Professor Kerryn Phelps AM

HOW TO KEEP YOUR BRAIN YOUNG

Preserve memory, reduce dementia risk, harness neuroplasticity and restore function

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About *How To Keep Your Brain Young*

Professor Kerryn Phelps AM, Australia's most trusted GP, reveals how to keep our most important organ at its best throughout our lives.

In her standout new book, Professor Phelps addresses what we all fear: losing mental function as we age. While ageing physically is inevitable, ageing mentally is not. In this accessible book, Professor Phelps lays out the basics of the brain and the simple, everyday practices for keeping our brains younger for longer.

Through the ongoing science of neuroplasticity, we know that our brains are continually capable of rewiring and relearning. Professor Phelps applies this knowledge to an array of simple, sustainable lifestyle habits, showing how anyone, whether starting at 40 or 80, can age gracefully and keep mentally sharp. *How to Keep Your Brain Young* details the fundamentals of a healthy brain, from diet and exercise to gut microbiome and mindfulness techniques, and shows us how to feel sharper, kick out the brain fog and retain mental acuity in later life.

Drawing on years of clinical experience and the latest research, *How to Keep Your Brain Young* is the ultimate guide for happy, healthy grey matter.

Also by Prof Kerryn Phelps AM

General Practice: The Integrative Approach

Ultimate Wellness: The 3-Step Plan

The Cancer Recovery Guide

The Mystery Gut

(with Dr Claudia Lee & Jaime Rose Chambers)

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Professor Kerryn Phelps AM

HOW TO KEEP YOUR BRAIN YOUNG

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Contents

Newsletter

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To Jackie, our family and friends.

To my teachers and mentors.

To my patients and their families.

To the people who have challenged me
intellectually to search for ways to a better world.

You have all contributed to the experiences and
thoughts that form precious memories.

May they last a lifetime.

Introduction

One of the great questions you will face as you grow older is this: will your brain go the distance? Will your physical health remain strong, but your brain function fail to keep up?

Your brain is such a precious organ. It governs everything you do and everything you think. It's important to look after it throughout your entire life.

Like so many people, I was fascinated by the life story of Professor Stephen Hawking, who had so much to say about quality of life, despite his neurodegenerative physical disability caused by motor neurone disease, because he had an awesome intellect. He understood, perhaps more than anyone, just how precious the brain is.

'I have been very lucky that my disease has not been a serious handicap, indeed it has probably given me more time than most people to pursue the quest for knowledge,' he said.

Decades of medical practice and talking to patients about their health concerns have shown me that many people's greatest fear as they get older is the possibility of losing their intellectual capacity, and the implications that might have for their quality of life, independence and autonomy.

But other people just don't seem to understand how precious their brain is. Some actively or mindlessly damage their brains, while others just don't make the most of the brain they have.

In medical practice, we do what we can to identify risk factors so that we can predict and prevent disease, or intervene at an early stage. Then there are times when we diagnose an established disease at a stage when little can be done to reverse or cure it. In neurology, the ‘holy grail’ is the search for the keys to prevention or cure of dementia and other neurodegenerative diseases. In the meantime, we have to gather as much evidence as possible about what you can do to optimise brain function and to maintain your brain health into old age.

Some people are dealt a bad genetic hand, making them more likely to develop some form of dementia as they age. That does not have to be inevitable, however. The purpose of this book is to look at the many ways you can optimise your brain health, and encourage you to make changes that will protect and even enhance your brain’s essential functions throughout life.

I decided to write this book to help you do whatever you can to keep your brain young.

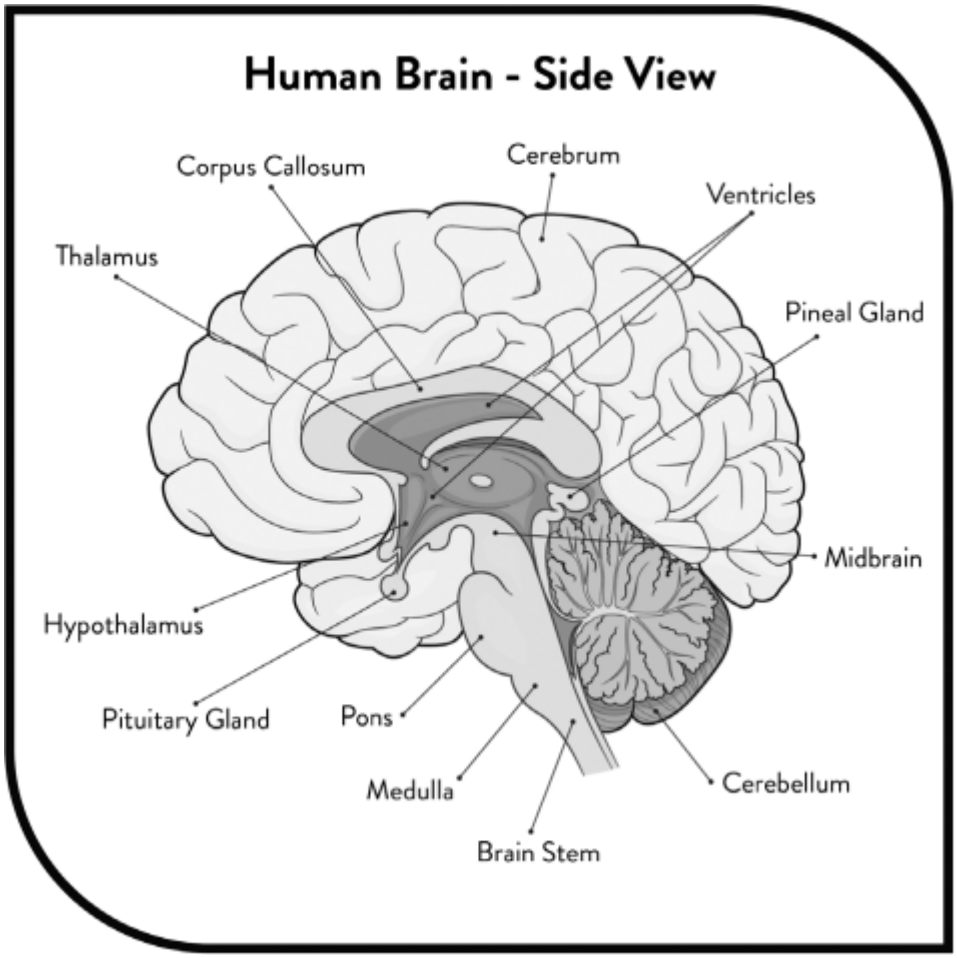
PART 1
BRAIN BASICS

1

How Your Brain Works

Before you can understand how to keep your brain young, you first need to understand how your brain works.

This is not a neurology or neurophysiology textbook, so I'll spare you a complex discussion about the brain's known and unknown physiology and biochemistry.



Still, we will need to discuss the various parts of the brain and what they do, in order to help you develop a clear understanding of how you can maintain your brain health.

The brain is divided into areas according to their anatomical positions. Each area has particular jobs to perform. It follows that when something goes wrong in a particular part of the brain, the functions of that area will be affected.

It is also worth looking, in broad terms, at what can go wrong with different parts of the brain, so that you can better understand the rationale behind the preventive strategies I recommend.

We'll start by looking at the main regions in the brain and what happens there.

CEREBRUM

The cerebrum is the largest part of the brain and is divided into the left and right hemispheres. The cerebral cortex is the so-called ‘grey matter’ of the brain, the folded outer layer of the cerebrum with white matter underneath. The two hemispheres are connected by a bundle of fibres called the corpus callosum, which transmits messages between the two sides. Each hemisphere controls the opposite side of the body, so if there is damage, say from a stroke in the left side, the right arm or leg might be weakened or paralysed.

The left hemisphere is dominant in over 90 per cent of people, explaining the predominance of right-handedness among the population.

It was once believed that you could be ‘right brain dominant’ or ‘left brain dominant’ and that this determined your personality and thinking style. You were a ‘left brain’ creative or ‘right brain’ rational thinker rather than intuitive. With more recent advances in imaging technology, it appears this is no more than a figure of speech. A study at the University of Utah in the United States in 2013 used specialised MRI brain scans to determine if there was more activity on one side of the brain or the other depending on personality. They found no correlation or gender differences.

The cerebral cortex is essential for consciousness, memory, attention, thinking, emotions, speech, decision-making and processing information from the outside world via the senses (sight, sound, smell, taste and touch).

The right and left hemispheres of the brain are further divided into lobes: occipital, temporal, parietal and frontal. The different lobes each have some distinctive roles, but they are also highly interconnected.

Occipital lobe: located at the back of the brain, the occipital lobe is responsible for processing vision, or making sense of what your eyes see. Damage to the occipital lobe can

result in difficulties with visual perception of light, colour and movement. At the extreme, this would mean total blindness.

Temporal lobes: You have two temporal lobes in your brain, the right and the left. This part of the brain is located near the temples.

The temporal lobes receive sound input from the ears and process them into meaningful information such as speech perception, as well as distinguishing non-verbal auditory information such as music. The temporal lobes also store memories and knowledge, and help to process emotions and language.

Temporal lobe damage can result in difficulty understanding spoken language, difficulty forming new memories and impaired long-term memory.

Deep in each temporal lobe is a key structure, the hippocampus, and these are critical for your ability to form new long-term memories of facts and events. They are an important part of the limbic system, which is responsible for regulating learning, motivation and emotion, and consolidation of memory.

Parietal lobes: The parietal lobes lie above the temporal lobes, towards the back of the brain. They process sensory information such as touch, taste, temperature and pain. They analyse information about the position of body parts, and process language and mathematics.

The parietal lobes contain the sensory cortex or the ‘somatosensory cortex’ (somato- refers to the human body so ‘somatosensory’ refers to sensations from the body). The somatosensory cortex is responsible for processing sensory information including pain, touch, pressure and temperature signals from different parts of the body.

Damage to the parietal lobes results in difficulty processing this sensory information as well as difficulty with

perception of length or depth. There can be trouble with speech, and agnosia (difficulty recognising common objects). A person with agnosia might be shown an apple but not recognise what it is. Distressingly, a person with parietal lobe damage may be unable to recognise familiar people.

A rare condition called Gerstmann's syndrome is caused by damage to a part of the dominant parietal lobe. Features of this condition include difficulty writing, confusion telling left from right and loss of mathematical ability.

Frontal lobe: The frontal lobe is at the front of the brain, behind the forehead. It controls essential functions such as thinking, planning, decision-making, attention, communication and fluency of speech, judgement, inhibition and important aspects of personality.

A disorder that affects the frontal lobe can cause a change in personality. The person may become irritable, socially inappropriate, impulsive and disinhibited, and emotionally unstable.

A person with frontal lobe damage may have impaired judgement and intellect, memory loss, difficulty making plans, loss of empathy and difficulty with speech.

Frontal lobe dementia accounts for 20 to 50 per cent of dementia cases in people under 65 years of age. The early signs include a change in personality and behaviour, and difficulty making plans. This eventually progresses to severe memory loss (compared with Alzheimer's disease, where the memory loss comes first, followed later by behavioural change).

LIMBIC SYSTEM

The limbic system is an interconnecting group of paired brain structures that together govern emotions, motivation and behavioural responses. It is particularly important for actions

necessary for survival, such as the fight or flight response, feeding, reproduction and caring for offspring.

The main areas of the brain involved in the limbic system are the hippocampus and the amygdala. The thalamus, hypothalamus and basal ganglia are also involved in the limbic system. The thalamus is located just above the brainstem and is a gatekeeper for motor and sensory messages between the brain and spinal cord. The hypothalamus controls emotions. It also regulates functions such as temperature, appetite and sleep.

THALAMUS

The thalamus is in the middle part of the brain between the cerebral cortex and the midbrain. It acts as a relay station; much of the information sent from the lobes of the cerebral cortex is relayed through the thalamus. Sensory information from the rest of the body is relayed via the thalamus to the cerebral cortex. It regulates consciousness, sleep and alertness, and interpretation of sensory signals from the body such as sight, sound, smell and touch.

HYPOTHALAMUS

The hypothalamus is located underneath the thalamus and above the pituitary gland. It influences the body's hormones and controls body temperature, the sensations of hunger and thirst, blood pressure and heart rate, and production of digestive juices in the gastrointestinal tract, as well as regulating fluid balance. The hypothalamus maintains equilibrium or balance in the body's functions either by releasing hormones itself or by modifying the release of hormones from other organs.

PITUITARY GLAND

The pituitary is a small gland at the base of the brain, underneath the hypothalamus, that regulates the hormones in your body. It is only about the size of a pea but it has a huge influence on the way your body functions. The pituitary gland produces substances that communicate with the hormone-producing glands in your body such as the thyroid, adrenal gland, ovaries and testes, acting like an accelerator and brake, telling these glands to increase or decrease their activity as needed.

PINEAL GLAND

This is a tiny area of the brain that produces the hormone melatonin, which modulates your sleep–wake cycle. Melatonin is produced cyclically, with maximum output during hours of darkness. It is also a strong antioxidant, with immune-boosting and anti-cancer effects.

Melatonin production deteriorates with age, and this may partly explain sleep problems in older people.

AMYGDALA

There are two amygdalae (plural of amygdala), each located close to the hippocampus, in the frontal part of the temporal lobe. It is comprised of twelve sub-nuclei with distinctive connections with other parts of the brain.

The amygdalae receive information about the external environment from the thalamus and the sensory cortices in the parietal lobes, and play an important role in processing emotional responses such as fear, anxiety and aggression, and interpreting the emotions of others. They are also involved in survival instincts, decision-making, motivation and the processing of memories.

People with damage to the amygdala are more likely to take big risks with little consideration of the consequences.

Studies have implicated abnormal activity in the amygdala in anxiety disorders, autism and addiction.

Neurogenesis – the creation and integration of new neurons (brain cells) – occurs during the development of the embryo. It has been discovered that the amygdala is one of three areas in the brain capable of adult neurogenesis. It has also been found to occur in the hippocampus.

FUN FACT

Your brain structure may determine the way you vote.

A study of healthy young adults correlated their brain structure with political liberalism or conservatism.

Liberalism was associated with increased grey matter volume of the anterior cingulate cortex (ACC). The ACC wraps around the front part of the corpus callosum in the front part of the brain. It has connections to the limbic system (involved with emotion) and the prefrontal cortex (involved in executive functioning). The ACC is thought to be involved in complex cognitive functions such as empathy, motivation, reward anticipation, assessing emotion, impulse control, ethics, problem solving and decision-making.

Conservatism was associated with increased right amygdala size.

HIPPOCAMPUS

The hippocampus lies deep within the temporal lobe on each side of the brain. It is associated primarily with learning and with processing short-term memory of experiences into long-term memory by sending memories to be stored in particular areas of the cerebrum and recalling them when required. It is also responsible for spatial navigation, and is important in regulating emotional responses driven by the amygdala.

A part of the hippocampus called the dentate gyrus retains the ability for neurogenesis throughout life. In adult humans, it has been estimated that 700 new neurons are added and integrated into existing neural circuits in each hippocampus

per day, with only a modest decline in neurogenesis during ageing.

Neurogenesis in the hippocampus can be increased with aerobic exercise, while depression has been shown to decrease neurogenesis.

Damage to the hippocampus causes loss of memory. The hippocampus is one of the first and most severely affected areas of the brain to suffer damage in Alzheimer's disease.

Neuroscientists are interested in how to use the discovery of adult neurogenesis to treat conditions including cognitive decline, dementia and mental illness in the future.

BRAIN STEM

The brain stem is located at the back of the brain, where it adjoins the spinal cord. The brain stem is made up of the midbrain, pons and medulla oblongata. It controls the flow of messages between the brain and the rest of the body.

Together, the parts of the brain stem are responsible for regulating breathing, digestion, sleep and wakefulness, and function of the heart and blood vessels (including heart rate and blood pressure).

CEREBELLUM

The cerebellum is located behind the brain stem. It is responsible for the coordination of voluntary movement and balance, coordination and posture. It contains the highest concentration of neurons.

Damage to the cerebellum can cause loss of coordination, tremors, abnormal gait and inability to judge distance.

CORPUS CALLOSUM

The corpus callosum is the bridge connecting the left and right sides of the brain, allowing information to pass from one side to the other and integrating the functions of the two hemispheres.

The corpus callosum can be damaged. There is also a rare congenital brain disorder where the corpus callosum is missing because it failed to develop in the foetus during gestation. The development of the corpus callosum is particularly vulnerable in foetal alcohol syndrome, the result of heavy drinking by the mother during pregnancy.

THE NERVOUS SYSTEM

The **central nervous system** consists of your brain and spinal cord. The **peripheral nervous system** is all parts of the nervous system that are not in the brain and spinal cord, comprising the nerves that connect them to the rest of your body.

The **enteric nervous system** is the nervous system of the gut. It controls the activity of the gastrointestinal system independently of input from the brain and communicates information back and forth with the brain.

The **somatic nervous system** is responsible for controlling all voluntary body movements. The **autonomic nervous system** controls involuntary body functions and consists of the **sympathetic** and **parasympathetic nervous systems**. The **sympathetic nervous system** activates your body's fight or flight response to perceived threats, mainly through the action of noradrenaline and adrenaline. When it is activated, the **parasympathetic nervous system** uses the neurotransmitter acetylcholine to slow your heart rate and breathing rate, lower blood pressure and regulate digestion. It plays a part in crying, releasing saliva, and sexual arousal.

BRAIN CELLS

Having discussed the parts of the brain that are responsible for performing specific functions, we can now zero in on the neurons – the cells within those sections of the brain that do specialised work.

The central nervous system has two main types of cells: neurons and glia.

Neurons

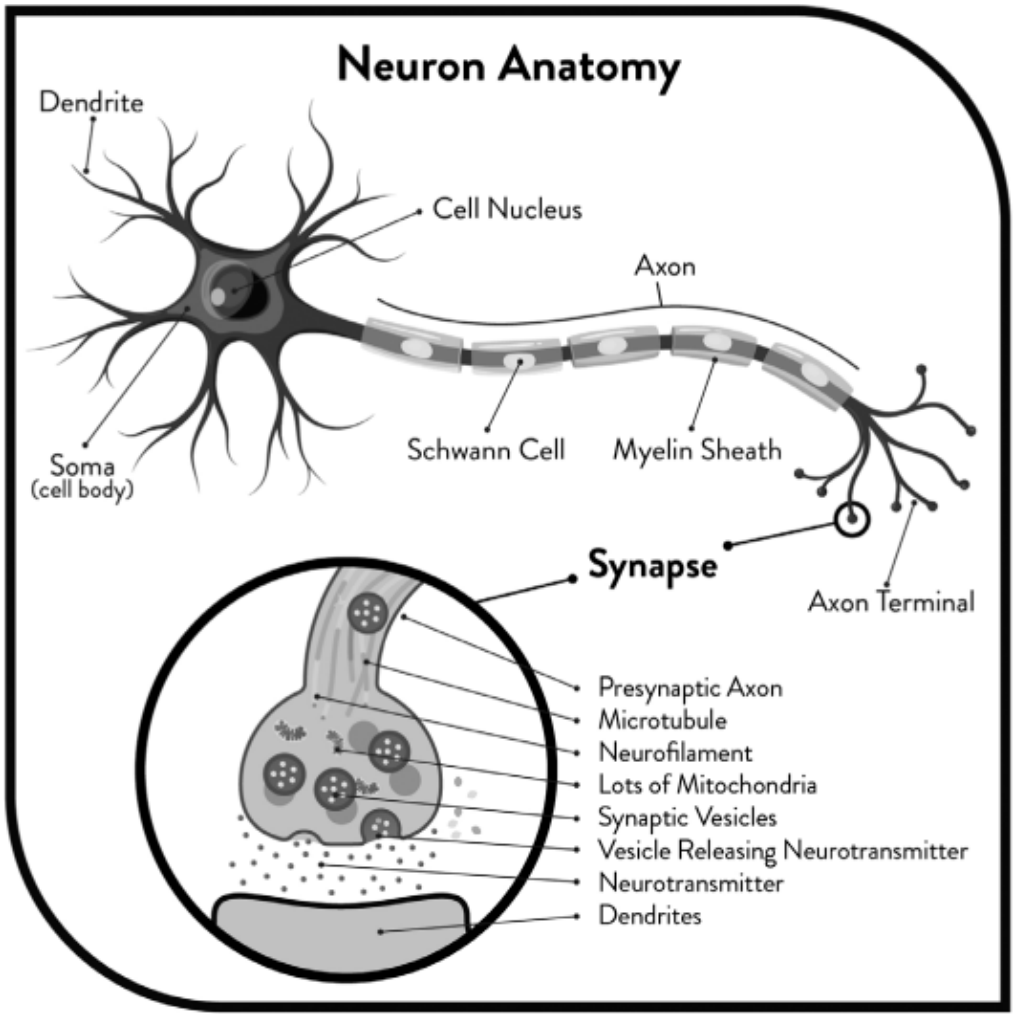
Neurons are the nerve cells of the brain and nervous system. They transmit information from the environment and from parts of the body to the brain and from the brain back to the relevant parts of the body using electrical signals and chemical messages. There are three types of neurons in the nervous system: sensory, motor and interneurons.

As their name suggests, sensory neurons carry information from sensory organs such as the eyes (vision), ears (hearing), nose (smell), tongue (taste) and the skin (touch, pain, heat) to the brain.

Upper motor neurons travel between the brain and spinal cord with messages about movement. Lower motor neurons travel between the spinal cord and muscles. Interneurons are found only in the brain and spinal cord, and they enable communication between spinal motor and sensory neurons and the brain.

Each neuron has three major parts: body (containing the nucleus and cell's genetic material), axon and dendrite. The brain is likely to have many different types of specialised neurons. Back when I was a medical student, accepted wisdom was that humans had pretty much all the neurons we were going to get by the time we were born. But in the 1980s, animal and bird studies began to show that new neurons are

created and incorporated into functional neural pathways in adulthood, in a process called adult neurogenesis.



Researchers built on those discoveries and found that the adult human brain is capable of neurogenesis in three parts of the brain, including the hippocampus and amygdala.

The opposite of neurogenesis is the destruction of neurons by disease processes or as a result of genetic mutations affecting specific parts of the brain. Examples are Parkinson's disease, Huntington's disease and Alzheimer's disease.

Parkinson's disease is a progressive neurodegenerative disease where dopamine-producing neurons are destroyed in a part of the basal ganglia called the substantia nigra in the mid-brain. This results in tremors and muscle stiffness, often initially on one side of the body, and slowing of movement. It

eventually causes difficulty with speech and swallowing. It can also affect memory, leading to dementia, and can cause depression and anxiety.

In Alzheimer's disease, waste, debris and protein fragments called beta-amyloid are not cleared away and clumps of beta-amyloid form plaques between neurons. Then there is abnormal accumulation inside neurons of another protein called tau, which forms 'neurofibrillary tangles' that damage the neuron's internal transport system as well as disrupting the communication between neurons at the synapses.

When affected neurons become damaged and die, people lose their capacity to lay down and recall memories, as well as losing their ability to do everyday tasks (see chapter 20: Dementia).

Glia or glial cells

Glial cells are not neurons or nerve cells. They outnumber neurons in the brain and nervous system, but they do not directly participate in the transmission of messages.

Glial cells form the support team for the neurons in the nervous system and each different type of glial cell has a different function, either by providing structural or nutritional support, regulating the fluid surrounding brain cells and the synapses or between neurons (or connections between cells). There are three types of glial cells: astrocytes, oligodendrocytes and microglial cells.

Astrocytes maintain the right chemical environment for neurons to send messages.

Oligodendrocytes lay down myelin, a protective sheath surrounding and insulating the ends of some axons.

Microglial cells throughout the brain and spinal cord are immune cells that mop up cellular waste produced as part of normal cellular activity or as a result of an injury. They are involved in synaptic organisation as well as brain protection and repair. Microglial cells and astrocytes are key regulators of inflammatory responses in the brain by releasing inflammatory substances including cytokines (chemical messenger in the body).

Microglial activation is one of the key factors in the progression of the pathology and the severity of symptoms in neurodegenerative processes such as Parkinson's disease, Alzheimer's disease and frontotemporal dementia (see chapter 20: Dementia).

GREY MATTER / WHITE MATTER

Now that we have paid some attention to the macro structures and the cell types that make up the brain, I want to spend a little time talking about the terminology of so-called grey matter and white matter.

The reason for the names is obvious. The grey matter looks grey and the white matter looks white. Grey matter is the outermost layer of the brain. It gets its colour from the high concentration of neurons. The grey matter surrounding the cerebrum is known as the cortex of the brain (or the cerebral cortex). Grey matter in the inner parts of the brain is known as nuclei. The grey matter in the brain enables information processing, movement, memory and emotions.

White matter is the deeper layer beneath the grey matter and it is white because it contains a high concentration of axons surrounded by myelin, the fatty insulating layer that forms around nerve cell axons and allows the rapid transit of electrical impulses along nerves which communicate between

different areas of grey matter. Because it is beneath the cortex, it is also referred to as subcortical white matter.

NEUROTRANSMITTERS

Neurotransmitters are chemicals in the brain that are produced within the neurons. They enable the neurons to do their work by conveying messages from neuron to neuron.

This can get very biochemically and anatomically complicated. For our purposes, the main thing is to understand the principles of brain structure and function with an emphasis on the actions you can take to keep your brain healthy throughout your life. To do this, you do need to be familiar with the seven major types of neurotransmitters:

- glutamate
- gamma-aminobutyric acid (GABA)
- dopamine
- serotonin
- histamine
- acetylcholine
- noradrenaline/norepinephrine.

Let's go through the list of neurotransmitters, their roles, and effects on neurons and brain function.

Glutamate

Glutamate is the predominant excitatory neurotransmitter in the brain, boosting the activity of neurons. It is abundant in brain tissue, but the highest concentrations of glutamate are found in synaptic vesicles at the ends of neurons.

Glutamate plays an important role in modulating signals between neurons to shape memory and learning. It also works

with GABA (see below) to control the brain's overall level of excitation.

In Huntington's disease, a rare genetic mutation causes over-production of glutamate in the basal ganglia. This results in the features of Huntington's disease, such as depression and other psychiatric disorders, behavioural changes and abnormal movements of muscles.

Gamma-aminobutyric acid (GABA)

GABA is an amino acid produced in brain cells that acts as the main inhibitory neurotransmitter in the central nervous system. When it attaches to a GABA receptor in the brain, it has an inhibitory effect, damping down or blocking the activity of some neurons in the brain. GABA is present in high concentrations in different brain regions, particularly the limbic system.

When it is mobilised, GABA produces a calming effect, inducing sleep, reducing emotional stress, and lowering fear and anxiety.

Low GABA levels can show up as anxiety, depression, difficulty concentrating, insomnia and headaches.

GABA also has effects on other organs of the body, and has properties that may reduce high blood pressure, combat diabetes and cancer, act as an antioxidant, reduce inflammation, and protect the liver, kidneys and gut.

It is found in various foods including green tea, soybean, adzuki beans and germinated brown rice. GABA is also present in a number of fermented foods, such as kimchi, miso, tempeh and yoghurt.

Dopamine

Dopamine acts as a neurotransmitter in the brain. It has several essential functions, including reward motivation, attention, learning, emotion, motor control and executive functions – the higher-level cognitive skills you use to govern thinking, problem-solving, impulse control, emotional regulation and self-control.

It is produced in three main parts of the brain – the substantia nigra and the ventral tegmental area (VTA), both in the midbrain, and in the hypothalamus.

Dopamine produced in the substantia nigra helps to initiate movement and speech. Dopamine from the VTA is involved in reward, or 'feeling good'.

In Parkinson's disease, a drop in dopamine levels in the substantia nigra results in uncontrolled tremors and trouble initiating movement.

Stimulant drugs like cocaine and nicotine cause enormous temporary boosts in dopamine levels. The amplified reward reaction causes people to repeatedly seek out that drug to experience the same 'high', and that can lead to addiction.

Conversely, lowering dopamine can cause you to lose pleasure in activities, a symptom known in psychological medicine as anhedonia.

Serotonin

Serotonin is perhaps the most well known of the neurotransmitters, playing a role in virtually every process in the brain.

Serotonin is not only found in the brain. It also regulates a range of body processes, including those of the heart, bowel and bladder.

Its work in the brain involves the regulation of human behaviours and processes relating to mood, perception,

reward, anger, aggression, appetite, memory, sexual desire and attention.

Low levels of serotonin have been associated with depression, and it appears that abnormal serotonin physiology is involved in the symptoms of a number of other disorders, including anxiety disorders, eating disorders, schizophrenia, impulse-control disorders and autism, as well as aggressive behaviours.

Many antidepressant medications are targeted at adjusting serotonin levels in the brain, particularly selective serotonin reuptake inhibitors (SSRIs), which specifically target serotonin receptors in the brain.

Histamine

When we hear the word histamine, most of us immediately think of *anti*histamines, the medications that counter allergic reactions mediated by histamine.

This same chemical is a neurotransmitter in the brain as well, where it promotes wakefulness. Brain histamine is also crucial for motivation and goal-directed behaviours.

There is some recent evidence to suggest that abnormal histamine signalling in the brain may be a key factor in addictive behaviours and degenerative disease such as Parkinson's disease and multiple sclerosis.

Acetylcholine

Acetylcholine is the neurotransmitter that is active at the neuromuscular junction – that is, the place where the neuron meets muscle. It is the main neurotransmitter (along with adrenaline and noradrenaline) in the autonomic nervous system. It also acts in the brain in functions such as the sleep–wake cycle.

Acetylcholine receptors are involved in the formation of memories in the amygdala, hippocampus and cerebral cortex.

A group of drugs called anticholinergics block the action of acetylcholine, causing muscle relaxation or paralysis. They are used to treat a range of conditions such as overactive bladder and chronic obstructive lung disease, some gut disorders, allergies, depression, Parkinson's disease and motion sickness.

These drugs, as well as organophosphate chemicals used as insecticides and the 'nerve gas' Sarin, block the action of acetylcholine. Long-term exposure to organophosphate chemicals can cause a range of neurological symptoms, including memory loss, muscle weakness, depression and confusion.

The use of some classes of anticholinergic drugs can cause impaired cognition in the short term. Prolonged use is a risk factor for the development of dementia, particularly anticholinergic drugs prescribed for antidepressant, urological and anti-Parkinson purposes, an effect that can be seen up to 20 years later. (See chapter 20: Dementia.)

Noradrenaline/norepinephrine

Noradrenaline, also known as norepinephrine, is a hormone and a neurotransmitter. Its main role in the body is to mobilise both the brain and body to action in the so-called 'fight or flight response'.

Operating as the main neurotransmitter of the sympathetic nervous system, noradrenaline readies your body for action by increasing heart rate and blood pressure and increasing blood flow to your muscles, and triggering the release of glucose from energy stores.

Levels of noradrenaline are lowest when you are asleep and highest when you are under stress or duress.

Noradrenaline helps your brain to focus attention, alertness and arousal, heightens vigilance, and enhances the formation and retrieval of memories.

THE DEVELOPING BRAIN

During pregnancy, a woman needs to provide her growing foetus with all the nutrients it needs for brain development, as well as avoiding toxic substances like alcohol that can cause abnormal brain development. We will look more closely at the preparation for a baby's brain growth and development from before conception through to early childhood in chapter 4: A Head Start.

Adolescence is a particularly dynamic and sensitive time in the brain's development. It is a time of great opportunity for healthy brain development, but also a time of great vulnerability.

During adolescence there is a dynamic reorganisation of the brain regions that are responsible for adult cognitive (thinking) and executive function (decision-making, self-control and organisational skills), working memory, reward processing, emotional regulation, and behaviour.

As a parent you hear horror stories about the risks your child faces when they start to exert their independence and head out into the world without the close supervision of childhood. Experimenting with alcohol and other drugs, accepting dares to perform risky behaviours, meeting a stranger on the internet … there is seemingly no end to the ways they can get into trouble.

If you ever wondered why an adolescent does something risky and apparently stupid, blame the 'teenage brain'. During adolescence there is a changing balance between earlier maturing, puberty-related limbic systems and later-maturing frontal executive function systems. As a result, the decisions

made by an adolescent are different from decisions guided by a mature brain. An adolescent is more likely to be guided by the reactive amygdala, without full consideration of the consequences of their actions, than by the logical frontal cortex, which matures later as you develop the ability to think before you act.

The best protection is a vigilant parent, parent-figure or other adult who tries to anticipate the risks a teenager might face and explain the possible consequences of their decisions.

AGEING AND THE BRAIN

The process of ageing in the brain seems to start by about the age of 40. Changes occur at different rates in different parts of the brain as you get older. There is also a great deal of variation from one individual to another.

The changes of ageing involve brain size and volume, and structures right down to cell and molecular level, blood vessels supplying brain tissue, and cognition. Neurotransmitter levels and hormones also play a part in brain ageing.

After the age of 40, brains shrink in volume by about 5 per cent per decade, particularly the frontal cortex and hippocampus.

Some myelin sheaths deteriorate from around the age of 40.

White matter may also decline with age and MRI studies have shown this is most pronounced in the pre-frontal white matter.

Blood vessels supplying the brain can change as part of systemic cardiovascular disease. The incidence of hypertension, blood vessel disease and stroke increases with age, and can cause damage to brain tissue. Other chronic diseases such as diabetes and impaired glucose metabolism

also become more common with age (see chapter 11: Glucose).

There are also changes in the levels of neurotransmitters and hormones, affecting the function of the brain.

When it comes to neurotransmitter levels, acetylcholine, serotonin and dopamine levels all decrease with age.

Dopamine levels decline by around 10 per cent per decade from early adulthood and this is associated with declines in cognitive and motor performance.

Reduced sex hormone levels can affect brain performance. The decline in hormone levels in women at the time of menopause can have an effect on brain function (see chapter 14: Menopause Brain). Low endogenous levels of testosterone may be associated with reduced cognitive ability in older men. However, testosterone supplementation in older men with low testosterone and cognitive impairment does not improve their memory or cognitive function.

Cognitive impairment is a relatively common part of the ageing process, but it is certainly not inevitable. Cognitive impairment includes many domains, such as memory, learning, mental flexibility, attention and executive function. In practical terms it may be evident as difficulty finding the right words or remembering names or details, and difficulty with multitasking.

The brain of an older person is still able to form new memories and learn new skills, although this may take longer than in your youth, and there are cumulative advantages gained through a lifetime of experiences and knowledge.

Memory is the area of cognition most widely affected by ‘normal’ ageing but that is not the same as Alzheimer’s disease or other forms of dementia.

Biological ageing is not entirely related to chronological age either, and the best defences against the rate of ageing on the brain are healthy brain lifestyle measures such as optimal nutrition, regular exercise, sleep, lifelong education, and avoiding tobacco, excess alcohol and other damaging toxins. We will examine these measures further throughout this book.

2

Neuroplasticity

It was once thought that the brain was hardwired, that you had all of the brain's neurons and connections from birth and that was that. We now know that your brain is in a constant state of change with every experience and every thought.

The brain is capable of rewiring itself in response to influences both within and outside the body to adapt its structure, function and neural connections. We call this capacity for change neuroplasticity.

Structural and functional changes in the brain can be induced by environmental factors, emotions, experiences, learning and behaviours. What an exciting prospect it is that we can consciously harness the potential for the brain to adapt by actively changing our thought patterns and behaviours.

We have learned a lot about the brain's capacity to change itself by studying the process that takes place after an injury to the brain, such as a stroke or a traumatic brain injury (see chapter 17: Brain Injury). The stimulus for neuroplasticity in these cases is inflammation, scarring of brain tissue or the death of brain cells.

The changes that occur through neuroplasticity can be helpful, neutral or harmful to brain health. Helpful changes are

those that enable the brain to restore function after an injury. Neutral effects provide neither practical benefit nor harm to the neuroplasticity reorganisation. A harmful or pathological effect means that the neuroplasticity changes have an adverse effect on brain function.

Neuroplasticity after an injury to the brain that results in structural or physiological changes in brain function happens in several phases.

In the first 48 hours after injury, neurons and other cells are recruited to replace the damaged cells, form scar tissue and restore blood supply to the affected brain tissue.

In the following weeks, a process of brain remodelling called axonal sprouting occurs, where undamaged axons grow new nerve endings to reconnect damaged neurons. Newly sprouted nerve endings can also form new neural pathways.

This process of remodelling and regeneration continues for weeks to months.

There is a great deal of research underway to understand the brain's connections and to harness the brain's neuroplasticity potential after injury, including targeted medications and stem cell therapies.

Building on this knowledge, there is a lot of evidence for the ability of the brain to change over time as a result of a range of experiences.

Emotions alter the structure of parts of the brain as well as the activity of neurons. Psychological therapies rely on the prospect of neuroplasticity changing both the function and physiology of the brain in a beneficial way.

An example of this was Swedish research which used neuroimaging techniques to see the effect of nine weeks of cognitive behaviour therapy (CBT) on brain structure and function in people with social anxiety disorder. People with

anxiety disorders exhibit excessive reactivity of neurons in the amygdala. Researchers found what they described as ‘compelling evidence’ that CBT changed both the physical structure and functional response of the amygdala.

This is informing our thinking about conditions like post-traumatic stress. Even though the initial responses to trauma might be protective or necessary for survival, stress-induced brain changes may have adverse long-term effects. The body’s stress response activates specific brain regions involved in the limbic system, including the hippocampus, amygdala and prefrontal cortex. A substance called brain-derived neurotrophic factor (BDNF) promotes cellular growth and synaptic changes crucial for neuroplasticity. Those neuroplastic changes can form lasting memories of the trauma. Even years later, a reminder of the initial traumatic effect can trigger the limbic system to respond in a similar ‘fight or flight’ way, out of proportion to the current triggering event.

Therapy aims to create positive neuroplasticity changes that lead to recovery from post-traumatic stress disorder.

Other activities and experiences can create positive neuroplasticity changes.

Musical training, for example, can enhance neuroplasticity and improve cognition.

A group of elderly people were given lessons in how to read music and play piano along with daily practice for four months against a control group who did other activities such as physical exercise, computer lessons and painting lessons.

There was a significant improvement for the piano group on executive function, visual scanning and motor ability. The piano lessons decreased depression, and improved their sense of wellbeing.

Exercise strengthens the underlying systems that support neuroplasticity, including neurogenesis, by increasing blood

flow to your brain, increasing growth factors in the brain and triggering the process of neuroplasticity (see chapter 23: Brain and Exercise). Exercise has been shown to improve episodic memory and processing speed, as well as decreasing age-related atrophy (deterioration) of the hippocampus. It also helps to maintain conditions in the brain for synaptic plasticity by enhancing clearance of beta-amyloid, one of the main contributors to the development of Alzheimer's disease.

Exercise also reduces risk factors for systemic diseases that can affect the brain, such as diabetes, high blood pressure and cardiovascular disease.

We know that many other interventions such as nutrition, targeted nutritional supplements, sleep therapies and stress management can harness your brain's neuroplasticity capacity, enabling you to maintain or improve your brain's performance.

3

DNA Predictions of Dementia

A growing number of patients have asked me whether they should have predictive genetic testing to discover what their risk of various diseases might be.

Discovering you have a higher risk of specific health problems is a double-edged sword. On one hand, this is a reasonable and arguably sensible thing to do. If finding out that you have a higher risk of type 2 diabetes or high cholesterol or heart disease means that you take early evasive action to correct your lifestyle, that is undoubtedly a positive thing.

But there is a dark side to this. What if your genetic test told you that you were at higher risk of a progressive and currently untreatable neurological disease? How would you react? How would it change your life plans or affect your mental health? What would you tell your children?

What if your predictive genetic test said that you were more likely to develop dementia? How would that change your life plans?

Like I said, it's a double-edged sword.

There is also the emerging issue of insurance companies using information from genetic testing to deny life insurance, but I will leave the ethics of genetic privacy aside for our purposes.

A ‘higher risk’ predicted by a genetic test does not necessarily mean it is inevitable that you will develop a disease. There are many forms of dementia, and genes do play a role in the development of some of these forms. The average lifetime risk of developing Alzheimer’s disease is 10–12 per cent in a 75–80-year life span. This risk at least doubles with the presence of a first-degree relative who has the disorder.

For example, if you have a parent or a sibling with Alzheimer’s disease, you are at higher risk of developing the disease. This does not mean that you will develop Alzheimer’s disease, however. In most people, the risk of developing Alzheimer’s disease is linked to variations in large numbers of inherited susceptibility genes. Some of these genes will increase susceptibility, while others will be protective.

The most common Alzheimer’s susceptibility gene to be discovered so far is called the Apolipoprotein e gene (APOE), found in chromosome 19. It provides instructions for making the protein involved in the metabolism of fat, also called Apolipoprotein e.

This gene has a number of variants. One variant, called e4, has been shown to increase the risk of developing Alzheimer’s disease over the age of 65. If a genetic test shows that you have this variant, this does not mean that you will develop Alzheimer’s disease, it just means a subtle increase in risk in some people.

Not all people with Alzheimer’s disease have the APOE e4 gene, and not all people who have the gene will develop the disease.

To put the risk into perspective, half of people aged 85 who have two copies of Apolipoprotein e4 (one from each parent) do not have symptoms of Alzheimer's disease.

So what do you do if you have a genetic test and it shows that you have the APOE e4 gene, or some other susceptibility gene?

This is the question you need to consider before you commit to genetic testing.

Of course, ideally you would do everything possible to optimise your brain health immediately, but our understanding of this disease offers no guarantees of prevention.

The other time people consider genetic testing is when an older family member is diagnosed with early Alzheimer's disease or another form of dementia. What is the risk that this could be passed on to my children? Again, this is an understandable question.

It is important to point out that there are no approved tests for the most common form of Alzheimer's disease. However, this situation could change as our knowledge of genetics increases and the technology becomes more accessible – the so-called democratisation of genetic testing. But it's important to consider the ethical and practical implications of discovering you have a statistically increased risk of a disease that has a limited scope for proven prevention, treatment or cure, either through pharmacological or lifestyle interventions before you consider having a test.

What if the test result tells you that there are no apparent susceptibility genes for Alzheimer's disease or other inheritable forms of dementia; does this mean you cannot develop dementia? Again, this is complicated. There are many forms of 'dementia' which is a term used to describe a decline in memory, intellect and cognitive functioning. Not all forms of dementia have any known genetic component.

While it might be reassuring to receive this news, you should not be reassured to the point of becoming complacent about optimising your brain health throughout your life.

Before you decide to have your DNA tested, carefully consider what you might find out, how that might affect you emotionally and the impact it might have on your life decisions and relationships.

Genetic counsellors are available to discuss the decision to have a test done, or to help you realistically assess your risk if you have done the test and want to figure out what the results mean for you. Your GP can begin this process for you.

If you are concerned about the risk of inheriting Alzheimer's disease, Dementia Australia provides professional staff who offer counselling and support. This service is confidential and sensitive. You can ring the National Dementia Helpline on 1800 100 500 to arrange an appointment with a counsellor.

Further information is available on the Dementia Australia website: www.dementia.org.au/information/genetics-of-dementia

PART 2

WHAT CAN AFFECT YOUR BRAIN

4

A Head Start

When you plan a pregnancy, there is so much to consider.

Birthing plan? Vaginal delivery or caesarean? Will you breastfeed, and if so, for how long?

Will it be a boy or a girl?

What colour eyes will they have?

Will they take after someone in the family?

How much time do I need to take off work?

Where will we live and where will they go to school?

But before all of that, there is an even more important consideration: how to create the ideal environment for a baby to be conceived, grow and develop.

The developing foetal brain has many different types of cells and connections between those cells that proliferate, differentiate and develop into their eventual form and function.

A woman needs to start planning for the development of her baby's brain even before she becomes pregnant. This is where brain health begins and has an impact for the rest of that baby's life.

If you are thinking about pregnancy, I always advise a trip to the GP, armed with a list of the questions you need to ask and the check-ups you need to organise.

You will need to consider the following things:

If you have any existing medical conditions like diabetes or asthma, hypertension or epilepsy, review your treatment plan. Make sure that any medications you are taking, either prescribed or over-the-counter, are safe for a pregnancy.

Is your cervical screening up to date?

Are your immunisations current? Your immunisation status needs to be checked, particularly for preventable infectious diseases likely to affect a pregnancy, such as rubella (German measles), varicella (chicken pox), hepatitis B and measles. If you are non-immune, rubella and varicella immunisation need to be given at least 28 days before planned conception.

Rubella (German measles) during pregnancy can cause catastrophic damage to an unborn baby, including brain damage, deafness and heart defects. Measles and chicken pox can also cause brain inflammation and long-term effects on brain structure and function.

Influenza in pregnant women has been linked to the later development of autism spectrum disorders, differences in cognitive test scores and bipolar disorder in the baby.

You can have a flu vaccine at any time during pregnancy, particularly if your second or third trimester falls during influenza season. It is now recommended that COVID-19 mRNA vaccines be offered to all pregnant women.

Parents and other close family members and child carers are advised to have a pertussis (whooping cough)/diphtheria/tetanus combination vaccine in the last trimester of their child/family member’s pregnancy. This is to protect the newborn baby from whooping cough in the early

weeks after birth, before they are old enough to have their immunisations.

According to the United States Centers for Disease Control and Prevention (CDC), about half of babies younger than one year old who get whooping cough require hospital care. The younger the baby with whooping cough, the more likely they are to be hospitalised. Of those babies with whooping cough who are treated in hospital, about 1 in 300 (0.3 per cent) will have encephalopathy (brain inflammation).

INVESTIGATIONS TO HAVE (PREFERABLY) BEFORE PREGNANCY

Your doctor will discuss a suite of prenatal investigations, which might include:

- full blood examination and blood group/antibody screen
- iron studies
- blood tests for German measles, chicken pox, hepatitis B and C, and measles immunity
- HIV status and syphilis test
- folate level
- urine protein
- urinary iodine
- blood glucose
- vitamin D
- thyroid function tests.

You will have a chance to talk about any relevant extended family history of both your biological parents to identify any potential genetic problems, and to discuss general health and lifestyle problems and improvements you can make.

Of course, not all pregnancies are planned, and despite your best intentions, you may become pregnant before you are quite ready. If there is any possibility you may become pregnant, the safest course of action is to behave in all things AS IF YOU ARE PREGNANT without knowing it yet.

STRESS

Pregnancy is not always a blissful time, no matter how much you want to have the baby. Numerous life events can cause stress during this time, such as financial pressure, the upheaval to your career or moving house to accommodate your growing family.

When you are pregnant, the stress hormones in your body are shared with the baby. These hormones cross the placenta and affect the baby's neurological and physiological development. For example, maternal stress, especially in the early stages of pregnancy, has been associated with reduced foetal growth, developmental problems and an increased risk of mental illness in the child.

The consequences of maternal stress on the baby depend on the cause, timing, duration and intensity of the stress and its context, as well as the mother's reactivity to stress and the genetic susceptibility of the foetus.

Exposure to excessive psychosocial stress during pregnancy may cause delays in the child's mental and motor development, difficult temperament and impaired cognitive performance.

Stress management

To optimise your child's future health, it is important to make a plan to adapt to the inevitable physical and emotional challenges that pregnancy and parenthood can bring. I speak from experience here. I had my first baby in June of my intern year. I was young and fit, but I still remember the physical load of late pregnancy while doing a full intern roster. I didn't know a single other person with children, certainly not any other young doctors, and I remember that sense of social isolation. I was lucky enough to have family help, but my friendship group substantially changed to people with young

children who could relate to that ‘new parent’ experience. I envisaged my peers all moving on with their training and their careers as I was changing nappies and figuring out breastfeeding routines.

Try to anticipate the potential for stress and consider how you might deal with it in practical ways as best you can. For example, plan modifications to your work schedule in advance. Maybe you can transition some of your work to be home-based for a time if your workplace allows. Develop a support group of other expectant mothers, friends with young children, work colleagues and family members so that you stay connected and have people you can call on when you need help or just an understanding listener.

The following activities and actions will also help manage stress:

- Make sure you get plenty of sleep when you can.
- Prioritise responsibilities so that you can pace yourself, allowing for fatigue.
- Avoid substances like alcohol, nicotine or unnecessary medications.
- Try practising yoga, tai chi, meditation and relaxation exercises.
- If you are finding it difficult to cope, ask for help from your support system, your doctor, a counsellor or a psychologist.

NUTRITION ESSENTIALS

It will probably come as no surprise that a mother’s nutritional status will determine the health of her growing foetus, because the foetus is entirely dependent on the mother’s blood circulation for all of its needs.

A serious micronutrient deficiency in the mother can have significant consequences for the baby's brain development, which may determine many of the outcomes of its life. Some of the most important contributors to a baby's nutritional health and development are iodine, folate and vitamin D.

Iodine

Iodine is a trace element that is essential for the production of thyroid hormones. If the thyroid gland (the butterfly-shaped gland at the front of your neck) is unable to make enough thyroid hormone for the body's needs, the pituitary gland at the base of the brain releases a substance called thyroid-stimulating hormone (TSH). If there is insufficient iodine to increase thyroid hormone production, the TSH continues to try to stimulate the thyroid gland to produce more thyroid hormone, resulting in thyroid gland enlargement, also known as a goitre.

The human body is unable to produce iodine, and so relies on food sources such as seafood, seaweed and iodised salt.

For people who do not eat seafood or seaweed, or communities whose food sources are away from the coast or where soils have been depleted of iodine due to flooding, deforestation or soil erosion, there is an increased risk of iodine deficiency. For this reason, many countries have mandatory iodine food fortification programs.

Iodine deficiency carries an even greater risk for a developing foetus. Severe hypothyroidism (low thyroid hormone) during foetal and early childhood stages of development causes severe and irreversible brain development problems, including learning difficulties, speech and hearing defects, and stunted physical growth.

Iodine deficiency today is the leading cause of preventable poor cognitive development in the world, and of lower IQ

levels in school-aged children.

With the reduced consumption of iodised salt, and dairy producers no longer using iodine compounds in sterilisation procedures, we are again seeing an increase in iodine deficiency, even in developed countries with plentiful food.

To ensure adequate iodine, either:

- eat fish one to three times a week.
- limit high-mercury types of fish during pregnancy. These will usually be larger predatory types of fish like orange roughy, swordfish, barramundi, ling, Southern bluefish tuna and shark. A foetus is most sensitive to the effects of mercury in the third and fourth months of gestation, resulting in later effects on the brain and nervous system affecting memory, language development and attention span.
- if using salt, use iodised salt.
- take a multivitamin for pregnancy that contains iodine.

Folate

Folate is a B group vitamin that occurs naturally in green leafy vegetables, citrus fruit, seafood, eggs and liver. It is also included in multivitamin supplements. Folate plays a crucial role in the development of a baby's central nervous system. Low folate levels in pregnant women are thought to be responsible for about 50 per cent of cases of neural tube defects such as spina bifida.

Folate was first discovered in the 1930s, but it wasn't until 1989 that Australian researchers Professor Fiona Stanley and Professor Carol Bower discovered the key role of dietary folate in reducing the number of babies born with neural tube defects such as spina bifida and anencephaly. Subsequent research showed that neural tube defects could be reduced by

up to 70 per cent by ensuring the mother consumed enough folate in very early pregnancy. This led to the global recommendation for women planning a pregnancy (or who believe there is a chance they may fall pregnant) to optimise their diets and to supplement with folate, ideally for three months prior to conception and then throughout pregnancy. In 2007 the Australian federal and state governments agreed to introduce the compulsory enrichment of bread-making flour with folate. What an incredible contribution to public health!

A daily supplement containing 500 mcg (0.5 mg) of folic acid is recommended for two months before you get pregnant and for at least the first three months of pregnancy. It is also advisable to eat foods rich in folate.

If you have a family history of cleft lip or congenital spinal problems or you are taking an anti-epilepsy medication, this dose may need to be greater. Please discuss this with your GP or obstetrician.

Vitamin D

We are increasingly recognising the role of vitamin D in many body processes. A foetus depends entirely on the mother's circulating vitamin D. Vitamin D deficiency is common, and in a pregnant woman this can have a significant impact on the development and function of the baby's brain.

One study published in *Pediatrics* found that vitamin D deficiency during pregnancy was associated with neurocognitive difficulties at age ten, increased risk of eating disorders in adolescence, and lower peak bone mass at 20 years. Other studies have found associations between vitamin D deficiency in pregnancy and later psychiatric problems.

Researchers from the University of Surrey and the University of Bristol discovered that pregnant women who were deficient in vitamin D were more likely to have children

who scored in the bottom 25 per cent in pre-school development tests for gross and fine motor development at age two-and-a-half years than children of vitamin D sufficient mothers.

In Australia, many women are deficient in Vitamin D. It makes sense to ensure that every pregnant woman has adequate vitamin D levels, either through sun exposure (without sunburn) or vitamin D supplementation before and during pregnancy.

Recommendation:

- The mother's vitamin D level should be assessed before or as early as possible in pregnancy.
- Vitamin D supplementation during pregnancy. The dosage will depend on the level of Vitamin D. Sometimes higher doses are needed at first to correct deficiency, followed by a lower maintenance dose.
- Vitamin D blood test performed again at 26–28 weeks.
- It is important to maintain adequate vitamin D levels when you are breastfeeding.

ALCOHOL

Drinking alcohol during pregnancy can affect the developing brain of the foetus. We have not established if there is any safe level of alcohol consumption during any stage of pregnancy.

The main concern is for the development of the baby's central nervous system. Total brain volume can be reduced, and some areas of the brain are particularly susceptible to the effects of alcohol, namely the corpus callosum (connecting the left and right brain), caudate nucleus (controlling motor abilities and cognition), hippocampus (controlling memory and learning) and cerebellum (regulating balance and coordination). This obviously has far-reaching implications for

the child's learning ability, physical development, behaviour and future potential.

Foetal alcohol spectrum disorder (FASD) is a range of physical, mental, behavioural and learning disabilities that are caused by a foetus being exposed to alcohol during pregnancy.

The risk of damage, including brain damage, to a foetus increases with the amount of alcohol a pregnant woman drinks. The impact on the brain development of the baby also increases with higher amounts of alcohol.

New research from the University of Sydney found that even low levels of alcohol consumption during pregnancy can have an impact on a child's brain development and is associated with greater psychological and behavioural problems in youth, including anxiety, depression and poor attention. Research also suggests that paternal alcohol consumption before conception can affect the baby's brain and behavioural development.

Recommendation: Stop drinking alcohol when you are planning to become pregnant. That goes for both birth parents. Biological fathers should not drink in the lead up to conception, and mothers are advised not to drink alcohol at all throughout a pregnancy. If you need counselling or other assistance to stop drinking alcohol, discuss this with your doctor.

NICOTINE

Tobacco smoke contains thousands of different chemicals, some of which have the potential to interrupt normal development of the brain and central nervous system. Nicotine itself can have adverse consequences on the foetus, so quitting smoking is essential to the health of an unborn baby. This needs to be done using counselling and behavioural techniques rather than nicotine replacement.

Recommendation:

- Don’t smoke.
- If you are a smoker, stop.
- If you are planning a pregnancy or you are pregnant, avoid any exposure to tobacco smoke.
- Ask your doctor for assistance if you find it difficult to stop smoking.

DRUG EXPOSURE

Back in the late 1950s and early 1960s doctors noticed an increased number of babies being born with deformities, including stunted limb growth. These babies were all born to mothers who had taken the drug thalidomide to help manage morning sickness.

I remember going to school with a boy who had no arms because his mother was prescribed thalidomide during pregnancy. Once this connection was recognised, the drug was taken off the market. This tragic episode demonstrated the potential for other medications taken by a pregnant woman to affect the developing baby. Some medications have the potential to affect brain development.

The effect on the baby will depend on the type of drug, the dose, the stage of pregnancy when the drug is taken and the individual response of the foetus to the drug. There will be other factors in play too, such as the nutritional status of the mother and any other health issues she might have.

Recommendation: If you are planning a pregnancy or there is a chance you could become pregnant, check any medication or supplement you are taking or planning to take including type, dose and combinations to ensure that it is not likely to cause a problem for an unborn baby. If you are taking regular medication for any reason, make sure you ask your GP or

medical specialist whether it is safe for pregnancy and what pregnancy-safe options are available to you. Don’t stop taking any medicines that are prescribed to manage a chronic or serious medical condition without advice from your medical advisors. And of course, avoid any illicit drugs.

5

Alcohol and Your Brain

The immediate short-term effects of alcohol on the brain are obvious. In small doses, alcohol can create a relaxing effect, reducing anxiety and lowering inhibitions. This is the main reason that most people drink alcohol.

Higher doses of alcohol create more harmful short-term effects on the brain, affecting virtually all its functions. If you have had too much to drink you will experience confused thinking, slurred speech, blurred vision, erratic moods, stumbling gait, poor judgement and slow reaction times. You may not remember details of conversations or the names of people you met.

More serious is the ‘Oh no! What happened last night?’ blackout, when there is absolutely no memory of the events of the night before. Blacking out does not mean falling asleep or being unconscious, although it is possible to pass out or have a seizure during a blackout. These are periods of complete memory loss, having no recollection of events that happened while drinking larger amounts of alcohol. Blackouts are thought to be caused by disruption of activity in the hippocampus, with intoxication blocking the ability to form memories. During a blackout period you might continue to have conversations (which may or may not make sense to

others), dance, eat a meal, have sex, even drive home. But no matter how hard you try to recall these events, the memories are not there to retrieve. Some people are more prone to alcohol-related blackouts than others.

It is clear that too much alcohol has an acute toxic effect on the brain. Anyone who has ever suffered a hangover will attest to that. But what about the effects of chronic and long-term excessive alcohol consumption?

Drinking too much alcohol over a long period of time causes permanent damage to parts of the brain. Chronic alcohol use particularly damages the frontal lobes, causing frontal lobe impairment. As discussed earlier, frontal lobe damage can cause a change in a person's personality. They may become irritable, socially inappropriate, impulsive and disinhibited, and emotionally unstable.

A person with frontal lobe damage may have impaired judgement, loss of intellectual capacity, memory loss, difficulty making plans, loss of empathy and difficulty with speech.

Long-term excessive alcohol consumption can also damage the cerebellum at the back of the brain, which is responsible for balance.

Prolonged heavy drinking over many years will take a toll on your brain health.

What about the effects of alcohol on your brain as you age, if you have only ever been a light or moderate drinker? Would it help you to keep your brain young by modifying the amount of alcohol you drink?

WERNICKE–KORSAKOFF SYNDROME

Wernicke–Korsakoff syndrome is a neurological disorder caused by a severe deficiency of thiamine (vitamin B1), combined with excessive alcohol consumption, often resulting in permanent brain damage. Alcohol interferes directly with

thiamine absorption from the gut and thiamine storage in the liver.

Alcohol also has direct toxic effects on the brain.

Wernicke–Korsakoff syndrome causes vision problems, confused mental state, apathy, difficulty concentrating, memory loss and unsteady gait with a wide stance.

THE BRAIN, AGEING AND ALCOHOL

'Is it just my imagination or do I get drunk more easily these days? When I was younger I used to be able to knock back a bottle of wine in an evening and still feel fairly normal. These days, I have two drinks and feel like I could just lie down and go to sleep.'

This was a conversation I had recently with a woman in her late fifties, and it's something many people experience as they get older.

It seems that sensitivity to the effects of alcohol does increase as you get older. Older people reach a higher blood alcohol concentration (BAC) than younger people after an equal amount of alcohol, so intoxication and other adverse effects do happen more easily. In other words, as you get older you have to drink less to feel drunk, and it takes less alcohol to do damage to your brain and other organs.

Excessive alcohol can cause premature ageing of the brain – in other words, it accelerates the normal ageing process.

Some recent media reports observe that people who don't drink in middle age are more likely to develop dementia. This raises the question of whether light occasional drinking might confer some neuro-protective effect. Is a little bit of alcohol good for your brain?

The evidence is conflicting. Some studies do show that light alcohol consumption might be beneficial. Other studies show no such advantage. Could it be that the people who

showed this effect abstained during middle age because they drank heavily in their younger years, and that early drinking was what did the damage? Or could there be some mechanism by which a small amount of alcohol can protect your brain?

The *British Medical Journal* paid some attention to this controversy, publishing a fascinating editorial in 2017 titled 'Alcohol Consumption and Brain Health'. They concluded that:

> 'After adjustment for numerous potential confounders, alcohol use was associated with reduced right hippocampal volume in a dose dependent manner; even moderate drinkers (classified as up to 21 units a week for men at the time of the study) were three times more likely to have hippocampal atrophy than abstainers, and very light drinking (1–6 units a week) conferred no protection relative to abstinence … drinking more than 14 units a week was associated with both brain pathology and cognitive decline.'

This confirms what we know about heavy drinking, issues a warning about brain damage caused by an average consumption of 14 to 21 drinks a week, and concludes that there is no brain health benefit to very light drinking of one to six drinks a week. The editorial also makes the point that even low levels of alcohol consumption carry a greater risk than abstinence for conditions such as breast cancer, and that any purported benefit is not sufficient to advise abstainers to drink for the sake of their brain health.

HOW MUCH ALCOHOL IS 'SAFE' FOR YOUR BRAIN?

Alcohol is very popular – so much so that in many social groups it is considered abnormal NOT to drink it at least

sometimes. On the other hand, excessive drinking is considered ‘normal’ for many people.

GP: How much alcohol do you drink?

Patient 1: You know, just normal.

GP: What is normal?

Patient 1: Every night I share a bottle of wine with my partner.

GP: That’s four standard drinks each.

Patient 1: No it’s only two glasses.

GP: Must be big glasses.

Later that day …

GP: How much alcohol do you drink?

Patient 2: You know, just normal.

GP: What is normal?

Patient 2: Two beers after work, a couple of wines with dinner most night. Fridays and Saturdays are usually big nights with my friends, maybe ten or fifteen if you count the shots. Who keeps count?

GP: How do you feel on Mondays?

The National Health and Medical Research Council (NHMRC) guideline gives advice on reducing (but not eliminating) risk of alcohol-related disease or injury for most mature adults. It says:

- healthy men and women should drink no more than 10 standard drinks a week and no more than 4 standard drinks on any one day.
- The less you drink, the lower your risk of harm from alcohol.

Of course this advice is for an entire population, and will not be suitable for every individual's circumstances. The question of what is a 'safe' level of alcohol consumption should be simple, but it isn't. The answer depends on who is asking the question and why. In some cases, we don't know what the 'safe' level might be for an individual.

I put 'safe' in inverted commas because the level of alcohol that is not going to cause harm is extremely difficult to predict for any particular individual. For some, the only safe level will be zero. Others may find they can drink much more without apparent long-term effects, but those long-term effects may not be seen for decades. There will also be individual, environmental and genetic factors that determine your ability to deal with alcohol as a toxin.

Public health authorities around the world have tried to provide uncomplicated advice about alcohol for people wanting to look after their health, but this can seem conflicting. The Australian guidelines developed by the NHMRC are one such attempt to reduce the risk of accidents, injuries, alcohol-related diseases and death from excessive alcohol consumption. The NHMRC adds that there is no level of drinking alcohol that can be guaranteed to be completely 'safe' or 'no risk'. See page 191 for more.

PREGNANT WOMEN

As discussed in chapter 4: A Head Start, there is no level of alcohol consumption for pregnant women that we can confidently say is risk free. Foetal brain development is extremely sensitive to the effects of alcohol throughout pregnancy, and there is no known safe level of alcohol consumption during pregnancy.

One of the strongest pieces of advice I give to women who are planning to get pregnant, or who have just found out that

they are pregnant, is to stop drinking alcohol altogether. The same goes for women who are breastfeeding.

ADOLESCENTS

During adolescence, the brain is going through a major period of growth and transformation. Your brain continues to grow and develop throughout your teens and at least into your mid-twenties. Drinking alcohol while your brain is developing can impair this process. As discussed previously, alcohol can have a damaging effect on the hippocampus – the part of the brain that is responsible for memory and learning. Studies have shown that adolescents who drink heavily have a smaller hippocampus and may damage the brain cells in that area, impacting on their learning and memory.

The prefrontal cortex is important for judgement, decision-making and language. Heavy drinking in adolescence and early adulthood causes physical changes in the prefrontal cortex, leading to permanent cognitive problems.

Adolescence is also a crucial stage for the maturing of synapses (connections between neurons). Synaptic plasticity is the ability of synapses to strengthen or weaken over time. Synaptic plasticity and the release of neurotransmitters may be disrupted by consumption of alcohol during adolescence. This can lead to remodelling of synapses and abnormal adult behaviour. For example, repeated binge drinking increases the risk for alcohol use disorder and other psychological problems including anxiety in adulthood.

While many Australians do start drinking at a young age, younger people are increasingly following advice not to drink at the crucial stage of adolescent brain development, with the age at which people first tried alcohol rising over time. The average age at which young people aged 14–24 first tried alcohol has steadily risen from 14.7 years in 2001 to 16.2 in

2019. In 2017, almost half of those aged 12–17 had drunk alcohol in the past year, and 27 per cent had done so in the past month. In another positive sign, there has been a long-term increase in the proportion of young people who abstain from alcohol: from 2007 to 2019, the proportion of people aged 14–17 who abstained increased from 39 per cent to 73 per cent, while for people aged 18 to 21 alcohol abstinence rose from 13.1 per cent to 21 per cent. (Refer to the endnotes for source information.) Adolescents are particularly vulnerable because they are more likely to take risks, including drinking excessive amounts of alcohol.

WHAT AGE IS SAFE TO START DRINKING ALCOHOL?

The NHMRC guidelines recommend that young people under 18 years of age do not drink alcohol at all. Given the emerging evidence about the impact of alcohol on the developing brain, I think that is setting the age way too young.

My advice is to delay the initiation of drinking for as long as possible, at least into the twenties, and that when a young person does start to drink alcohol they should be careful how much they drink, in order to protect their brain development.

MENTAL HEALTH AND ALCOHOL

Alcohol may increase the risk of or worsen some mental health conditions, such as depression and anxiety. Excessive alcohol use may cause mental health problems as a direct result of brain toxicity.

Alcohol has a depressant effect and is commonly used as a form of ‘self-medication’ by people trying to cope with feelings of stress or anxiety, or problems with sleep. This is generally a short-term effect, ultimately worsening the problems they are trying to relieve.

ALCOHOL AND OTHER DRUGS

Mixing alcohol and other drugs can be risky for your brain function. This goes for a long list of prescription drugs as well as some illicit drugs.

The combination of alcohol and other drugs can have a potent effect on your brain function, beyond the effect of either substance alone.

If your doctor prescribes a medication that interacts adversely with alcohol, they will usually warn you to avoid alcohol while you are taking that medication. To be certain, ask your doctor or pharmacist if you should avoid alcohol while you are taking a prescription medication, and make sure you read the information sheet that comes with the medication to see if it is likely to interact with alcohol. Some over-the-counter medicines such as cold and flu preparations, antihistamines or painkillers can cause drowsiness, which can be exacerbated by alcohol. This is potentially dangerous if you are driving or need to be alert for any reason. It can also increase the risk of falls or accidents, especially in older people.

Illicit drugs are always more tricky and unpredictable than pharmaceutical preparations because you may not know what you are taking, and doses can be inconsistent. Illicit drugs are not standardised, and there is no quality control.

Alcohol may compete with stimulant drugs like cocaine, but can exacerbate a depressant drug like heroin. For further information about this, see chapter 9: Illicit Drugs and Your Brain.

SO, IN SUMMARY, HOW MUCH ALCOHOL IS SAFE FOR BRAIN HEALTH?

If you are trying to work out your ‘safe’ level of drinking, you need to consider your gender, age, whether you are pregnant or planning to get pregnant, your mental health, history of addictions, other drug use, medications, any existing medical conditions and any previous diagnosis of cancer.

Different people will give you different answers as to what is ‘safe’ for you. My focus is on keeping your brain healthy as you get older. With that aim in mind, let’s go over the current advice.

To protect the development of an unborn baby’s central nervous system, there is no known safe level of alcohol consumption. If you are of child-bearing age and there is a chance you could get pregnant, make decisions as if you could be pregnant. That means no alcohol after ovulation (usually mid-cycle), and never more than one or two drinks in a 24-hour period. Stop drinking if your period is late.

Alcohol appears in breast milk, so the best course is to avoid alcohol while you are breastfeeding.

With respect to brain health and ageing, your tolerance levels will decrease as you get older. I see a lot of older patients who choose to drink much less than when they were young, because they recognise that the effects of alcohol are amplified.

Light drinking, between one and six drinks total in any week (but no more than four on any given day) seems to show similar outcomes for brain health when compared to abstinence.

Despite reports that light drinking may confer some (likely disproven) benefit to brain health, this is not a reason to start drinking if you do not usually drink alcohol.

If you have specific health issues, your doctor will help you with advice about alcohol for your personal situation.

For more information, refer to:

- NMHRC alcohol guidelines www.nhmrc.gov.au/health-topics/alcohol-guidelines
- Drinkaware UK www.drinkaware.co.uk

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Medications

Some medications may affect your brain function. You might experience brain fog, sleepiness, confusion, trouble concentrating or memory loss as a side effect of certain medications. In severe cases, medication side effects can even mimic the early stages of dementia.

Older people are at particular risk of adverse medication side effects because they are more likely to have one or more chronic diseases and so are more likely to be taking multiple medications, and there are age-related changes in the way the body processes drugs. Generally, older age is associated with increased blood concentrations of drugs and altered metabolism, reduced effectiveness, and increased risk of adverse reactions for many medications.

One of the ways you can look after your brain is to check for potential brain side effects before you start a new medication. Or, if you are already on medication and you suspect it may be affecting your thinking or concentration, ask your doctor or pharmacist to review your medications for the possibility that one or a combination of them may be causing the problem. Specifically ask about any brain function effects. You can also search for side effects on credible sites on the internet.

The list of medications that can cause or worsen problems with brain function is a long one. Some of the medications are common and obvious suspects, but in other cases, we have to hunt through the reports of side effects in the medical literature to identify potential problems.

Your doctor will need to take a careful and detailed history, including the timing of starting or changing any medications. If you are having trouble concentrating or remembering details, it is helpful to have someone you trust and who knows you well to attend the consultation with you. They can provide their observations and also help you recall the advice you were given.

Sometimes we can't find brain/cognitive/memory/mood changes on the list of reported side effects. In the case of medications that are new to the market, it can take some time for side effects to be recognised and reported.

In this chapter I am going to list some of the medications that may have an effect on your ability to think. Some medications have a temporary effect on brain function, experienced only while you are taking them, while others have the potential to cause permanent and irreversible brain problems. There is also an individual genetic element to whether a particular medication works for you, or has an adverse effect on you. Pharmacogenomic testing is in the early stages of clinical use, and as more evidence becomes available and testing becomes more accessible, we will develop a greater understanding of individual risk and potential benefit with specific medications based on your own body's genome.

STATINS

Statins have become one of the most popularly prescribed medications for lowering cholesterol, and there is no shortage of controversy around them.

You may be aware of reports that statins can cause cognitive impairment. Other reports suggest that statins reduce the risk of dementia, Alzheimer's disease and cognitive impairment. Where does the truth lie?

There is evidence that statins can cause reversible cognitive impairment in some people, particularly in high doses. The original trials of statins were not set up to detect cognitive impairment as a side effect, but there have since been many case reports of reversible cognitive impairment.

This led the Federal Drug Administration in the United States in 2012 to issue a warning:

> Information about the potential for generally non-serious and reversible cognitive side effects (memory loss, confusion, etc.) and reports of increased blood sugar and glycosylated hemoglobin (HbA1c) levels has been added to the statin labels. FDA continues to believe that the cardiovascular benefits of statins outweigh these small increased risks.

This is certainly something we see in general practice from time to time, such as the following case study about Ken.

> *Ken and his wife Laura had both noticed that Ken had been having problems with his memory. He seemed very confused at times, and was forgetting details – even his friends' names. Laura explained that Ken was usually the designated driver and he had such a great sense of direction that he rarely had to use the GPS in their car. But one day he took a wrong turn on the way to their local shopping area and became confused about where he was. When we went through his medical history, it became apparent that the changes seemed to coincide with him finding out he had high cholesterol and starting statin medication. After a trial off that statin medication, Ken was back to his old self.*

While the evidence is still being established, it's important to be alert to the possibility that any cognitive decline you experience after starting to take a statin may be due to the statin. A trial off medication, under medical monitoring, will show whether the changes you have noticed are reversible.

Depending on your cardiovascular risk factors, you may be advised to trial a different cholesterol-lowering medication or a lower dose of the statin you were taking.

Again, the cognitive impairment of statins is reversible, so if the statin is responsible, the condition should reverse itself.

There are other reports that statins decrease the risk of dementia, Alzheimer's disease and cognitive impairment in some people. Again, randomised controlled trials have not been able to establish clear evidence for this.

The decision to take a statin is not as clear cut as it once seemed. It's best to be guided by the doctors who know your individual medical condition, especially your risk of heart disease or stroke, and to discuss the balance of risks and benefits with them.

BENZODIAZEPINES

Benzodiazepines are some of the most commonly prescribed medications. They are used to reduce anxiety, treat panic attacks, as a sedative and as an anticonvulsant. You can usually recognise them because the generic form of the drug name ends in 'azepam'.

Benzodiazepines (or, as they are popularly known, 'benzos') with brand names including diazepam (Valium), oxazepam (Serepax) and temazepam (Normison), and the more potent clonazepam (Rivotril), lorazepam (Ativan) and alprazolam (Xanax) are so commonly prescribed that their potential for causing serious problems is too often overlooked or understated.

They enhance the effect of gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter in the brain. The resulting effects are sedating, sleep-inducing, anxiety-relieving, anticonvulsant and muscle relaxing.

Side effects of benzodiazepines

Most people take a benzodiazepine because of a desired effect it has on their brain.

Similarly, unwanted effects, or side effects, are mostly also related to the effect on the brain. These include:

- confusion
- impaired coordination, increasing the risk of falls in elderly people
- dizziness
- drowsiness
- mood swings and depression
- dependence
- poor sleep quality.

The benzodiazepine story began in 1960 when the compound chlordiazepoxide (Librium) was launched in the UK, followed by diazepam (Valium) in 1963. By the late 1970s benzodiazepines had become the most aggressively marketed and commonly prescribed of all drugs in the world. Marketing was particularly targeted at women, coining a widely used term for benzodiazepines: ‘Mother’s Little Helper’.

By the early 1980s there were 17 benzodiazepines on the market, worth billions of dollars worldwide. There are now almost 30 different variations.

As a general practitioner, I sometimes see patients who get into trouble with side effects or addiction to benzodiazepines

and then have terrible difficulty learning to manage without the medication.

It can start simply enough. A prescription for something just to get you over a period of insomnia related to a stressful time in your life. Then the stressful period passes, and you find that you need to take the medication to get to sleep every night. You can't sleep without 'taking something'. In some cases, that dose won't work anymore, and now you need two tablets, and then an even higher dose, to get the same effect. It can take as little as a few weeks for dependence or addiction to develop. But these are not the only problems.

Over the years, concern about the long-term use of benzodiazepines has grown, particularly the effect this has on brain function.

A 2012 French study published in the *British Medical Journal* found that the recent commencement of benzodiazepines in elderly people was associated with an increase of approximately 50 per cent in the risk of dementia. The authors wrote: *'Benzodiazepines remain useful for the treatment of acute anxiety states and transient insomnia ... Our data add to the accumulating evidence that use of benzodiazepines is associated with increased risk of dementia, which, given the high and often chronic consumption of these drugs in many countries, would constitute a substantial public health concern.'*

More recent studies suggest that any related memory impairment is primarily recent recall and is often mild and largely reversible when benzodiazepines are discontinued. Elderly people may be more vulnerable to this side effect. A subsequent prospective population-based study in 2020 showed 'no evidence of a causal association between benzodiazepine use and dementia.'

In addition to the side effects of muscle weakness, blurred vision, panic attacks, poor sleep quality, confusion, clumsiness and memory problems, benzodiazepines are also related to mental health problems. They figure prominently in worsening depression and suicide attempts.

Mixing benzodiazepines with other sedative drugs or alcohol increases the risk of accidental death.

Benzodiazepines also cross the placenta; babies born to mothers who are taking benzodiazepines may need to spend time in a special care nursery because they are likely to have trouble feeding, have a low body temperature, appear floppy and lethargic, and have breathing problems. They may be very irritable and suffer their own form of drug withdrawal. Reduction of the drug during pregnancy needs to be carefully managed and medically monitored.

Benzodiazepines are meant to be prescribed for occasional short-term use only. Even the guidelines for the management of anxiety and insomnia warn against using them for longer than two to four weeks, and this is particularly the case for the more potent, longer lasting or higher dose types.

If you have been taking a benzodiazepine regularly, and for longer than a few weeks, it is important to withdraw carefully and gradually, and under medical supervision. Stopping abruptly can be dangerous; possible withdrawal effects include convulsions.

If you are taking a benzodiazepine and you are concerned that it is having an adverse effect on your brain, I would advise you to speak to your doctor about how you can reduce or stop taking it. You will be advised on how to safely wean off the medication. As you reduce your dependence on a benzodiazepine, you also need to address the underlying reasons you started taking the medication or continued to take it.

Some people will need to switch to a different class of medication. There are also other ways of reducing the need for medication and managing your symptoms, such as talk therapy (counselling), exercise, meditation and lifestyle change.

ANTICHOLINERGICS

Another group of prescribed medications that has recently come under scrutiny is the anticholinergics. There is a long list of medications that are either anticholinergic or have anticholinergic effects. These include drugs to treat depression, psychosis, urinary incontinence, allergies, asthma, Parkinson's disease and eye conditions. They all have the effect of blocking the neurotransmitter acetylcholine.

In the brain, acetylcholine is involved in memory and learning. In other parts of the body, it stimulates muscle contractions. An *anti*cholinergic drug will block those effects.

These drugs are widely prescribed. Use of these drugs becomes more common in older people. It has been estimated that in Australia, 33 per cent of people over the age of 65 years take enough medications with anticholinergic effects to potentially increase their risk of harm.

Common side effects of anthicholinergic drugs include dry mouth, urinary retention, drowsiness and blurred vision. If you take more than one anticholinergic medication, it can have an additive effect. It is not clear whether this effect is entirely reversible once the medication is stopped. There is also a suggestion that the risk of mild cognitive impairment is increased in people taking anticholinergic drugs. Recent research showed that older people taking larger cumulative doses of some of these drugs had a higher risk of developing dementia than those who were not taking them. A possible explanation for some of this effect is that people who are

developing dementia may be more likely to be prescribed one of the medications in this category.

Dementia Australia has a fact sheet listing the common drugs in this category. You can also check any medications you are taking with your GP, specialist or pharmacist.

Until the situation is more certain, the best advice is to ask whether there is an alternative medication, one without anticholinergic effects, especially as you get older. If there is no alternative available, work with your doctor to find the lowest effective dose and reduce the number of medications you are taking with this effect.

CARDIOVASCULAR MEDICATIONS

Heart disease becomes more common with advancing age, and so does cognitive impairment. The question is whether a medication for treating heart disease or its risk factors, such as high blood pressure, might be contributing to the brain function changes experienced with ageing.

In 2016, a review was published examining drug-induced cognitive impairment caused by cardiovascular medications. The review found that, in general, use of all antihypertensives, especially in the case of multiple drugs or the wrong doses, can lead to low blood pressure and/or slow heart rate, and that these effects could lead, in turn, to cognitive impairment due to decreased blood flow to the brain. Of course, uncontrolled high blood pressure is a risk factor for stroke and vascular dementia so it is a matter of getting the medication choice and the doses right to keep blood pressure in the safe range.

The use of diuretics to reduce fluid retention and to decrease blood pressure can cause electrolyte imbalance, resulting in confusion and delirium.

In addition, cardiovascular agents that have an effect on the brain, such as digoxin and some of the medications that

treat abnormal heart rhythms, can also carry a risk for cognitive impairment. Digoxin can cause headache, weakness, dizziness, apathy, confusion and mental health problems (such as anxiety, depression, delirium and hallucinations).

Again, the same principle applies. If cognitive impairment or mental health symptoms become a new or worsened problem, then a full medication review is necessary.

Any decision about medication for cardiovascular disease prevention or treatment is a high stakes issue and needs to balance the risks of adverse medication effects against the benefits of lowering the risk of heart and blood vessel disease.

ANTIDEPRESSANTS

Major depression is a common and debilitating condition, and effective treatment may include the careful use of medication.

Depression itself has effects on your ability to think, to concentrate, to make decisions and to function optimally at work or in your social and family life. Fatigue and sleep disturbance can also contribute to the cognitive impairment of depression.

Depression can also be a feature of the onset of dementia.

Sometime in the future we may be able to test for the right antidepressant medication for each individual case, but until then, deciding which medication will be most effective, with the least side effects, is largely a matter of experience as well as some ‘trial and error’.

The cognitive impairment that occurs with episodes of major depression may improve with treatment and resolution of depressive symptoms, but cognitive deficits can still be detected even in people who respond well to treatment and achieve a period of remission.

The combination of the right antidepressant along with psychological therapies will improve cognition in people with major depression. However, some antidepressants may have the effect of making cognitive impairment worse.

Some studies have found that the treatment of depression with a selective serotonin reuptake inhibitor (SSRI) improved cognition, while others have found that people taking SSRIs can show a decline in their memory function within the first eight weeks of starting on the SSRI.

Some antidepressant groups have anticholinergic effects that can have an adverse impact on cognition. These include tricyclic antidepressants such as amitriptyline, often used for anxiety treatment and pain management, and doxepin.

If you are taking an antidepressant medication and you think that it is adversely affecting your memory or thinking ability, talk to your doctor. The problem may be the medication, but it could also be the underlying depression. Your doctor may recommend a change of medication, but it is important not to simply stop your medication without medical advice and supervision.

CORTICOSTEROIDS

Corticosteroids are widely used to treat a range of conditions where inflammatory reactions or the immune system need to be suppressed.

Common examples we see in general practice are acute flares of asthma, treatment of Crohn’s disease or rheumatoid arthritis, and severe allergic reactions.

However, they do also have some serious side effects, particularly with long-term use, including abnormal glucose metabolism, osteoporosis, cataracts and hypertension.

Corticosteroids also have effects on brain function, including insomnia, euphoria, mood changes, agitation, abnormal behaviours and poor concentration.

About 20 per cent of patients receiving high doses of corticosteroids develop psychiatric disorders, including depression, mania and psychosis needing drug treatment. Psychiatric symptoms appear to be dose-dependent and generally occur during the first few weeks of therapy. In most cases, the brain-related side effects happen in the first five days of treatment, but they can come on at the beginning, during or at the end of treatment.

Most psychiatric symptoms are reversible when the corticosteroid use is discontinued.

If you do experience psychiatric symptoms or other brain side effects related to corticosteroids, the dose will need to be reduced or treatment discontinued only under medical supervision. Sometimes the symptoms will need to be mitigated with other medications, usually in consultation with a specialist.

MEDICATIONS THAT DEPLETE NUTRIENTS

Medications are supposed to make you feel better, cure disease or help you to manage illness. Unfortunately, as we have seen they can also have side effects, and some interact with other drugs, herbs or supplements. This is an issue that is always front of mind for a doctor prescribing a new medication.

A less-recognised downside of many pharmaceutical and over-the-counter medications is that they can deplete one or more essential nutrients. This can occur because of interference with the normal processes of nutrient absorption, or because of a chemical interaction within your body affecting the activity of the nutrient in body tissues.

The medication may help you, but it could also be causing harm. Nutrient depletion can cause additional health problems on top of the problem you are trying to solve by taking the medication.

It is unfortunately common to see a side effect of one drug caused by nutrient depletion (such as indigestion or depression) being treated with another drug, potentially compounding the problem. If you recognise and treat a possible drug-induced nutrient depletion, this could help you tolerate an essential medication.

In chapter 24: Brain Food, we look at the nutrients essential for the smooth operation of your brain. Where there is an anticipated nutrient depletion, it may not be possible to address this by increasing food intake alone; often nutritional supplements are necessary to avoid deficiencies and maintain adequate nutrient levels.

Here are some commonly prescribed drug groups and their known nutrient-depleting effects. If you are taking one of these medications, you will need professional advice on using supplementation to counter the effects, or finding a different way to manage your medical condition:

- oral contraceptives (birth control pills): B vitamins, vitamin C, magnesium, selenium and zinc
- hormone replacement therapy: vitamin B6, vitamin B12, folate and magnesium
- anti-diabetes drug (metformin): folate, vitamin B12, coenzyme Q10
- anti-inflammatory (examples: ibuprofen, aspirin): folate, iron
- oral diabetes medication: vitamin B12, folate
- indigestion and anti-ulcer drugs used to lower stomach acid: vitamin B12, folate, vitamin D, magnesium, calcium,

iron and zinc

- statins (cholesterol-lowering drugs): coenzyme Q10
- diuretics (fluid tablets): B vitamins, magnesium, zinc and potassium
- beta-blockers: coenzyme Q10, melatonin
- digoxin: calcium, magnesium, phosphorus, vitamin B1 and potassium
- SSRI antidepressants: folate
- antipsychotics: vitamin B2 (riboflavin)
- benzodiazepines: calcium, endogenous melatonin
- antibiotics: many antibiotics can deplete B vitamins. Also, while gut flora are not strictly nutrients, depletion of the important bacteria in your gut can affect the absorption and metabolism of some important nutrients. A probiotic is essential if you are taking or have recently taken a course of antibiotics.

You will see from this list that the nutrients that are depleted by these commonly prescribed medications are all necessary for your brain to function well. But how often is a nutritional supplement recommended when you are prescribed one of these medications?

Some nutrient levels can be checked with blood tests, such as iron, folate, vitamin D and vitamin B12. Other nutrients, such as coenzyme Q10, are not easy to test for, or the test is unreliable or expensive.

It is best not to wait for a nutrient depletion to affect you. We have to anticipate the likely nutrient depletions or judge clinically what might be needed to counter the expected side effects of medication.

My advice is to review all of your medications with your doctor or pharmacist. If you are taking a medication that can

cause nutrient depletion, make sure you get advice on whether the medications you are taking are all necessary, and whether there are non-drug alternatives that are safe and effective for you. If you need to continue your usual medication, you will need to adjust your diet and take appropriate doses of supplements to make up for the possible nutrient depletion caused by the medication. See chapter 25: Herbs and Supplements for Brain Health. Also check out www.dementia.org.au.

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Cancer, Chemotherapy and Brain Function

The relationship between brain function, cancer and cancer treatments is complex. There are many types of cancer, and many combinations of cancer chemotherapy drugs, surgical and radiotherapy procedures with the potential to cause brain function problems.

Cognitive impairment is more commonly seen in patients with cancer than in those in remission. This can be a direct effect of the cancer itself, it can be associated with other medical issues, or it can be a side effect of cancer treatment.

A review of medical literature on cancer-related cognitive impairment (CRCI) found that CRCI is highly prevalent: ‘these problems can be detected in up to 30% of patients prior to chemotherapy, up to 75% of patients report some form of CRCI during treatment, and CRCI is still present in up to 35% of patients many years following completion of treatment’.

There is evidence that the presence of a cancer itself can affect brain function even before adding chemotherapy, although some types of chemotherapy definitely make cognitive problems worse. This is turn affects quality of life and daily functioning.

An interesting study at Sydney Medical School at University of Sydney found that a cancer diagnosis itself can cause brain function problems. The study found that people diagnosed with colorectal cancer are three times more likely to have cognitive impairment when tested soon after their cancer diagnosis (but before starting any chemotherapy) than healthy people in the control group, and that this effect was sustained at 12 months post-diagnosis. The research also found that more people who received chemotherapy had cognitive symptoms after six months (about the time chemotherapy ended), but by 12 months there was no difference in cognitive symptoms between the groups. The cognitive problems did not seem to be related to stress, anxiety or depression.

We do not yet know why the presence of a cancer elsewhere in the body might affect brain function. There are some theories, however, including inflammation, direct neurotoxic effects, dysfunction in the body's immune system and genetic factors.

CHEMO BRAIN

'Chemo brain' is a term I often hear from patients who are having chemotherapy for cancer treatment. They are referring to the effect of the chemotherapy drugs on their brain's ability to function normally. It is well recognised that some forms of chemotherapy can have cognitive side effects.

Of course, cancer affects more people in older age groups, so some people diagnosed with cancer will have some level of pre-existing cognitive deficit, and chemotherapy may tip them into a worse state. There are many different types and combinations of chemotherapy and, as with all medications, some people will have more side effects than others undergoing the same treatment.

People with chemo brain describe mental fogginess, trouble with memory, being forgetful, taking longer than usual to finish things or make decisions, having trouble multitasking or doing complex tasks, being disorganised and having trouble remembering names and dates.

These changes might only occur during the course of treatment and for a short time after, or the effect may be prolonged. This seems to be a feature of some but not all types of chemotherapy.

Changes in the brain's structure and function have been documented in studies using brain imaging techniques, including structural and functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scanning. These brain scans have shown reductions in grey matter volume or density, reductions in white matter microstructure, and changes in brain activation and connectivity.

The areas most affected by chemotherapy treatment include brain hub regions such as the prefrontal cortex and hippocampus. However, recent studies provide increasing evidence that CRCI may be associated with widespread disruption of brain network connectivity rather than regionally specific effects.

As you can imagine, chemo brain can have a major effect on your life, having an impact not only on day-to-day activities but also on work performance. It is not always easy to detect more subtle changes in your brain function with standard medical investigations, but you will notice the change.

There can be a direct toxic effect of chemotherapy on brain function. However, it is important not to assume that any problem with thinking or other brain functioning is a result of

chemotherapy. Many other factors can also have an effect on your brain functioning, and they need to be checked.

These include: other drugs or medications such as opioid painkillers or hormone treatments, anaemia, nutritional deficiencies such as iron deficiency, infection anywhere (including urinary tract infection), tiredness related to insomnia, cancer-related fatigue, anxiety and depression.

In the case of breast cancer, women treated with the hormone blocker anastrozole have been found to have lower executive function scores than women in the control group up to 18 months after the start of treatment. We see some cognitive effects in men treated with hormone blockers for prostate cancer too.

So far, medical science has not found a specific way to prevent or treat CRCI. There are, however, some practical ways to manage. All of the advice in this book will help you keep your brain as healthy as possible, and applies to recovery after treatment. This includes all of the advice about intellectual stimulation, nutrition, exercise, avoiding toxins, not smoking, avoiding excess alcohol, getting good quality sleep, reviewing your use of medications, optimising the management of any other chronic diseases and more.

Psychological therapies including cognitive behaviour therapy and cognitive brain training can assist.

See your doctor to work out if there is a treatable underlying cause of your mental fogginess, such as a micronutrient deficiency or an infection (such as a urinary tract infection), or a drug side effect.

Coping with chemo brain

- Get yourself organised with a detailed diary of the things you need to do. Try to focus on one task at a time, and don’t over-commit yourself.

- Learn to delegate where you can.
- Take a rest during the day if you feel tired.
- Let your close family and friends know about the difficulties you are having, and tell them what they can do to make things easier for you.
- Nutrition: a diet with plenty of antioxidant-rich fruit, a variety of vegetables and sources of omega-3 fatty acids (as found in seafood, nuts and seeds such as flaxseed or chia seeds, and plant oils such as flaxseed oil).
- Practise daily yoga and meditation.
- Take regular aerobic exercise.

Herbs and supplements for chemo brain

Most of the studies on herbal medicines and supplements related to brain function have focused on age-related cognitive decline or dementia. Few have looked specifically at the use of herbs and supplements for preventing or treating chemo brain.

Given that medical treatments for this distressing side effect are very thin on the ground, it is worth looking at some low-risk complementary therapies.

Chapter 25: Herbs and Supplements for Brain Health details evidence for some of the major micronutrients and herbs used to support brain health.

The information in this chapter relates to general support for brain health. In applying this to chemo brain, I am conscious that there is a lack of specific research in this area to date and decisions will need to be made in collaboration with your medical oncologist.

Nutrients that may help with chemo brain include omega-3 fatty acids, acetyl-L-carnitine, Coenzyme Q10,

phosphatidylserine, phosphatidylcholine and the herbal medicines ginkgo biloba, Bacopa and Gotu Kola.

Make sure you ask for professional advice on doses and combinations.

If you are planning to take herbs for this purpose while you are going through chemotherapy, I would recommend you see a practitioner who is qualified to prescribe and monitor herbal medicines. It will be particularly important to check for any herb/supplement/drug interactions, and to be aware of special precautions.

Resource:

The Cancer Recovery Guide, Phelps K. Pan Macmillan, 2015.

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Anaesthetic Brain

If you are advised to have surgery, you may have many questions about the risks of the procedure. You may not have the luxury of deciding whether or not you will have surgery, but you still need to be informed about the potential benefits and risks of the procedure, and the likelihood of its success. It is also important to know what you can do to prepare for surgery, and to plan your post-operative recovery and rehabilitation.

It is largely because of modern anaesthesia that we have access to the surgical procedures that save lives and relieve suffering, yet the part of any surgical procedure that usually gets the least attention is the anaesthetic.

There are different types of anaesthetic. There is the local anaesthetic, like the injection under the skin used to repair a small laceration. This does not affect the brain.

There is a regional anaesthetic, which blocks sensation from a larger section of the body. This may be accompanied by a ‘twilight’ drug to cause sedation, reduce awareness and block your memory of the procedure.

Then there is a general anaesthetic, which is induced by a combination of drugs. The aim is to maintain all of your

normal physiological functions, but to make you completely unconscious and unaware, so that you feel no pain, cannot move and have no memory of the procedure.

Commonly used anaesthetic agents target neuronal receptors, altering the activity of specific neurons in the brain either by increasing the activity of the inhibitory GABA (gamma-aminobutyric acid) receptors, or blocking excitatory NMDA (N-methyl D-aspartate) glutamate receptors, decreasing the ability of the nerve cell to fire.

The general assumption is that you have a general anaesthetic to get you safely through surgery and then once it wears off after few hours in the recovery ward, you wake up and your brain is entirely back to normal. While that may happen most of the time, this interruption to the normal functioning of the brain can have longer-lasting effects in some people.

The longer-term brain effects following general anaesthesia have only recently been recognised.

Post-anaesthetic delirium is now recognised as a common surgical complication. It is particularly prevalent in older adults, but it can occur at any age. According to a study in the United Kingdom, this affects around 20 per cent of people in the hospital who need intensive care.

In recent years there has been some investigation into the effects of a general anaesthetic on the function of the brain after the anaesthetic is expected to have worn off. Recent studies indicate that even once the initial confusion dissipates, attention and memory can be affected for months or, in some cases, years.

There is evidence that an ageing brain is more vulnerable to the effects of anaesthetics than a younger one, particularly if there is an existing cognitive disorder such as Alzheimer’s disease.

Anaesthetics can also affect the developing foetus in late pregnancy, potentially resulting in learning or behavioural problems in infants and toddlers under three.

In 2016 in the United States, the Federal Drug Administration issued a warning about repeated or lengthy general anaesthetics and sedation drugs in infants and toddlers under three, and in pregnant women in their third trimester, because of the possible effect on the development of the child's brain. Of course, any decision has to be weighed against the risk of delaying or avoiding necessary surgery.

You are more vulnerable to delirium as you age if you have a pre-existing problem with memory or cognitive skills, have hearing or vision problems, are physically frail, have other underlying medical conditions, abuse alcohol and/or drugs, or if you have had a similar experience with previous anaesthetics.

The state of memory loss and confusion after an anaesthetic is called Postoperative Cognitive Dysfunction (POCD), or delirium.

In rare cases, this effect on brain function can persist for several months and, in some cases, for years after long anaesthetics for major surgery. This is more commonly seen in elderly patients, particularly after heart surgery, although up to 40 per cent of people are affected for one week after non-cardiac procedures. Up to 15 per cent of people continue to be affected after three months.

In my experience in general practice, the vast majority of people have no problem recovering from a general anaesthetic, but I have seen a number of patients whose cognitive skills have been affected for weeks or even months.

RECOGNISING POSTOPERATIVE COGNITIVE DYSFUNCTION (POCD)

Potential adverse effects of general anaesthesia include:

- delirium
- confusion
- dizziness
- memory problems
- impaired judgement
- blurry vision
- insomnia or reversal of usual sleep–wake cycle
- personality changes, becoming anxious, angry, paranoid or aggressive.

PREPARING YOUR BRAIN FOR AN ANAESTHETIC

As the awareness of the post-anaesthetic effect on the brain has grown, so have efforts to find ways to prevent it.

This introduces the concept of ‘prehabilitation’. Where rehabilitation is the plan for recovery after an illness or procedure, prehabilitation is about anticipating the physical and mental challenges of a surgical or medical intervention, and taking preventive steps to optimise your health and avoid some of the predictable adverse effects.

Many of the fundamentals of prehabilitation are reminiscent of the fundamentals of a healthy brain lifestyle. But if you are able to plan for an anaesthetic, there are some measures you can take:

- Make sure you are maintaining healthy nutrition (see chapter 24: Brain Food).
- Have blood tests to identify nutritional deficiencies (including iron studies, vitamin B12 and folate levels), correct diet and supplement where necessary.
- Review all current medication.
- Quit smoking and drinking alcohol.

- Exercise regularly within your capability. If your medical condition and the reason you are having a surgical procedure make it difficult for you to move around, an exercise physiologist can assess your capabilities and tailor an exercise program around what you can do.
- If you are having sleep problems, speak to your doctor about what you can do to get a better night's sleep (see chapter 28: Sleep).
- Have hearing and vision checks, and take hearing aids or prescription glasses with you to hospital.

AFTER THE ANAESTHETIC

- Have a medication review. It is possible that painkillers and other medications taken after surgery could exacerbate the effect of the anaesthetic on brain function.
- Get moving as soon as it is safe and medically advisable after surgery.
- Re-establish routines for nutrition and sleep as soon as possible.
- Make sure you have exposure to daylight.
- Minimise the use of narcotic analgesia.

CASE STUDY

Patrick was 78 when he visited his doctor, accompanied by his son. He was agitated and seemed confused, having trouble recalling names and events. His son Paul said the family was very concerned about him because he had previously been living independently, had a big group of friends and was involved in a busy schedule of activities. He had recently needed to have an orthopaedic procedure and was under anaesthetic for almost three hours. Patrick had spent some

weeks in rehabilitation to improve his strength and mobility after the surgery, but while the result of that was very successful, he had emerged from the anaesthetic very confused and now, several weeks later, he was having such difficulty managing his day-to-day life that his sons were considering moving him from the rehabilitation facility into permanent supervised residential aged care. He was having trouble getting to sleep because of anxiety, and he was waking frequently during the night. He was not able to do the morning crossword.

His doctor's personalised plan included these elements:

- a diet rich in vegetables and fish with other proteins
- supervised daily exercise with morning sunlight exposure
- gradual weaning off opioid painkillers
- an antidepressant medication at bedtime as a temporary measure to assist sleep, stabilise his mood and assist with pain management
- melatonin in the evening
- coenzyme Q10 supplement daily
- vitamin D supplement to address deficiency
- fish oil supplement for omega-3 essential fatty acids
- an extract of Bacopa (*Bacopa monnieri*) or brahmi (a herbal medicine used to enhance memory, recall and attention span)
- regular visits to an exercise physiologist.

Much to his family's relief, over the following months, his mental state improved, his anxiety settled, his sleep cycle was restored, and his motivation returned so that he was able to continue with his exercise program and return home. He gradually returned to his previously active social life.

RECOMMENDATIONS

- If elective surgery is recommended or planned for a child or toddler, or a pregnant woman, consider whether the surgery is necessary and whether it can reasonably be delayed without jeopardising the child's or the mother's health.
- If surgery is elective, plan a program of prehabilitation, starting at least a month before surgery.
- Minimise the use of narcotic analgesia or other medications likely to cause sedation.
- Avoid alcohol.
- After surgery, put the 'How to Keep Your Brain Young' plan into action (see Part 4 of this book).
- Seek expert healthcare advice about herbs and supplements.

9

Illicit Drugs and Your Brain

There is no question that illicit drugs have an effect on the physiology of your brain. We know that there are short-term effects, which are the very reason people use psychoactive drugs: to alter their brain's experience of reality. But what about the long-term effects of psychoactive drug use on brain health, once the immediate short-term effects have worn off?

Each drug will have different effects on different people. Some of these are expected and common, while others are less common and may be unexpected. Different people will experience different reactions to the same drug, because of their unique genetic code.

Of course, that's presuming you know what you have taken.

WHAT ARE YOU TAKING?

Illicit drugs are not standardised or regulated in the way that pharmaceutical preparations are. Not knowing what is in the pill or substance that you are planning to take means you may not be able to predict the effect it will have on your brain or

other parts of your body, either in the short term or the long term.

That is one of the reasons I became a strong supporter of pill-testing trials at music festivals, and the reason they have been backed by the Australian Medical Association and other medical groups. Pill testing has been shown to save lives.

There has been a lot of debate about the politics of pill testing at music festivals, following the deaths of a number of young people at festivals in the Australian summer of 2018–2019.

The debate has been reminiscent of the debate about heroin-injecting rooms and needle exchange programs decades ago. Young people were dying in the streets from overdoses and there was other collateral damage such as HIV and Hepatitis B and C infection. Back then, we heard the same arguments about legitimising drug use. From a medical point of view, however, it was about saving lives and removing some of the other health consequences of injecting drug use.

I looked into the operations and results of pill-testing trials at music festivals. One of the key things these trials revealed is that the pills people are buying often do not contain the drugs they think they are buying.

A UK pilot trial was undertaken with the aim of reducing drug-related harm. Test results revealed that one in five illicit substances was not as sold or acquired. People who bought the drugs on-site at the festival were more than twice as likely to have been sold something other than what they thought they were buying.

The advice that we give about illicit drugs and harm minimisation assumes that you know what you have taken or are planning to take. But in some cases, the substance is completely different to what the person thinks they are taking.

In other cases, there is a combination of known substances and dangerous substances, and variation in doses and fillers.

One of the first Australian trials in 2019 at the Groovin the Moo music festival in the ACT found that more than 230 festival-goers were reported to have used the pill-testing service, with seven substances found to contain the potentially lethal stimulant n-ethylpentylone. All but one of the people who were told their drugs contained the dangerous substance dumped them in amnesty bins provided by the pill-testing service, while one person said they planned to dump it. The testing is also accompanied by professional advice.

Different festivals have found different results, which only emphasises the unpredictability of illicit drug ingredients.

The other problem is dosage. One pill may contain far more of an active ingredient than another, meaning that the potential for overdose is greater.

The fundamental question I had to ask myself was whether pill-testing would entrench drug-taking culture at music festivals, or whether it would prevent death, brain damage or other serious health problems by giving people the information they needed to make an informed decision. In the end, I was guided by my concerns as a doctor and as a parent, convinced by the evidence that further trials would give us the answer to that question.

I have long held the view that harm minimisation is the way to go. A lot of people in government and in the community fantasise that if you just tell people to say ‘no’, and if you make penalties large enough, people won’t take illicit drugs. But that has never worked. We just need to be smart about this.

The top four illicit drugs used in Australia are cannabis, ecstasy, cocaine and methamphetamines. In this section of the

book, I will concentrate on what we know about these substances.

As we go through this list, bear in mind the findings of the various pill-testing trials mentioned above. Remember, you may not know what you have taken or its potential effects on your brain and other organs of your body. This should act as an extra precaution in thinking about your future brain health.

CANNABIS (MARIJUANA)

Cannabis is a drug that is derived from the *Cannabis sativa* plant.

Cannabis comes in different forms such as dried leaves and flowers of the plant and it can be smoked, eaten or vaporised.

According to the Australian Institute of Health and Welfare (AIHW), cannabis is the most widely used illicit psychoactive drug in Australia.

Some people use cannabis for its therapeutic or medicinal properties, while others use it recreationally for its effect on the brain.

Cannabis is used more frequently than other illicit drugs. Thirty-seven per cent of people who used cannabis did so as often as weekly or more, compared with only 6.7 per cent for ecstasy and 4.5 per cent for cocaine users.

Use of cannabis in the Australian general population increased significantly between 2016 (10.4 per cent) and 2019 (11.6 per cent). Some of that increase has likely been because the federal government legalised access to medicinal cannabis in 2016.

I have been looking at the issue of medicinal cannabis for many years. Back in 1996, I was working as the health reporter for the *Today Show* and I was sent over to California to look at the then proposed legalisation of medicinal cannabis

use. This was at the time of the HIV/AIDS epidemic, and cannabis was a lifeline for managing HIV wasting syndrome, for which there was no medical treatment available. I spoke to people with HIV, neurological disorders and chronic pain. I spoke to their doctors, to legislators and to researchers, and was absolutely convinced that medicinal cannabis could have an important place in our armamentarium. That was a quarter of a century ago.

So, technically speaking, because of the legalised access for medicinal use, cannabis may or may not be illicit depending on the context and reasons for its use. That position may also change with time as the laws concerning non-medicinal cannabis use are changed.

The difference between illicit and medicinal cannabis (apart from the legal framework and the business model) is that medicinal cannabis is not the whole plant, with all the variations of species and subtypes. It is produced and standardised in the way that pharmaceutical preparations are made.

There is evidence for cannabis being effective in treating a number of difficult conditions, including:

- cancer-related nausea, loss of appetite, weight loss and debilitation
- nausea and vomiting related to chemotherapy
- some forms of chronic pain, including nerve pain
- muscle spasms of multiple sclerosis.

Cannabis will not cure the underlying problem, but may help in managing the symptoms and reducing the reliance on other pharmaceutical medications.

The cannabis plant produces more than 70 identified cannabinoids and about 300 non-cannabinoid chemicals. The two main cannabinoids that have been found to have

therapeutic benefits are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). The main psychoactive component of the cannabis plant is THC. CBD moderates the psychoactive effect of THC.

Cannabinoid receptors exist throughout the brain, so cannabis use affects a diverse range of the brain's cognitive processes, including executive functioning, reward processing and memory.

For the purposes of this discussion about the impact of illicit drugs on brain health, we are going to focus on recreational use of cannabis (marijuana).

How cannabis is used

Cannabis is most commonly used by inhalation of smoke or vapour, in food, tea, capsules or a sublingual spray.

Smoking is the most popular method, and the smoke can damage your lungs and airways, and cause inflammation in your nose, throat and sinuses. In countries with medicinal cannabis programs, inhalation is recommended via a specific type of medical vaporiser.

The effects of cannabis use will vary depending on individual responses, any pre-existing medical or mental health conditions or predispositions, the amount and type of cannabis used, and the way it is taken.

Short-term effects of cannabis use

Cannabis alters normal brain communication by attaching to cannabinoid receptors on nerve cells in the brain and activating them, disrupting the normal function of the body's own neurotransmitters.

It is a central nervous system depressant, so it causes a sense of euphoria and relaxation and reduces inhibition. In

some cases, it can paradoxically and unpredictably cause confusion, panic and paranoia. Some people will experience dizziness, rapid heart rate, headaches and red eyes.

During use, THC decreases learning, attention and memory. It also alters sensory perception, with a distortion of time and intensification of ordinary experience. In larger doses, cannabis can trigger an episode of acute psychosis, to the point of hallucinations and delusions and a loss of personal identity.

THC disrupts functioning of the brain areas that regulate balance, posture, coordination and reaction time (the cerebellum and basal ganglia).

Cannabis is one of the most common drugs found in traffic accident deaths because of its effect on coordination and reaction times. According to the AIHW, cannabis was the second most common drug type identified at toxicology for traffic accident deaths in 2016.

THC also alters dopamine pathways. It can alter the functioning of the hippocampus and orbitofrontal cortex, brain areas that make it possible for you to form new memories and shift your focus of attention.

Long-term effects of cannabis use

Smoking causes long-term damage to the respiratory and cardiovascular system. Smoking cannabis brings with it some of the same risks as smoking tobacco, such as lung disease and lung cancer. If you have a medical recommendation to inhale cannabis, a vaporiser is the safer and more reliable method. In Australia, medicinal cannabis is tightly regulated. Approved products are mostly taken orally and are formulated so they have the greatest medical effect and the fewest possible side effects.

It is difficult to say exactly what long-term effects cannabis use has on brain health, because cannabis users frequently use other drugs as well, such as alcohol and pharmaceutical medications, meaning there could be some combination effects. There could also be underlying reasons why different people use cannabis for its short-term therapeutic effects, such as relieving a pre-existing anxiety condition or stimulating appetite.

That said, the published literature shows that chronic cannabis use does have long-term effects in some people, including dependence. Physical dependence is marked by withdrawal symptoms if you stop chronic use.

WITHDRAWAL EFFECTS

Cannabis is addictive, so if you use it at high doses regularly for weeks or months, physical dependence is a real possibility. This also means that if you stop using it, you can experience a withdrawal syndrome including several days of irritability, restlessness, sleeping problems, nausea, hot flushes and appetite disturbance.

There are several ways of assessing the effect of cannabis on the brain. One is by comparing brain structures. The other is to look at brain function.

Studies on the long-term effects of cannabis on brain structure are inconclusive. One study found that heavy, chronic users of cannabis have lower orbitofrontal cortex (OFC) grey matter volumes than people in the non-using control group. The OFC is situated at the base of the frontal lobe above the eye sockets and it is particularly involved in social behaviour and decision-making. Damage to the OFC can change the way you respond to emotions, which may contribute to impulsive and socially inappropriate behaviour and poor decision making. The study also found that brain changes depended on the age that cannabis use started, and the duration of use.

The question of the long-term effects of cannabis use on the developing brain of an adolescent has been the subject of some research.

Because the brain is in a constant state of development until at least the early twenties, the developing brain of a young person is going to be more vulnerable to positive or negative environmental effects than someone a few years older.

A study of adolescent cannabis users looked at verbal learning, verbal working memory, attention and vigilance, and time estimation. Participants completed a brief neuropsychological battery of tests on three occasions: after three days, two weeks and three weeks of stopping cannabis use.

They detected ‘poorer verbal learning and verbal working memory among adolescent marijuana users that improved during three weeks of abstinence, while attention deficits persisted’. This suggests a long-term effect of cannabis use on thinking ability, and the possibility that not all of the effect is reversible.

Early and regular cannabis use predicts an increased risk of cannabis addiction compared to people who don’t start using cannabis until later, as adults.

It is also reported that cannabis use at an early age can impair short-term memory, judgement and coordination.

There is an increased risk of chronic psychotic disorders including schizophrenia in people who have a predisposition to psychosis and who use cannabis.

Long-term cannabis use has a negative impact on both structure and function of the brain, and those effects are greater with an earlier starting age and with prolonged use of the drug.

COCAINE

Cocaine is a powerful stimulant that speeds up the activity of your brain. It is a white powder, usually snorted or sniffed into the nose, and is rapidly absorbed through the tissues lining the nasal passages. Sometimes it is injected or smoked (as 'crack'). Street cocaine is sometimes found to be mixed with impurities like powdered milk, baking powder or bleach.

AIHW data shows that cocaine use in Australia is most prevalent among those who are employed and who live in major cities or the highest socioeconomic areas.

Between 2016 and 2019, recent use of cocaine increased from 2.5 per cent to 4.2 per cent. However, 57 per cent of cocaine users said they used it only once or twice in the previous year.

Short-term effects of cocaine use

Cocaine has both desirable and undesirable effects. It is used for its immediate effects of increasing energy and alertness, a sense of exhilaration, self-confidence and sexual arousal.

On the negative side, it can also cause a racing heart, high blood pressure, fast breathing, sleeplessness, body overheating, and erratic and unpredictable behaviour.

The immediate high tends to last for about 30 minutes, followed by a low. It is then common for a user to repeat the dose to maintain the effect. Over a period of hours this can lead to unpredictable aggressive behaviour, hallucinations, paranoia, agitation, nausea and vomiting, and chest pain.

High doses of cocaine can cause heart complications, including constriction of coronary arteries and dangerous abnormal heart rhythms, and lead to a heart attack in a young, otherwise healthy person.

Noradrenaline is a neurotransmitter that is released from nerve cells in the sympathetic nervous system, responsible for the so-called fight or flight reactions. Its normal role is to prepare the brain and body for action under a perceived threat. Cocaine inhibits the reuptake of noradrenaline, causing the sympathetic nervous system to go into overdrive.

If you are planning a pregnancy and you are using cocaine, even occasionally, stop. Using cocaine during pregnancy may cause miscarriage, premature labour or stillbirth.

Long-term effects of cocaine use

Regular cocaine use has been shown to cause abnormalities in the blood vessels in the brain, causing complications such as haemorrhagic or thromboembolic strokes or cerebral haemorrhage (bleeding in the brain).

With repeated use of cocaine, tolerance increases, meaning it takes more and more cocaine to achieve the same effect. Tolerance to cocaine can develop quickly.

Repeated snorting damages the nasal lining and results in nose bleeds, loss of sense of smell, sinus infections and perforation of the tissues between the nostrils.

Patients I see who have run into problems with long-term use of cocaine usually present as ‘underweight, wired and tired’.

The withdrawal effect from cocaine can last for months, with difficulty concentrating, agitation, exhaustion, fatigue after exercise, loss of pleasure, sexual dysfunction, depression or anxiety, nightmares, increased appetite and craving for cocaine.

ECSTASY (MDMA)

Ecstasy is the street name of an illicit synthetic drug 3,4-methylenedioxy-methamphetamine (MDMA). It is usually taken in tablet or capsule form.

It is one of the most commonly used illicit drugs in Australia, with 3 per cent of people using it in the past 12 months according to the 2019 National Drug Strategy Household Survey, although about a half of people using it reported that they used it only once or twice a year.

The short-term effects of ecstasy on the brain kick in within 20 to 60 minutes of taking the drug. The feelings of emotional warmth, disproportionate empathy towards other people, elevated mood and sense of wellbeing or ‘ecstasy’ are the result of a huge surge in the levels of neurotransmitters serotonin and noradrenaline, and to a lesser extent dopamine.

The surge subsides and for days later there is a depletion of serotonin in the brain, which causes delayed after-effects. As the effect of ecstasy wears off, the user experiences the opposite to the acute effects of taking it, such as depression, insomnia, poor memory and attention, anxiety, aggression and irritability.

There are some acute adverse effects including light-headedness, hallucinations, panic attacks and long-term cognitive problems. Fatalities related to ecstasy are not common, but it is one of the drugs reported to cause dance party deaths. Potentially lethal adverse effects include raised blood pressure, increased body temperature, dehydration, loss of consciousness and seizures.

Taking ecstasy can also lead to brain swelling, overheating, dehydration and electrolyte imbalances. Additional doses can cause unpredictably high levels of the drug in the blood, which can increase the potential for organ damage.

One of the problems for people taking ecstasy, or what they think is ecstasy, is that they don't always know what they are buying, or the strength of the dose, because it is not standardised.

Without pill testing or any form of standardisation, it is impossible for people to know for sure what they are taking, whether a pill contains what they think it does or whether it contains potentially toxic substances or other drugs. However, MDMA can itself cause deaths, even if a person knows what they are taking. It is likely that some people are more susceptible to adverse effects than others and doses vary from batch to batch.

A study from the European Monitoring Centre on Drugs and Drug Addiction (EMCDDA) from April 2016 looked at the issue of dosage. The study states that:

> *… in the 1990s and 2000s the average MDMA content of tablets was somewhere between 50–80 mg, as reported by drug checking services and forensic institutes. Currently, however, the averages are closer to 125 mg MDMA per tablet, while there are also 'super pills' found on the market in some European countries with a reported range of 270–340 mg. There are reports of large variations in the dosage in similar looking tablets*.

The unpredictable dosing obviously amplifies the danger of overdose, brain damage and accidental death.

That is the acute danger. Then there are the longer-term issues for brain health. Research tells us that continued use of MDMA can cause damage to serotonin-containing brain cells, which can result in long-term damage.

PET scanning shows lasting effects in several parts of the brain, including the amygdala and hippocampus, as well as the prefrontal and parietal cortex and medio-temporal areas of the

brain. This can be experienced as impaired memory, depression, anxiety, confusion, paranoia, impulsivity, sleep disturbance and difficulty with attention.

METHAMPHETAMINE (‘Crystal Meth’, ‘Ice’)

Methamphetamine or ‘ice’ is a highly addictive illegal street drug with serious consequences, both for brain health and for the community.

The drug can be smoked in a pipe, sniffed, injected intravenously or swallowed. Methamphetamine is considered to be the drug of most serious concern to the general community.

In 2019 1.3 per cent of people aged 14 and over in Australia reported using methamphetamine. Sixty-five per cent of people going to prison in 2018 reported using illicit drugs in the 12 months before being imprisoned, with the most common being methamphetamine (43 per cent). Those numbers alone show the impact of the drug on the community.

Methamphetamine causes an initial sense of euphoria, confidence and loss of inhibition because it briefly and dramatically increases dopamine in the brain. The effect wears off, which encourages the user to take more to regain the effect, and then more, leading to overdose or addiction.

Methamphetamine use has a strong association with mental illness. People who already have a mental illness and who use methamphetamine long term will be at greater risk of brain damage related to abuse of the drug than people who have no previous mental health problems or who use it less intensely or over a shorter period of time.

Meth dependence causes a marked reduction in the brain’s grey matter volume in multiple areas of the brain, due to damage and destruction of brain cells. Once destroyed, the lost neurons usually cannot be recovered. The effects are serious,

with damage to a range of abilities and brain functions, including:

- impaired attention, focus and concentration (damage to the frontal and prefrontal cortex)
- impaired judgement, impulse control and problem-solving
- increased susceptibility to psychiatric conditions
- delusions and hallucinations
- mood swings, depression
- aggression, hostility, violence, irritability
- impaired memory
- possible impairment of reaction times and coordination and you might observe erratic and jerky movements and tics.

There has been a rapid increase in the number of deaths involving methamphetamine and other stimulants, with the death rate in 2019 four times higher than that in 2000 (two deaths compared with 0.5 deaths per 100,000 population, respectively).

In addition, long-term methamphetamine use causes gums and teeth to rot. It also causes pimples and sores on the skin that the person picks at and that are difficult to heal.

It really doesn't have a lot going for it.

RECOMMENDATION

Illicit drugs are treacherous territory for brain health. While people will think they are 'getting away with it', maybe for years, there is the potential for unexpected ingredients and unexpected adverse events, including brain damage and death.

In the long term, the use of illicit drugs can cause structural and physiological changes to your brain that can result in problems with mental health and thinking ability, as

well as causing personality changes. There is no room for negotiation with an illicit substance. It will either cause immediate or long-term harm or it won't.

Your brain health now and into the future is a crucial part of the decision-making process for each individual. You are the only one who can decide if it is worth the risk.

10

Gluten Brain

Most people who eat a sandwich or a croissant, a cake or a bowl of cereal containing gluten will have no problem with it. But people with coeliac disease or non-coeliac gluten sensitivity certainly will.

Gluten is a protein that is found in a number of grains, notably wheat, rye, triticale and barley. It is also present in many packaged or processed foods as a thickener or food additive.

Exposure to gluten in a gluten-sensitive person can lead to gut symptoms such as bloating, abdominal pain, diarrhoea and/or constipation.

The diagnosis of coeliac disease is confirmed by testing blood for a number of different antibodies, including anti-endomysial antibodies (EMA), anti-tissue transglutaminase antibodies (tTG), and anti-gliadin antibodies (AGA), and then direct biopsies from the tissues of the small intestine.

Non-coeliac gluten sensitivity (NCGS) is a syndrome diagnosed in patients with symptoms that respond to the removal of gluten from their diet, after investigations have ruled out coeliac disease and wheat allergy.

In addition to the well-described gut symptoms of coeliac disease and gluten intolerance and the symptoms of gluten allergy, gluten can also have an effect on the brain and nervous system in some people. These effects include headache and brain fog. We also see problems with memory, attention and cognitive function resulting from gluten ingestion in people with untreated coeliac disease or who are affected by gluten sensitivity.

Iron deficiency is a common complication and can explain some of the apparent behavioural manifestations, such as lethargy and apathy.

More serious neurological consequences of gluten ingestion in people with coeliac disease or gluten sensitivity include gluten ataxia, peripheral neuropathy, seizures, and apparent cognitive impairment, mood disorders, other psychiatric disorders and behavioural problems.

‘BRAIN FOG’

Many people report experiencing ‘brain fog’, a transient blunting or slowing of their ability to think, concentrate, make decisions or perform academically, if they are exposed to gluten. This condition is also called gluten-induced cognitive impairment.

Long term, this can be misinterpreted as depression, or raise concerns about the onset of dementia, particularly in older people.

In people who are diagnosed with coeliac disease and who suffer from brain fog, improvement occurs gradually over a year once they have been diagnosed and are on a strict gluten-free diet. For someone who is already on a gluten-free diet, it can take at least several days after an accidental exposure to gluten before you feel that you are thinking clearly again.

The primary cognitive domain affected appears to be the speed of processing. The most likely cause is an increase in circulating cytokines associated with generalised inflammation, resulting in inflammation of parts of neurons in the brain.

GLUTEN ATAXIA

Ataxia is a movement disorder that can cause difficulty with coordination, dexterity and gait, and may cause slurred speech. Gluten ataxia is an immune-mediated disorder that may happen when a person with coeliac disease or gluten sensitivity is exposed to gluten in food, and antibodies to gluten attack the cerebellum in the back part of the brain.

I have seen a case of sporadic ataxia in a person with coeliac disease who was not strictly observing a gluten-free diet. The man had developed writhing movement of his hands. He became unable to do up the buttons on his shirts and he was having difficulty with balance.

His gliadin antibodies were elevated, reflecting his lack of commitment to avoiding foods containing gluten. We removed all sources of gluten from his diet, and after some months the ataxia resolved and did not return, as he remained on a gluten-free diet.

This experience reflects the findings of a research study into this condition, which showed that after one year there was improvement in ataxia in people who adhere to their gluten-free diet.

GLUTEN AND CHILD BEHAVIOUR

Children with gluten sensitivity or untreated coeliac disease can appear to have behavioural problems. This presents some significant challenges for the child, and also for the parent, carer or teacher trying to manage their behaviour. They might

be lethargic, refuse to eat, be unable to settle into a task, have difficulty in the classroom and refuse to follow instructions.

There is also a variety of gluten-associated neurological disorders that we might see in children with untreated coeliac disease and non-coeliac gluten sensitivity. These include chronic headache, developmental delay, hypotonia, poor attention span, learning difficulties and ADHD-like symptoms. There has also been a case report of psychosis diagnosed in a child, which I will describe on the next page.

Studies show that ADHD-like symptoms are markedly overrepresented among people with untreated coeliac disease, and that a gluten-free diet may improve symptoms significantly within a short period of time. This means, of course, that a child who shows symptoms of ADHD-like behaviour should be tested for coeliac disease and trialled on a gluten-free diet as part of their initial assessment.

It is important to note that coeliac disease and non-coeliac gluten sensitivity can begin to manifest at any age, not just in childhood. That means we need to be alert to the possibility of a gluten effect on the brain when any new symptoms present at any age.

ADOLESCENTS

Untreated coeliac disease in adolescents has been associated with an increased prevalence of depressive and disruptive behavioural disorders. One study in Finland in 2005 found a significant decrease in psychiatric symptoms at three months on a gluten-free diet compared to their baseline condition, coinciding with significantly decreased coeliac disease activity.

The researchers concluded that ‘serotonergic dysfunction due to impaired availability of tryptophan may play a role in

vulnerability to depressive and behavioural disorders among adolescents with untreated coeliac disease'.

GLUTEN AND PSYCHIATRIC SYMPTOMS

Several psychiatric manifestations can be seen with gluten exposure in people who are vulnerable to its effects. These include an increased association with anxiety, social phobias and panic disorder.

Depression and mood disorders are also associated with coeliac disease and gluten sensitivity with improvement after introducing a gluten-free diet.

Schizophrenia in children with coeliac disease has been documented as long ago as 1953 and studies showed that gluten-free diets accelerated recovery.

There was a case report of psychosis triggered by gluten exposure in a 14-year-old girl. She was admitted to a psychiatric ward experiencing apathy, self-neglect and hallucinations. She improved in hospital, but did not return to normal. Four months later she presented with crying spells, confusion, ataxia, severe anxiety and paranoid delirium after eating pasta. She also had gut symptoms, and tests excluded coeliac disease. She was treated with anti-psychotic medication.

More than a year later a nutritionist trialled her on a gluten-free diet. Her symptoms completely resolved within a week, and she was able to cease anti-psychotic medication, with her behaviour and personality returning to normal.

THE CAUSES OF GLUTEN'S EFFECT ON THE BRAIN

Medical research offers a number of suggested causes for the effects of gluten on the brain, including some gluten-mediated

immune response, nutritional deficiencies, elevation of circulating cytokine levels due to systemic inflammation, and low brain serotonin levels.

The interaction of a leaky gut with the brain has also been postulated. However, the definitive cause or causes for the effect of gluten exposure on the brain remain elusive.

The medical literature describes cases of cerebral blood flow abnormalities in people with untreated coeliac disease. In a 2004 study, regional cerebral perfusion (blood flow) was assessed using a scanning technique called single photon emission computed tomography (SPECT) in untreated coeliac patients, comparing them with coeliac patients on a gluten-free diet and with healthy patients. The study showed the reduction of regional blood flow in the brains of 73 per cent of the untreated coeliac patients, compared with only 7 per cent of Crohn's disease patients on a gluten-free diet. The effect was not seen in any of the people who did not have coeliac disease.

Considering each single region, significantly lower cerebral perfusion was found in untreated coeliac patients compared to controls in 7 of the 26 brain regions evaluated. There were no significant differences in cerebral perfusion between untreated patients and those on gluten-free diets, or between patients on gluten-free diets and healthy people in the control group, reflecting a beneficial effect of a gluten-free diet.

Similar cerebral blood flow changes have been reported in patients suffering from different psychiatric disorders.

A previous paper reported a case of brain perfusion abnormalities, assessed by SPECT examination, in a coeliac patient with schizophrenia; the relief of both cerebral hypoperfusion and schizophrenic symptoms was observed after six months of a gluten-free diet. Psychiatric and/or neurological disorders in people with coeliac disease could be

related, in part, to changes in blood-flow patterns in the brain. These blood-flow changes seem to be linked to coeliac disease activity, and they resolve after a gluten-free diet.

What is clear is that both coeliac disease and non-coeliac gluten sensitivity can affect the body and the brain in many ways. A strict gluten-free diet should be introduced as soon as either condition is suspected and, if confirmed, should be continued for life.

11

Glucose

Given how common insulin resistance, impaired glucose tolerance and type 2 diabetes are in the community, it is important to look at how blood glucose relates to brain health. High blood glucose and insulin resistance-associated conditions are well-recognised risk factors for cognitive impairment, with diabetes increasing the risk of vascular and Alzheimer's-type dementia.

Your body relies on the hormone insulin, produced in your pancreas, to transport glucose into body cells, where it provides the energy you need for all of your body's functions. The insulin sends a message for glucose to enter the cells to provide them with the fuel they need. Insulin regulates expression of the neurotransmitters acetylcholine and norepinephrine, both of which are known to influence cognition. Insulin may also increase glucose metabolism in brain regions important for learning and memory. Insulin resistance is when cells resist or are unable to receive this message. The pancreas responds by making more insulin to keep blood glucose levels in the normal range.

If your blood glucose level is higher than normal, but not high enough for a definitive diagnosis of diabetes, the next step is to arrange what we call an oral glucose tolerance test

(or OGTT). This is to see how your body deals with the glucose load over time, taking place over two hours.

If your glucose level is elevated after two hours (but not high enough to be in the diabetes range), then you fit the criteria for impaired glucose tolerance, which suggests that your body does not process glucose effectively.

Impaired glucose tolerance does not mean you have diabetes, but it is considered a warning sign. That's why it was previously known by the term pre-diabetes – impaired glucose tolerance means that, unless you make some changes, you have a much higher risk of developing type 2 diabetes.

As GPs, we monitor some patients closely for impaired glucose tolerance. These include women with polycystic ovarian syndrome or a history of gestational diabetes, patients who are overweight, have a family history of diabetes or heart disease, and people with a sedentary lifestyle.

HIGH OR LOW? EFFECTS OF BLOOD GLUCOSE ON THE BRAIN

Glucose is the energy supply to all tissues of the body. Low blood glucose is referred to as hypoglycemia. This means there is insufficient glucose supplying energy to the brain to perform its complex functions.

You can suffer the effects of hypoglycaemia if you are taking too much oral medication or insulin to lower blood glucose, or if you eat less than usual or exercise more than usual after taking diabetes medication. If you do not have diabetes, blood glucose can drop if your body produces too much insulin after you eat.

The symptoms of hypoglycaemia reflect the body's organs, including the brain, being starved of energy, and include muscle weakness, fatigue, dizziness, blurred vision, difficulty

concentrating, confusion and strange behaviour (sometimes mistaken for drunkenness). In extreme cases, hypoglycaemia can lead to loss of consciousness and coma and, if untreated, can be fatal. This is why it is so important for people with diabetes to wear an identifying bracelet so that first responders know what to do if they find you unconscious or unable to tell them what the problem is.

Hyperglycemia or high blood glucose is the opposite of hypoglycaemia. It means elevated blood sugar levels, and is a feature of suboptimal control of diabetes.

We know that higher fasting blood glucose over time is associated with cognitive impairment and cerebral atrophy (shrinkage).

A 2012 study found that even mildly elevated plasma glucose levels were associated with atrophy of the hippocampus and amygdala, both parts of the brain that are relevant to ageing and neurodegenerative processes, and accounted for 6–10 per cent of volume reduction.

Even plasma glucose levels in the high normal range of millimoles per litre (<6.1 mmol/L) were associated with greater atrophy of these parts of the brain.

Type 2 diabetes is associated with approximately a 1.5- to 2.5-fold increase in the risk of dementia. A large community-based prospective cohort study followed patients over a 20-year period and found that diabetes in midlife was associated with a 19 per cent greater cognitive decline over that period.

In chapter 28: Sleep we will look at the relationship between obstructive sleep apnoea (OSA) and cognitive impairment. There is also an intersection of sleep apnoea and abnormal glucose metabolism.

In women with obstructive sleep apnoea, insulin is an indicator for the possible development of cognitive

impairment. Greater cognitive declines were observed in people with greater increases in insulin resistance.

It is estimated that 15–30 per cent of people with obstructive sleep apnoea have insulin resistance or type 2 diabetes mellitus, and treatment of their sleep apnoea improves their glucose metabolism. This suggests that the cognitive impairment we see in OSA could be, at least in part, caused by insulin resistance.

It is well established that diabetes brings an increased risk of cardiovascular disease, which suggests that the cognitive effects of abnormal blood glucose could also be due to the effect on the blood vessels in the brain.

It is also believed that insulin has a role in regulating neurons in the central nervous system and affects beta-amyloid metabolism, which accelerates Alzheimer-related pathology.

I will explain more about the role of beta-amyloid in Alzheimer's disease later in the book when I am discussing the various forms of dementia. In brief, beta-amyloid is a naturally occurring peptide (a short string of amino acids, the building blocks of protein). It accumulates around the outside of neurons in the brain, triggering a sequence of abnormal reactions: the 'amyloid cascade' that interrupts the connections between neurons, ultimately leading to the destruction of neurons in parts of the brain.

So what is the role of insulin in brain health?

Increasingly, the role of impaired clearance of beta-amyloid from around neurons, rather than the actual increased production of beta-amyloid per se, has been recognised as a key factor in the development of Alzheimer's disease. Insulin has significant effects in the so-called amyloid cascade. It is thought that low levels of insulin in the brain may interfere with amyloid clearance.

Insulin is also thought to play a role in inhibiting the formation of a protein called tau that forms what we call neurofibrillary tangles, and which are also involved in the damage leading to Alzheimer's disease.

In addition to these effects, insulin resistance is associated with oxidative stress, inflammation and impaired neurogenesis (the formation of new neurons).

There is a link between diabetes and depression and anxiety. People with depression have a higher chance of developing type 2 diabetes, estimated to be around double the average risk. Depression may develop because of stress or the burden of treatment, but also may result from the metabolic effects of diabetes on the brain. Changes in the brain which are structural, functional or neurochemical may all increase the risk of depression in people with diabetes.

All of this evidence means it is vital to diagnose insulin resistance and diabetes at the earliest possible stage, and to make lifestyle changes such as weight loss, nutrition and exercise to bring blood glucose levels down. This is important at any age, but takes on an added urgency in midlife, to protect against cognitive decline in later life.

What do you do if you are at risk of abnormal glucose metabolism or you have been diagnosed with a glucose problem?

The importance of finding out that you have impaired glucose tolerance is that you know you are at risk of cognitive decline and cardiovascular disease, so it is time to act. Lifestyle changes are the most important.

- If you are overweight, find out your healthy weight range and take steps to lose weight.
- Assess your diet. Eat more plant-based and high-fibre foods and less fat and high-kilojoule foods. Try to eliminate processed foods and drinks with high sugar

content. There is also evidence that eating only in a restricted eight-hour window during the day (the 16:8 diet) helps with glucose metabolism. This is a form of intermittent fasting.

- Exercise at a moderate intensity every day for at least 30 minutes. We know that the combination of diet improvement and exercise is the most effective way to improve glucose metabolism and reduce the risk of developing type 2 diabetes.
- If you are a smoker, stop – smoking puts you at higher risk of heart disease or stroke.
- Your doctor will discuss whether medication called metformin, taken in conjunction with lifestyle measures, will help to delay or prevent diabetes. Metformin works by reducing the amount of glucose released from the liver into the bloodstream and allows the body's cells to better respond to blood glucose levels.
- You may need to be referred to a psychologist to help you with stress management or coping skills strategies. Other activities such as mindfulness, tai chi or changing exercise routines and correcting sleep difficulties may also help.

DIABETES MEDICATION REDUCES DEMENTIA RISK

A new research study, conducted over six years in the Sydney Memory and Ageing Study in 1037 Australians (aged 70 to 90 years old at baseline), has revealed that individuals with type 2 diabetes who used metformin experienced slower cognitive decline with lower dementia rates than those who did not use the medication.

According to Sydney's Garvan Institute of Medical Research, people with type 2 diabetes have a 60 per cent risk of developing dementia.

In people in the study with type 2 diabetes who were taking metformin, there was no difference in the rate of decline in cognitive function over six years compared to those without diabetes.

We do not know whether metformin is helpful in people with normal glucose metabolism.

If you have type 1 or type 2 diabetes, lifestyle measures such as diet and exercise are still central to stabilising blood glucose levels. If you are taking medication, either oral glucose-lowering agents or insulin injections or a combination of both, expert guidance is needed to monitor and stabilise your blood glucose levels.

Careful monitoring and management of blood glucose control is essential to your future brain health.

12

Smoking and Your Brain

You would have to have been living in a cave on a deserted island without internet access to miss the point that there are no long-term health benefits of smoking tobacco. The toxic effect smoking has on the heart, lungs and blood vessels is now common knowledge.

Your brain doesn't escape the toxic effects of smoking either.

If you are a smoker, you need to think about the long-term implications on your brain health and what that might mean for your future.

Nicotine inhaled into your lungs is absorbed rapidly into the bloodstream. It increases blood pressure and pulse rate and constricts your arteries.

Once in the bloodstream, nicotine reaches the brain in seconds, where it activates 'feelgood' dopamine receptors. It also mimics the neurotransmitter acetylcholine. In the short term, nicotine has been shown to increase arousal and attentiveness, lift working memory and improve reaction time. Nicotine can improve mood and relieve anxiety, decrease appetite, and under certain conditions can be neuroprotective.

Because of the positive short-term effects of nicotine on cognition and mood, it also means nicotine is highly addictive.

We need to see these positive effects of nicotine in balance with the health problems caused by smoking and by nicotine itself.

Nicotine also suppresses the immune system by increasing cortisol levels, reducing antibody formation in B cells and reducing T-cell activity. B cells and T cells are types of blood cells called lymphocytes, and they are responsible for identifying and neutralising threats on the body from attacks, for example from bacteria and viruses.

This applies to nicotine from smoking or vaping with e-cigarettes. We are going to need to focus a lot of research attention on the effects of nicotine use and addiction on the adolescent brain. After years of successful campaigns to reduce the rates of teenage smoking, we are now seeing a rapid rise in teenagers becoming addicted to vaping, reversing the trend of declining nicotine use. In 2015, the US Surgeon-General reported that e-cigarette use among high school students had increased by 900 per cent from 2011 to 2015, and 40 per cent of young e-cigarette users had never smoked regular tobacco. Concerningly, a 2018 National Academy of Sciences, Engineering and Medicine report concluded that there was moderate evidence that e-cigarette use increases the frequency and intensity of cigarette smoking in the future. According to the US Surgeon-General, 'Youth and young adults are also uniquely at risk for long-term, long-lasting effects of exposing their developing brains to nicotine. These risks include nicotine addiction, mood disorders, and permanent lowering of impulse control. Nicotine also changes the way synapses are formed, which can harm the parts of the brain that control attention and learning.'

It's not just about nicotine though. Nicotine is just one of many chemicals in tobacco smoke, many of them toxic and

dangerous to your health.

You don’t have to be a smoker yourself for cigarette smoke to have a damaging effect on the brain. Exposure to cigarette smoke in the environment can affect brain function from an early age. A study of children aged between 6 and 16 years tested their serum cotinine levels. This is a biomarker, or a way of testing for exposure to tobacco smoke. Their intelligence and academic abilities were also tested. The results showed that children who had been exposed to even low levels of tobacco smoke in their environment had cognitive deficits in areas such as reading and mathematics.

Smoking during adolescence, when the brain has not finished maturing, increases the risk of developing psychiatric disorders and cognitive impairment in later life. Adolescent smokers also suffer from attention deficits, which worsen with the length of time someone has been smoking, making it harder to concentrate and to learn and lowering impulse control. Adolescents are also more vulnerable to addiction than adults.

Smokers experience more rapid cognitive decline than non-smokers and current smokers are 30 per cent more likely to develop dementia.

There are many possible ways that smoking can harm your brain in the longer term, including inflammation, oxidative stress and atherosclerosis.

Atherosclerosis is a build-up of plaque causing thickening and hardening in the blood vessels in the brain. The main risk factor for atherosclerosis is smoking, along with hypertension and high cholesterol. If the plaque obstructs blood flow in a blood vessel, this keeps blood from reaching the area of the brain supplied by that blood vessel (causing ischaemia or lack of oxygen). If a tiny bulge or aneurysm forms and ruptures

(causing bleeding into brain tissue), this damages those sections of brain – this is also known as a stroke.

The damage caused by cerebral atherosclerosis can sneak up over time, with many micro-haemorrhages and minor subclinical strokes building up, eventually, to vascular dementia with cognitive loss such as changes in personality, agitation, apathy, depression, difficulty with organising or planning, and memory loss.

Cigarette smoking can also cause oxidative stress, which creates inflammation, which in turn causes nerve cell damage.

The antioxidant defence system depends on the presence of a range of antioxidant micronutrients. A study found that, compared with non-smokers, on average, active smokers have more than 25 per cent lower circulating concentrations of the antioxidants ascorbic acid (vitamin C), alpha-carotene and beta-carotene (precursors to vitamin A), and cryptoxanthin.

According to the study, even in former smokers, average circulating concentrations of alpha-carotene, beta-carotene and cryptoxanthin were found to be 16–22 per cent lower than in people who had never been smokers.

This provides just a small insight into the complex mechanisms underpinning the role of inflammation in the damage caused to the brain by smoking.

IS VAPING RISK FREE?

Swedish research showed for the first time that e-cigarettes with nicotine cause a stiffening of the arteries, increased blood pressure and heart rate within 30 minutes. This raises the possibility that chronic exposure to e-cigarettes with nicotine may cause permanent effects on arterial stiffness in the long term, increasing the risk of heart attacks and strokes in later life compared to people who are nicotine-free. The Centers for Disease Control and Prevention website has lots of extra great information on this.

MEDICINAL NICOTINE

There is a pharmaceutical form of nicotine used in nicotine replacement therapy (NRT) to help people quit smoking. It is worth looking separately at the effects of NRT versus the effects of smoking tobacco.

Medicinal nicotine is used for harm minimisation, reducing the harm caused by the many toxic chemicals in tobacco smoke and managing the addiction by providing a dose of the addictive component, nicotine, in a pharmaceutical form.

Medicinal nicotine is available as skin patches, chewing gum, nasal sprays, oral sprays, inhalers, lozenges and tablets that deliver nicotine through the body to the brain.

The aim is to use medicinal nicotine to reduce the urge to smoke, then use behaviour therapies to gradually reduce the dose of nicotine over time and eventually stop. Because of the addictive nature of nicotine, it is not uncommon for people to become addicted to medicinal nicotine instead of cigarettes and we are seeing this same effect in the rise of vaping among young people. Advocates of medicinal nicotine justify this as doing less harm than smoking. There are two questions here that need to be answered.

Firstly, is medicinal nicotine a better option for your brain health than smoking? Secondly, does using medicinal nicotine have long-term consequences for your brain health? This second question is important, given the addictive nature of nicotine.

Regarding the first question, the short answer is yes. If you have tried unsuccessfully to stop smoking cold turkey, or by gradually reducing the number of cigarettes smoked, you may need the assistance of medicinal nicotine. Nicotine in pharmaceutical form is far safer than smoking a cigarette,

which contains hundreds of other chemicals. However, it is not risk-free.

There are a number of long-term effects of medicinal nicotine. I have already mentioned dependence or addiction, and the effect of nicotine on the immune system. Aside from this, there is evidence that pure nicotine has an effect on the cardiovascular system. Nicotine can also increase blood pressure, cause blood vessels to constrict and increase blood sugar levels, although I would reiterate that it is a lower risk to cardiovascular health than smoking.

So, switching to medicinal nicotine does not eliminate the increased risk of heart disease over non-pharmacological methods of quitting.

The overall success rate of those who quit smoking with medicinal nicotine is higher than those who attempt it without medicinal nicotine because it helps to relieve withdrawal symptoms and cravings, but overall it is still not high, and there is also the potential for addiction to the medicinal nicotine. The success rate for quitting increases with psychological strategies to help overcome dependence.

The use of medicinal nicotine is not recommended in pregnant women, children, teens or young adults.

How do you make a decision? If you want to keep your brain young, I'd suggest the following:

- Don't smoke.
- If you do smoke, quit.
- If you cannot go cold turkey, try cutting down gradually with behaviour therapies to aid quitting.
- If you cannot quit without more help, look into medicinal nicotine with counselling.

- If you use medicinal nicotine, make a plan for reducing over time to zero.
- Don’t start vaping.

13

Brain, Blood Vessels and Blood Pressure

High blood pressure is one of the most important risk factors for heart disease and kidney disease.

It is well known that hypertension (high blood pressure) also has a profound impact on your brain health, affecting brain structure and function.

Hypertension in midlife increases the risk of cognitive decline, vascular dementia and Alzheimer's disease, so knowing your blood pressure by checking it regularly and keeping it in the healthy range is essential to ensuring your brain is functioning at its best.

STROKE

The most immediate effect of high blood pressure on the brain comes in the form of a stroke. There are two types of stroke: ischaemic and haemorrhagic.

'Ischaemic' means a loss of blood flow to an area of brain tissue. Ischaemic strokes are by far the most common type. They can happen when a blood vessel supplying blood to a part of the brain becomes blocked by a blood clot. The clot can

form in a diseased blood vessel in the brain, or it can travel from a clot formed elsewhere, such as the carotid artery or inside the heart. A clot inside the heart may be the result of an abnormal rhythm of the heart called atrial fibrillation.

'Haemorrhagic' means a bleed into brain tissue from a ruptured blood vessel. A large bleed into the brain or just outside the brain can cause the features of a stroke. The deficit in brain function depends on the size of the haemorrhage and its location in the brain.

MICROBLEEDS

Multiple tiny bleeds are called 'microbleeds', and are thought to be caused by pathological changes in cerebral small vessels. Disease in these small blood vessels in your brain can be either ischaemic or haemorrhagic.

Repeated microbleeds cause damage that can build up over time. Microbleeds are very important in the context of cognitive impairment and Alzheimer's disease.

MICROBLEEDS AND DEMENTIA

In a study known as the Rotterdam Study, MRI brain scan results showed a high microbleed count to be associated with an increased risk of cognitive deterioration and dementia. This means that microbleeds are likely to be markers of damage to the small blood vessels of the brain, and the presence of a high microbleed count is associated with an increased risk of dementia.

It is worth looking more closely at the results of this study:

- Study participants had a mean age of 59.6 years.
- Microbleed prevalence was 15.3 per cent.
- The presence of more than four microbleeds was associated with cognitive decline.
- Lobar (with or without cerebellar) microbleeds were associated with a decline in executive function, information processing and memory function.
- Microbleeds in other brain regions were associated with a decline in information processing and motor skills.

- The presence of microbleeds was associated with an increased risk of dementia, including the dementia of Alzheimer's disease, after adjustment for age, sex and educational level.

With the increasing availability of imaging techniques like MRI, we have found that cerebral microbleeds (CMB) are common in healthy individuals and become more common with ageing, but they are known to precede ischaemic and haemorrhagic stroke and dementia.

The most important factor in prevention of stroke and progression of microbleeds is careful management of hypertension and vascular health. Measuring your blood pressure is an important feature of a medical check-up.

I make sure I check my patients' blood pressure at least once a year to ensure we detect any persistent elevation in blood pressure as early as possible. High blood pressure is much more than a couple of numbers. More often than not, though, it comes as a surprise.

Patients are often surprised when their blood pressure readings are high because they have no symptoms. In many ways, of course, it's a good thing to have no apparent symptoms from hypertension. But the problem is that if you feel okay, there is not the same motivation to make changes to your lifestyle or to take long-term medication. The longer term and serious consequences of high blood pressure need to be understood so that the importance of taking action is made clear.

Sometimes, on questioning, patients with newly diagnosed hypertension will admit to a low-grade headache. Sometimes women going through perimenopause or menopause will mistake the flushing from hypertension for hormonal hot flushes.

Your blood pressure can fluctuate across the day and night in response to physical exertion, sleep and emotional stress. It

can increase with some medications (particularly non-steroidal anti-inflammatory drugs) and with drinking alcohol.

A single elevated blood pressure reading will not trigger a diagnosis of hypertension or have your doctor prescribing medication, unless that reading is dangerously high. However, it is a signal to pay attention to your blood pressure. This may mean having you check your own blood pressure at home under different circumstances and at different times.

Your doctor may request a 24-hour ambulatory blood pressure reading. This involves wearing a blood pressure cuff and electronically recording your blood pressure every 15 minutes for 24 hours. This way we can see what your blood pressure is like at different times of the day and night, awake and asleep and with your usual activities.

If your blood pressure is persistently elevated, or has significant spikes of systolic pressure (the higher number on a blood pressure reading), then you will need to get it under control.

Treating high blood pressure reduces the risk of stroke. It also reduces the risk of memory loss of mild cognitive impairment, vascular dementia, and even Alzheimer's disease.

Depending on the severity, treatment of hypertension may be achieved with or without medication. If your hypertension is mild to moderate in severity, you may be able to treat it initially with lifestyle measures. I have seen many patients get their blood pressure under control by committing to lifestyle improvements. You might also be advised to start medication while you get the recommended lifestyle changes underway.

The lifestyle changes that really work to reduce high blood pressure are:

- Determining your healthy weight range for your height, and if you are overweight or obese, reduce your weight until you are in that range.

- Increasing the plant-based foods (fruit, vegetables and wholegrains) in your diet.
- Reducing animal fats and increase fish in your diet.
- Reducing processed foods.
- Reducing salt in your diet. Don't add salt to your cooking, and check the sodium content in packaged or processed foods to avoid hidden salts.
- Quitting smoking.
- Reducing alcohol to a maximum of one to two standard drinks a day.
- Exercising regularly.
- Checking any medications you are taking to see if they might cause an increase in blood pressure.
- Managing stress.

Even if you are taking medication you will still need to make these lifestyle changes.

If you are prescribed medication, you will need to monitor your response. We most often do this with a home blood pressure monitor, so you can measure your own blood pressure in real life.

Some people with a genetic predisposition or underlying reason for hypertension, and anyone who has had a stroke, may need to continue taking medication. However, as your lifestyle measures take effect, you may be able to reduce the dose or even cease medication.

Getting your blood pressure under control will help you to keep your brain young.

Resource:

Aronow WS. 'Hypertension and cognitive impairment'. *Annals of translational medicine*, vol. 5, no. 12, 2017; p. 259.

14

Menopause Brain

If you are a woman in your forties or fifties, you may at times have found yourself standing in a room wondering why on earth you are there, or forgotten the names of people you know well, or started a sentence and forgotten what it was that you needed to say. A lot of women worry that these are early signs of dementia.

If these experiences coincide with changes in your hormone levels and maybe a few (or many) hot flushes, they are far more likely to be signs of menopause than the onset of dementia.

Menopause brain is not ‘all in your mind’. The physical and emotional symptoms related to the changes in your hormone levels are very real, and can be debilitating.

Women approaching menopause are in the phase we call ‘peri-menopause’. The experience of menopause is individual for each woman. Some women do not notice any changes, while others can be severely affected by hot flushes. Some women are irritable and have difficulties with mood or concentration, while others are predominantly affected by sleep disturbance.

The early signs that you may be in peri-menopause usually relate to the onset of hot flushes, menstrual periods becoming irregular, and mood changes like irritability and a short-temperedness.

Periods can become heavier or lighter, more frequent or less frequent. Peri-menopause can also be a time when your memory and thinking start to be affected by hormone disturbances.

You have ‘officially’ entered menopause when you have not had a period for 12 months. You can have a blood test to check your hormone levels. If you are in menopause, these will show low oestradiol and progesterone levels, and an elevated follicle stimulating hormone (FSH).

Menopause often coincides with other significant life events, such as adult children leaving home, the arrival of grandchildren, the development of chronic diseases such as diabetes or heart disease, either in the woman or her partner, ageing parents requiring care, planning for transition to retirement or, conversely, having the time to take your career up a gear.

Therefore, any symptoms related to menopause, including the effects on brain function, have to be seen in the context of everything else that is going on in your life.

HOW YOUR BRAIN CAN BE AFFECTED DURING MENOPAUSE

There is a lot of speculation about why some women suffer more from menopause brain than others. It may be related to oestrogen levels, or to the interaction between hormone levels and neurotransmitters in the brain in individuals. It is also suggested that lifelong brain health habits (such as intellectual activity or physical exercise) provide some protection of brain function.

In peri-menopause and the early stages of menopause, women describe changes in their ability to think clearly, make decisions and function well mentally. Some describe this as ‘brain fog’. They may experience difficulty assimilating and making use of new information.

We now know that this form of brain fog affects around two-thirds of menopausal and peri-menopausal women. The cause is related to the effects of changing hormone levels on the female brain. The first hormone level to drop is usually progesterone, and this can be related to irritability, mood swings and brain fog. The drop in progesterone can also cause sleep disturbance. Sleep disturbance in itself can affect the brain’s ability to function optimally.

Dips in oestrogen levels cause the well-recognised symptoms of menopause, including hot flushes, mood changes, irritability, mental confusion and decreased energy. These things can all further contribute to hormone-related brain fog.

There is an association between loss of verbal memory skills (being ‘lost for words’) and the severity of hot flushes. One study showed that the women who experienced the most hot flushes in a day also had the worst scores for verbal memory performance. However, even if there are no other menopausal symptoms, memory can still be affected by the drop in hormone levels.

In medical consultations, many of my patients are enormously relieved when I tell them that their problems with brain function are most likely caused by the state of their hormones, and that it is likely to be temporary.

For women going through menopause-related memory and thinking problems, it is a relief to know that ‘menopause brain’ is:

- temporary

- not linked to any increased risk of dementia or Alzheimer's disease.

One study at the University of Rochester in New York looked at 117 middle-aged women and conducted a battery of neuropsychological tests for cognition. Researchers assessed their menopausal symptoms, and measured their hormone levels (oestradiol and FSH). They found decreases in attention/working memory, verbal learning, verbal memory, and fine motor speed may be most evident in the first year after the final menstrual period.

It has been shown that women who had a hysterectomy and their ovaries surgically removed at a younger age were more prone to the effects on the brain of the absence of hormones produced by the ovaries.

Another research study found that women who had their uterus and ovaries removed and then took hormone replacement therapy had a slower rate of cognitive decline than women who did not take hormones. The study did not say how long a woman would have to take hormones to protect against this effect.

You have to consider all of the other problems related to menopause that could contribute to brain fog. Some women going through the changes around menopause experience disturbed sleep, hot flushes and night sweats, and a depressed mood. All of these can contribute to difficulties with thinking and memory.

Menopause brain is temporary. The first year is likely to be the worst, and memory and learning ability generally rebound to normal after the menopause process is complete.

WHAT YOU CAN DO ABOUT MENOPAUSE BRAIN

While you are waiting for your menopause transition to run its course, there are things you can do to manage the situation. Bear in mind that for some women, this transition can last for several years. Menopause is also a time to reflect on all of your health habits and make adjustments that will take you into healthier middle and older age.

General health check

See your GP for a check-up to make sure your symptoms relate to menopause and not some other cause. This is also an opportunity to keep up to date with your regular health checks, particularly preventive health checks.

Check your blood pressure regularly (see chapter 13: Brain, Blood Vessels and Blood Pressure). Hypertension (high blood pressure) can cause hot flushes. It can also increase the risk of cognitive impairment, vascular dementia and Alzheimer's disease, even if you are on medication if blood pressure is not well controlled. Women with very high blood pressure or higher despite antihypertensive drug therapy have been shown to have a 30 per cent increased risk of developing cognitive impairment. Importantly, antihypertensive drug therapy significantly reduces the incidence of dementia.

Report any difficulties you are having with cognition so that any underlying causes other than menopause can be investigated.

Exercise

Exercise daily (see chapter 23: Brain and Exercise). Exercise is essential for the prevention of chronic disease, and it is also helpful for managing irritability, helping you sleep, and maintaining a healthy weight, strong bones and muscles.

Aerobic exercise and resistance (or strength) training will also help your brain function. Just as all body structures need

good blood flow to function and repair, the brain similarly requires good blood flow to maintain optimal function.

Exercise your mind

Make lists to help you stay organised. Think of ways to challenge your mind each day with brain stimulations such as crosswords, reading, studying something new, or learning a new language or a musical instrument. Arrange regular social interactions too.

Sleep

Disturbed sleep or lack of quality sleep impairs normal brain function and contributes to brain fog. (See chapter 28: Sleep.) Give yourself time to get to sleep. Make sure your bed and pillows are comfortable and your bedroom is quiet and dark. Don't keep electronic devices in your bedroom that emit light or make noise.

Nutrition

Look after your diet (see chapter 24: Brain Food). Eat plenty of vegetables and fruit, and other unprocessed whole foods. Avoid eating animal fats and trans fats.

Diet drinks

Compared with people who say they do not consume diet drinks, people who drink at least one per day have been shown to suffer three times more strokes, and to be three times more likely to develop dementia. My advice? Avoid artificial sweeteners such as aspartame, and switch to water as a thirst-quencher.

Alcohol

Many women find that when they drink alcohol around the time of menopause, it makes their hot flushes, night sweats and insomnia worse. Alcohol also increases body weight (because of added kilojoules) and increases blood pressure.

Healthy weight

Achieve and maintain your ideal weight. A study presented to the Endocrine Society in 2013 showed that memory improved in post-menopausal, overweight women after they lost weight by dieting. Functional MRI imaging showed that after weight loss, brain activity actually changed in the regions of the brain that are responsible for memory tasks. Activity increased during memory encoding in the brain regions that are important for identification and matching of faces, and memory retrieval was more efficient.

Smoking

Don’t smoke. (See chapter 12: Smoking and Your Brain.) Tobacco smoking affects cerebral blood flow, which has an adverse effect on brain function. Smoking may also worsen the hot flushes of menopause, and increases the risk of heart and blood vessel disease and some cancers.

Acupuncture

Some women find acupuncture helpful in treating hot flushes, fatigue, anxiety and sleeping problems. Acupuncture can also relieve memory problems. In my clinical experience it may help some women but not others. This may be due to the specific points used, the skill of the acupuncturist and other factors.

Meditation and mindfulness

Relaxation strategies such as meditation, tai chi, yoga, and breathing techniques can help with anxiety, irritability and sleep problems.

Medication review

As you get older, you become more likely to be prescribed various pharmaceuticals for chronic health conditions. Some of these may have an effect on your memory and brain function. These include sleeping pills, medications for high blood pressure, antidepressants and statins (to lower cholesterol). If you notice your brain function has worsened after starting one of these medications, ask your doctor or pharmacist to review the medication you are taking and see if you can trial something different – either a different medication or a non-pharmaceutical option.

Herbs and supplements

Some of the herbs and supplements we use to treat the hot flushes and mood swings of menopause may also help brain fog and memory problems. You will need the advice of a health care professional if you are exploring this option. Some common examples include black cohosh, red clover, ginkgo biloba, *Bacopa monnieri*, and dong quai.

Ensure you have adequate vitamins B6 and B12 to support cognitive function through menopause and beyond. Make sure you are not taking high doses of niacin, found in many multivitamin preparations. A ‘niacin flush’ is a side effect of taking high doses of supplemental niacin (Vitamin B3). This can mimic menopausal hot flushes.

If you have a vitamin D deficiency, this can exacerbate memory loss. Have a blood test to ensure you have adequate vitamin D levels, and increase sun exposure and/or supplement with vitamin D.

Menopause hormone therapy

MHT (also known as Hormone Replacement Therapy or HRT) refers to a range of hormonal treatments that can reduce menopausal symptoms. For our purposes, I will refer to it as menopausal hormone therapy, or MHT. MHT can be considered when other options have been unsuccessful. Current thinking has shifted more favourably to the use of MHT where it is needed. The general rule is to use the lowest effective dose for only as long as necessary, preferably for five years or less because of the increased risk of breast cancer with longer term use. Brain fog and other symptoms may reduce or disappear after a year or two, although they are more persistent in some women.

MHT comes in a range of forms and combinations (usually oestrogen and a progestin), and can be taken as pills, applied as patches or injected as an implant. If the main problem is vaginal dryness, oestrogen can be used topically as a cream. Newer options include compounded bio-identical MHT (which has the same risks and benefits as other forms of MHT and may be inaccurate or inconsistent) and micronised progesterone. MHT is not routinely recommended for menopause brain, and certainly not as an initial response. There is no strong evidence that hormone therapy benefits brain function around menopause, and it is important to consider the risks as well as the benefits. Research also tells us that long-term hormone therapy does not protect against cognitive impairment or the various forms of dementia.

The decision really depends on how severely cognitive problems and other menopausal symptoms are affecting your quality of life and your work performance, and what else you have tried. Hormone therapy tends to be most useful for brain function in the peri-menopausal stage.

15

Your Brain and Your Gut

We have always had a ‘gut feeling’ that the brain and the gut interact. Expressions such as ‘butterflies in your stomach’ to describe the gut reaction to anxiety, or the ‘nervous bowel’ experienced by some people during times of heightened stress demonstrate that these interactions are, in a macro sense, well accepted.

The past decade has seen an exponential increase in our understanding of the role of the gut, the enteric nervous system, the trillions of microorganisms in the gut microbiome and their interactions with the brain.

The microbes in your gut act collectively as an endocrine organ to create more than 30 neurotransmitters, many which are identical to those in the central nervous system. Neurotransmitters are chemicals that send signals to the brain. This interaction is termed the Brain–Gut Microbiome Axis, and involves two-way communication between the nervous, endocrine and immune systems. So it follows that if your gut is imbalanced, your brain may be affected, in turn affecting outcomes like anxiety, depression and cognition.

The more we learn about the gut, the more we recognise the impact of gut function on brain function, and the more we

realise we are yet to discover about the constellation of interactions between the gut and the brain.

Disturbances of the Brain–Gut Microbiome Axis have been associated with sleep disturbances, depression and lower emotional quality of life, anxiety, Parkinson's disease, and increased and decreased cognitive abilities. There is some evidence that specific probiotics can help boost mood and cognitive function and lower stress and anxiety.

Over the years I have treated many people with a range of conditions we broadly call 'gut dysbiosis'. Any medical term starting with 'dys-' means bad or disturbed. '-biosis' means a form of life. So, dysbiosis means a disturbance in the normal balance of microorganisms in the gut.

One of the intriguing symptoms we see in particular cases of gut dysbiosis is brain fog. I remember one middle-aged woman who had developed such a problem with brain fog that she was unable to manage her business efficiently. She could not concentrate on ordering or keeping accounts.

She had known for a long time that she had gluten intolerance, so she was on a gluten-free diet, but she still had an uneasy feeling in her gut, trouble sleeping, trouble concentrating and difficulty with decision-making.

Because of her gut symptoms, she had been investigated by a gastroenterologist who had ruled out the usual suspects such as coeliac disease or colitis. A suite of blood tests including thyroid function and iron levels gave no clues, so we decided to do a gut microbiome test before proceeding to formal neuropsychiatry testing. The result came back with a familiar dysbiosis pattern, a preponderance of streptococcus and hardly any *E. coli* with low lactobacillus levels. This can be associated with lethargy, fatigue, difficulty concentrating and making decisions, and sleep disturbance. With a combination of antibiotics and probiotics and a change of diet,

including the elimination of refined sugars, her gut symptoms settled and over several months her brain function returned to normal. Since then she has been able to function normally. There have been periods of time when the brain fog started to return, but another round of the treatment protocol has put things back on track again.

Here are some of the facts we now know:

- The brain and the gut are the only organs with their own nervous systems.
- The gut contains more neurotransmitters than the brain.
- Gut cells produce around 50 per cent of the body's calming hormone dopamine, and around 90 per cent of the mood hormone serotonin, so you can see the important link between how you feel and your gut health. They also produce GABA. All of these neurotransmitters have a key role in regulating mood.
- Bifidobacteria can produce and increase plasma levels of the serotonin precursor tryptophan, which is essential in regulating mood, appetite and gut function.

Your unique gut microbiome is established early in life, and its composition can be influenced by many factors. These factors can include your genetic inheritance, your mode of birth delivery (vaginal or caesarean birth), your diet, a history of gut infection, taking antibiotics and environmental factors.

Stress is a potent influence on the Brain–Gut Microbiome Axis at all stages of life. Just consider the interaction of stress and altered gut function in conditions like irritable bowel syndrome and inflammatory bowel disease.

We also know that your gut microbiome becomes less diverse with age. A greater richness of diversity in your gut microbiome supports a stronger and more stable immune system.

There is a constant two-way connection between your gut and your brain. The microbiome and the brain communicate with each other via various routes, including the immune system, the vagus nerve and the gut's own nervous system.

Just as the gut microbiome can be altered in ways that adversely affect your health, it is also possible to manipulate the balance of your gut flora to achieve better health outcomes.

HOW TO IMPROVE THE DIVERSITY OF YOUR GUT MICROBIOME

In addressing gut issues, there is a lot of crossover between the lifestyle advice and the more specific advice on the management of inflammatory conditions, cardiovascular disease, diabetes and cognitive impairment.

The aim is to eliminate or minimise potential or known factors that adversely affect gut health. This can be done in a number of ways.

- Check for undiagnosed medical conditions that may be affecting gut function, including nutrient absorption.
- Adjust your diet. Eat whole foods that are rich in fibre and low in sugar, with an emphasis on a wide variety of plant-based foods. Avoid processed foods and food additives. Identify food allergies and intolerances and avoid those foods, if necessary, under the guidance of a dietician. If you are not vegetarian or vegan, include bone broth in the gut healing phase.
- Reduce dietary advanced glycation end products (dAGEs) or glycotoxins in food. dAGEs are known to contribute to increased oxidant stress and inflammation, which are linked to the recent epidemics of diabetes and cardiovascular disease, ageing and degenerative diseases. Animal-derived foods that are high in fat and protein are

generally dAGE-rich and prone to new dAGE formation during cooking. They include red meat, butter, some cheeses, fried foods and highly processed foods. Excessive dAGEs accumulation disturbs synaptic transmission, contributing to a decline in cognitive ability during the ageing process and an acceleration in progression from mild impairment to Alzheimer's disease.

- Include prebiotics. Studies have shown that prebiotics which selectively stimulate the growth of beneficial bacteria in the human colon might offer protection against dAGE-related pathology in people at risk of developing type 2 diabetes. Prebiotic foods are fibrous foods that feed the bacteria in the gut. Examples of foods with high prebiotic content include vegetables such as Jerusalem and globe artichokes, fennel, sweet corn, garlic, onion, leek, shallots, spring onion, asparagus, beetroot and cabbage. Prebiotics are also found in lentils and other legumes, such as soybeans, red kidney beans and chickpeas. Fruit containing high amounts of prebiotics include nectarines, peaches, grapefruit, banana, apple and watermelon, pomegranate, figs and dates. Prebiotics are also present in grains, nuts and seeds.
- Reduce toxins that could adversely affect the microbiome: nicotine, excess alcohol, and chemicals and unnecessary pharmaceuticals, particularly non-steroidal anti-inflammatory drugs.
- Supplement if low in any nutrients, particularly zinc, magnesium, vitamin D, B vitamins and essential fatty acids. Consider gut healing supplements such as l-glutamine.
- Managing stress is integral to gut health. This will involve an assessment of the sources of stress and learning how to manage situations to reduce stress. It may involve improving relationships and social networks, and practising

meditation and mindfulness. Find out more in my last book, *The Mystery Gut*.

- Have more probiotics. Probiotic foods include yoghurt, kefir, kombucha, tempeh, miso, pickles and sauerkraut. There are many different types of probiotic, and they are referred to according to their species. Each one has slightly different activity in the human gut. Some examples of commonly used types are:
  - ***Lactobacillus acidophilus*:** *Lactobacilli* produce the enzyme lactase, and may improve lactose intolerance in milk-sensitive infants and children. These probiotics have even been shown to reduce the duration of cold and flu symptoms in children, as well as reducing the number of days off pre-school because of illness.
  - ***Bifidobacterium lactis*:** *Bifidobacteria* make up approximately 90 per cent of the endogenous beneficial bacteria in the adult large intestine. In breast-fed babies, bifidobacteria account for 99 per cent of the beneficial bugs in the gut. They stop the growth of many dangerous gut bacteria, help stimulate the immune system and promote the production of B vitamins.
  - ***Lactobacillus plantarum* 299v:** This calms the symptoms of irritable bowel syndrome, and reduces non-specific bloating, wind, diarrhoea and constipation. It also relieves inflammation in the gut from Crohn's disease and colitis.
  - ***Lactobacillus rhamnosus*:** Lactobacillus rhamnosus is useful in calming the immune system in allergy and eczema, and in prevention of diarrhoea and respiratory infection.
  - ***Saccharomyces boulardii*:** This is a yeast useful for treating gut infections like traveller's diarrhoea and

preventing and treating antibiotic-associated diarrhoea.

It is important to know that not all probiotics are the same, or have the same action, so if you are considering probiotics as supplements, it is important to know which preparation is best for your situation.

It is thought that regular exercise, particularly in youth, can lead to a more favourable diversity of gut-flora. Exercise can also help maintain a better gut flora balance in adulthood. For example, athletes have been found to have more diverse microflora than sedentary people of the same age and gender.

One study found that exercise promoted the growth of the bacteria that produce the fatty acid butyrate, which can reduce mucosal permeability, reduce inflammation and promote repair of the gut lining.

Recent evidence also suggests that aerobic exercise improves the diversity and abundance of microbes in the *Firmicutes* group (the *Firmicutes* phylum contains over 250 genera of bacteria, including *Lactobacillus*), which may be the link between the positive effects of exercise on the gut and brain. There are many justifications for including exercise (see chapter 23: Brain and Exercise) in a plan for a healthy brain, and maintenance of a healthy gut microbiome is one emerging area of interest.

The gut microbiome can affect your sleep physiology. Research has found that total microbiome diversity is associated with better sleep efficiency and total sleep time, and less episodes of waking after the onset of sleep. The researchers also found an interesting association between the richness and diversity of the gut microbiome and interleukin-6 (IL-6), a cytokine indicating inflammation in the body. Specifically, disordered sleep is associated with increased daytime levels of the inflammatory cytokine IL-6.

Further, the researchers found that a preponderance of some types of gut microbes (bacteroidetes and firmicutes) were good for sleep efficiency, interleukin-6 concentrations and abstract thinking, while others had a negative effect. This is one example of the connections between gut microbiome composition, sleep physiology, the immune system and cognition. This is quite recent research, so it adds to our knowledge of the links between the gut, the brain and sleep in a way that may lead to future research on improving sleep and brain function through manipulation of the gut microbiome.

This is an exciting time as knowledge about the link between the gut and its microbiome, probiotics and the brain rapidly advances. In the coming years we will see the results of more research into the influence of the gut on brain health, including the use of specific probiotics or probiotic combinations to achieve clinical outcomes in conditions such as mild cognitive impairment, Alzheimer's disease, Parkinson's disease, sleep disorders, anxiety and depression, and more.

16

The Dementia Mimics

One of the lessons I took from my medical training is to maintain a high level of suspicion about a diagnosis of dementia in elderly patients who appear to be confused, cognitively impaired or ‘demented’, particularly if the changes are recent.

There is a battery of tests called a ‘dementia screen’ to make sure that when an elderly patient presents with confusion, agitation, has trouble concentrating or appears to have a cognitive deficit, all diagnostic possibilities are considered. This is because there are many conditions that mimic dementia in an older person. It is important to consider this list of conditions that may be reversible or treatable, and to avoid making assumptions based on first impressions.

The dementia mimics are also a reminder of just how many medical conditions can have more subtle effects on your brain function at younger ages. We doctors must keep our diagnostic radar tuned to these possibilities. Obviously we want to identify any treatable conditions and fix them.

Some of these conditions may not be reversible, but getting the diagnosis right means you can avoid unnecessary tests or procedures, and ensure that people with genuine cases of dementia can get the most appropriate care.

If you or somebody close to you has started to show some of the signs of early dementia (confusion, disorientation or memory problems), you need to rule out these conditions, which can trick even the most experienced physician.

There are many dementia mimics. Some of the most common that we encounter are:

- vitamin B12 deficiency
- iron deficiency or low ferritin
- underactive thyroid
- urinary tract infection
- depression
- head injury
- subdural haemorrhage
- normal pressure hydrocephalus
- liver disease
- kidney disease
- uncontrolled diabetes
- heart or lung disease
- problems with hearing or vision
- sleep deprivation
- drug reaction
- alcohol withdrawal.

As you can see, it is a long list. Let's take a look at some of them and what can be done about them.

VITAMIN B12 DEFICIENCY

Vitamin B12, also known as cyanocobalamin, is an important B-group vitamin. It is essential to the production of brain

chemicals that affect brain function and moods.

The main dietary sources of vitamin B12 are meat, milk, cheese and eggs. Vitamin B12 and another B-group vitamin, folate, depend on each other. Vitamin B12 deficiency is one of the more common nutritional deficiencies I see, and in my clinical experience there are a few main causes: a limited diet (usually vegan), pernicious anaemia or poor absorption related to a gut problem, excessive alcohol consumption or older age.

Vitamin B12 deficiency results in a type of anaemia called megaloblastic anaemia. The symptoms include tiredness, dizziness, fast pulse, painful tongue, abnormal gut function and easy bruising.

B12 deficiency also causes a type of neuropathy (nerve damage) affecting the cerebral cortex of the brain, the spinal cord and peripheral nerves. If this goes undetected or untreated, the damage is likely to be permanent.

We recognise the symptoms of neuropathy as loss of sensation in the hands and feet, a pattern we call ‘stocking and glove’. Later in the course of the deficiency, there can also be muscle weakness and paralysis. This affects gait.

Later effects on brain function can include dementia, depression and mania. The effect of vitamin B12 deficiency on the brain is the reason it is included as a ‘dementia mimic’ and should be considered in any potential diagnostic list.

Vitamin B12 deficiency can be corrected by dietary change and/or supplementation. If you are unable to absorb vitamin B12 through the lower gut, you can still absorb it through the mucous membranes lining your mouth, so an oral spray is an effective, painless and easily accessible alternative to three-monthly injections.

IRON DEFICIENCY OR LOW FERRITIN

Iron deficiency and low iron stores are very common. Ferritin level on a blood test is a reflection of iron stores. If you have low ferritin, you may experience symptoms without your circulating blood iron levels being under the normal range, and regardless of whether you have anaemia.

Iron deficiency or low ferritin are considered dementia mimics because of their effect on cognitive function in the elderly, but the effect on cognition can be seen at all ages. Infants with iron deficiency test lower on cognitive, motor, social-emotional and neurophysiological development. We need to be alert to this possibility in children, because although the cognitive effects can be prevented and/or reversed with treatment earlier in development, or before iron deficiency becomes severe or chronic, children may not be able to fully catch up from a long-term untreated deficiency during brain development. This is because iron deficiency can cause abnormal development of brain structures such as myelination and the development of the brain's neurotransmitter systems.

The first step in ensuring children have adequate iron for their brain development is by monitoring the mother's iron levels throughout pregnancy.

During infancy and childhood there are some behavioural signs that can indicate iron deficiency, such as irritability, apparent apathy or disruptive behaviour.

Children and adolescents are at risk of iron deficiency because of the increased need for iron to fuel their rapid rate of growth. If a child or adolescent is found to have iron deficiency, we look for the cause. This is most commonly inadequate dietary intake, or a gut absorption problem such as coeliac disease. In the case of adolescent girls, heavy periods and restrictive dieting often contribute to iron deficiency or low ferritin. Menstruation means that young adult women are more likely to be iron deficient than healthy young men.

One study of women aged between 18 and 35 found that the effects of iron deficiency on cognition were not confined to the developing brain. The study found that women with adequate iron levels performed better on cognitive tasks and completed them more quickly than women with iron deficiency. Women who had anaemia related to their iron deficiency performed worst, and anaemia was related to processing speed. After treatment, a significant improvement in serum ferritin was associated with a substantial improvement in cognitive performance.

Iron deficiency (with or without anaemia) understandably affects cognitive performance in elderly people as well. Because of age, it is easy to assume that forgetfulness or difficulty concentrating are early signs of cognitive decline or dementia. In elderly people, anaemia accelerates cognitive decline. This is why it is essential to consider iron deficiency and to test for it routinely in these situations.

When we detect low iron or ferritin, we need to look for a reason. There are four categories for investigation:

- inadequate dietary intake (usually vegan or vegetarian)
- excessive blood loss (heavy periods in women or gastrointestinal bleeding from inflammation, polyps or bowel cancer)
- poor absorption from the gut
- chronic disease, infection, inflammation or cancer.

Iron deficiency needs to be medically investigated, and you need professional advice about supplementation because it is possible to over-supplement with iron. Where a diet is inadequate, that needs to be corrected.

If there is a treatable medical cause, that should be addressed. Your general practitioner will guide you in

investigation and referrals where appropriate; for example, to a dietician, gynaecologist or gastroenterologist.

In the case of children, you will need professional advice on specific age-related iron supplementation and preparations. In adults, the treatment depends on the severity of iron deficiency and individual preference. In pregnancy, a very low ferritin is best treated with an intravenous iron infusion because the result is instantaneous, and foetal brain development needs to be considered as a priority. Intravenous iron supplementation has been shown to be safe and effective in a general practice setting where the practice has the equipment and protocols to do it.

There are also many different types of oral iron supplementation. Your GP can advise you on what is best for your situation.

THYROID DISEASE

Thyroid hormones regulate many of our metabolic processes. Underactivity (hypothyroidism) and overactivity (hyperthyroidism or thyrotoxicosis) are conditions we commonly see in general practice. Most thyroid conditions have an underlying autoimmune cause and have a tendency to run in families.

You need sufficient dietary iodine in the production of thyroid hormones.

The symptoms of hypothyroidism include:

- depression and other neuropsychiatric disorders
- brain fog, memory problems, difficulty concentrating
- weight gain
- fatigue
- intolerance to cold environment

- hair loss
- dry skin
- constipation
- enlarged thyroid gland.

The symptoms of hyperthyroidism include:

- anxiety
- agitation
- sweating
- intolerance to hot environment
- rapid pulse
- fatigue
- diarrhoea
- may have bulging eyes (exophthalmos)
- enlarged thyroid gland.

We test thyroid function by measuring the amount of thyroid hormone produced by the thyroid gland at the front of the neck, and the amount of TSH (thyroid-stimulating hormone) produced by the pituitary gland at the base of the brain. As its name suggests, TSH is released to stimulate the thyroid gland if the pituitary gland perceives that there is not enough circulating thyroid hormone. The level is increased if the thyroid is underactive and needs to be stimulated to produce more thyroid hormone, and decreased if the thyroid is overactive. Iodine is needed to produce thyroid hormone. The link between congenital hypothyroidism and profound effects on foetal brain development has been known for over a century. This is why we monitor a mother's thyroid function and avoid iodine deficiency during pregnancy.

Thyroid dysfunction in adults shows different patterns of cognitive impairment, and may not be fully reversible once the

thyroid function is returned to normal. Still, it is extremely important to identify whether thyroid dysfunction is a contributing factor where cognitive function seems to be affected, particularly if the patient has experienced recent changes in memory or concentration.

URINARY TRACT OR OTHER INFECTION

Urinary tract infection, or UTI (infection of the bladder and/or kidneys), becomes more common in older people. UTIs are also more common in women than in men, because women have a shorter urethra and the bacteria causing the infection have less distance to travel to the bladder. The lack of oestrogen after menopause in women can also make the vaginal and urethral tissues more prone to infection. Men with prostate enlargement are also more prone to UTIs than other men because of obstruction to the outflow of urine.

The usual symptoms that alert us to a UTI are frequency of and a burning sensation during urination, abnormal urinary odour, pelvic pain (sometimes loin pain if a kidney is infected), and sometimes fever. Interestingly, UTIs can be ‘silent’, and those symptoms may not be present in older adults. The first sign could be the acute onset of confusion, agitation, emotional sensitivity, withdrawal or other change in behaviour. This can be misinterpreted as the onset or worsening of dementia.

Treatment with antibiotics will quickly resolve the cognitive issues that were precipitated by the infection.

DEPRESSION

People with depression (see chapter 19: Depression and Anxiety) often experience symptoms that can look like the onset of dementia. They can appear confused, forgetful,

disoriented and vague, and appear to not concentrate and to have lost interest.

Depression can occur in older age as a response to many life changes, including loss of a partner, retirement, social isolation, illness or disability, or financial stresses.

In the case of Alzheimer's disease, the memory loss comes first, and depression may be a response to the awareness of memory loss and cognitive decline.

When depression is suspected in an older person, treatments include counselling, social supports, cognitive behaviour therapy and other psychological techniques, exercise programs and nutritional correction.

HEAD INJURY

A fall or a knock to the head can cause concussion. This can result in temporary confusion, which should spontaneously resolve over hours or days.

A head injury (see chapter 17: Brain Injury) can cause bleeding inside the skull, called a subdural haemorrhage. The effect of a subdural haemorrhage depends on the size and location of the bleed and its impact on the brain.

A subdural haemorrhage is a bleed that is inside the skull but on the outside of the brain. It is called subdural because it is under the membrane (dura) surrounding the brain. The most common cause is head trauma from a fall. Bleeding is usually very slow, and as the amount of blood increases, so does the pressure on the brain.

An acute subdural haemorrhage develops in the minutes to hours after a significant head injury and is a life-threatening condition needing emergency medical treatment. A chronic subdural haemorrhage (bleed) or haematoma (blood collection) is one of the most common causes of reversible

apparent dementia in an elderly person, as it causes gradual memory loss and personality changes.

A chronic subdural haemorrhage takes days to weeks to gradually develop, and the symptoms similarly develop gradually. A common scenario is an older person who has had a fall and hit their head. The blow to the head might have been quite minor, and they may have no recollection of the incident. Symptoms might include a mild headache, nausea with or without vomiting, clumsiness and loss of balance, weakness or numbness in limb(s) on one side, change in personality, memory difficulties and double vision. The gradual loss of memory and changes in personality can be mistaken for dementia.

If there is a suspected chronic subdural haematoma, a brain scan will be arranged, and if a significant bleed is confirmed, surgery will be performed to drain the collection of blood.

NORMAL PRESSURE HYDROCEPHALUS

Normal pressure hydrocephalus is the result of an abnormal build-up of cerebrospinal fluid (CSF) in the ventricles (network of cavities) of the brain. If there is a blockage in this network, the build-up of fluid can result in memory loss, confusion, mood changes, depression, trouble walking and loss of bladder control.

This is more common in older age, so the symptoms can be mistaken for the onset of Alzheimer's disease.

It is important not to miss this diagnosis, because it is one of the few causes of dementia that can be treated and reversed with a surgical procedure.

KIDNEY DISEASE

In chronic kidney disease, the kidneys are unable to effectively remove toxins from the bloodstream. Renal failure can cause mental confusion, depression and agitation, as well as other neurological problems as toxins accumulate in the brain. Treatment needs guidance from a renal medicine specialist.

PROBLEMS WITH HEARING

It is surprisingly common for an older family member to appear to be mentally vague or unresponsive because they have a hearing problem. Perhaps they grumble about other people mumbling, or avoid groups or crowds because they are unable to follow conversations.

The lack of responsiveness or social engagement and the irritability that can be caused by hearing loss is sometimes misinterpreted as the onset of dementia.

The most common cause of treatable hearing loss that I see in general practice is a gradual build-up of ear wax. The hearing loss can sneak up on you gradually. Wax build-up needs to be considered in the case of any recent hearing loss. It can also cause tinnitus (ringing in the ears) and loss of balance. Removing the wax can be as simple as using wax softening drops for a couple of days, then having the wax removed by water syringing or suctioning with special instruments. If this is the cause, the treatment will instantly restore your hearing.

Benign, slow-growing tumours of the acoustic nerve (acoustic neuroma) can cause one-sided hearing loss. These can be removed surgically. There is also a condition known as exostoses, bony growths in the ear canal which can block off hearing. These need to be surgically removed.

Some medications can also affect hearing, such as the antibiotic gentamicin and some chemotherapy drugs. Talk to your doctor about any medication you are prescribed and

check whether it has a side effect of hearing loss. Discuss whether the medication is necessary, and whether there is an optional medication.

If you suspect you suffer from hearing loss, see your doctor to investigate the cause. Treatable causes need to be dealt with as soon as possible. Permanent hearing loss can be managed with an individually fitted hearing aid.

DRUG REACTION

There are many medications with a sedating effect that can give the appearance of cognitive impairment and raise the possibility of the onset of dementia. It's a long list, including:

- sedating antihistamines
- some antidepressants
- anti-anxiety medications and sedatives
- painkillers, especially opioids such as codeine or oxycodone
- some anticonvulsants.

If you are experiencing difficulties with memory or concentration and you are taking a medication, particularly if you have noticed a change in yourself since starting a new medication, speak to your doctor about your medicines to see if what you are experiencing is a likely side effect, and whether a different medication (or stopping unnecessary medication) is worth a try.

Refer to chapter 6: Medications for more information about these medications.

ALCOHOL

Alcohol is a central nervous system depressant. Heavy chronic alcohol use can cause a range of brain issues. It shrinks the

brain's frontal cortex and underlying white matter, and the cerebellum, and expands the ventricles.

This damage can have numerous consequences, including memory loss, confusion, poor decision-making, loss of coordination, loss of concentration and loss of abstract-thinking ability. These effects can be misinterpreted as dementia.

Some of these effects will be reversible if you stop drinking alcohol. If you are a heavy drinker, the effort to stop drinking alcohol will benefit your brain health. Different parts of the brain recover at different rates, however. Research has shown that abstinence from alcohol can start to show recovery of brain volumes in the frontal lobe and cerebellum and decreased ventricular volume within the first few months. Some damage, though, will be irreversible. Refer to chapter 5: Alcohol and Your Brain for more information.

17

Brain Injury

Boxer Muhammad Ali was famous not only for his astonishing athletic ability, but also for his particularly provocative and engaging brand of speech and swagger.

He reportedly encouraged sparring partners to hit him in the head to 'build up resistance'. This made it all the more poignant when he later developed Parkinson's disease, a progressive brain deterioration, reportedly the result of many thousands of punches to his head over his career.

If you step into a boxing ring, you know you are signing up for a potential brain injury. After all, the aim of the game is to knock your opponent unconscious, or at least have them so neurologically injured that they are unable to continue.

In my career as a health communicator and as President of the Australian Medical Association, I argued that if the area 'below the belt' was out of bounds then the area above the neck should be given similar consideration. In other words, if the testicles deserve protection, so does the brain. I said in 2002 about professional boxing, 'I just don't think that in this day and age, with all that we now know about the delicate functioning and the nature of the brain, that (boxing) can be tolerated in a civilised society.'

The Australian Medical Association, the American Medical Association, the British Medical Association and the World Medical Association are all in agreement that boxing is a dangerous sport that should be banned.

TRAUMATIC BRAIN INJURY

More severe traumatic brain injury (TBI) is recognised as a risk factor for a variety of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS). Recently, large epidemiological studies have also identified mild traumatic brain injury as a risk factor for dementia.

Repeated mild TBI has also been linked to the neurodegenerative disease now known as chronic traumatic encephalopathy (CTE), which was first described in boxers. It has since been recognised in a variety of contact sports.

The symptoms of chronic traumatic encephalopathy can occur immediately after an injury, or they can be delayed. They are signs that the damaged brain is malfunctioning.

Mild traumatic brain injury

Symptoms of mild traumatic brain injury can include:

- a brief loss of consciousness (seconds to minutes) or a period of feeling dazed and confused following a knock to the head
- headache
- nausea or vomiting
- drowsiness or fatigue
- problems with speech
- visual disturbances

- tinnitus (ringing in the ears)
- abnormal smell sensation
- sensitivity to light or sound
- sleep disturbances
- dizziness, balance problems
- difficulty with attention, concentration and memory
- mood swings
- irritability, anxiety or depression
- frustration.

Moderate to severe traumatic brain injury

The severity of symptoms will depend on the seriousness of the original injury and the duration of unconsciousness. Symptoms can include:

- loss of consciousness for minutes to hours
- persistent or worsening headache
- nausea or vomiting
- difficulty with attention, concentration and memory
- impaired judgement
- confusion
- trouble understanding and expressing language
- slurred speech
- problems reading and writing
- vision problems
- tinnitus
- convulsions or seizures

- weakness or numbness in extremities
- movement disorders (lack of coordination, clumsiness, paralysis)
- behavioural and emotional changes (aggressiveness, irritability)
- difficulty in social situations
- delayed neurodegenerative disorders (Parkinson's disease, Alzheimer's disease).

In the case of boxing, the injury is repetitive and intentional. It differs from other sports in that brain injury in the form of a 'knockout' is the aim of the sport, rather than an incidental occurrence.

There are other sports, such as rugby, soccer (round-ball football) and other activities, where brain injury is a possibility and where precautions can avoid or reduce the severity of a brain injury.

American Football

The 2015 Will Smith movie *Concussion* dramatised the sudden death of American National Football League (NFL) player Mike Webster and a form of brain disease, chronic traumatic encephalopathy (CTE), previously associated only with boxers. Webster was the first American football player to be diagnosed with CTE, at autopsy after his death.

Set in 2002, the film tells the story of Dr Bennet Omalu, a forensic pathologist who fights against the NFL's efforts to suppress his research on CTE.

Since then, it has been recognised that former players with CTE have battled depression, memory loss and in some cases dementia.

Significant changes were eventually made to the sport's concussion protocols in December 2017.

Football (soccer)

Football (or soccer) mostly involves kicking a ball along the field and into goal. In the goal area, players can 'head' the ball to pass it to another player or direct it into goal. In other words, a heavy object strikes a player's head and is deflected at high speed. Research has shown that repetitive heading of a soccer ball contributes to the development of neurodegenerative disorders of the kind we saw in Muhammad Ali and American professional football players.

Shake the brain up often enough and it starts to exhibit abnormalities like memory problems, anger, anxiety, depression, headaches and sleep disorders. Later in life, it can also lead to movement disorders and dementia.

Researchers at University College London found evidence that repetitive soccer heading produces cumulative brain damage and dementia later in life:

> … 14 retired soccer players who developed dementia later in life were followed up until their deaths. Most of them had started training and heading the ball during childhood. The researchers obtained next-of-kin permission to study the brains of six players. All six brains showed evidence of damage associated with chronic repetitive head impacts, including Alzheimers' Disease, and four of the six brains revealed the characteristic damage associated with Chronic Traumatic Encephalopathy (CTE), originally associated with boxers.

More than 50,000 soccer concussions were reported among US high school players in 2010. In 2014, a group of parents and players filed a lawsuit in a US district court

charging FIFA, US soccer and the American Youth Soccer Organization with negligence in treating and monitoring head injuries.

The lawsuit was resolved in 2016 when the American Youth Soccer Organization introduced new safety measures, specifically improving concussion awareness and banning heading for all players under 12, and limiting heading in practice for 12–13-year-olds.

There have been calls for heading to be banned for all child and youth soccer, and indeed for the rules to be changed to ban heading at all levels.

In 2018, the Australian soccer players' union and Football Federation Australia called for 'more research' after the Union of European Football Associations (UEFA) announced it was considering an international ban on juniors heading the ball.

Rugby

Rugby is another contact sport that has come under increased scrutiny in recent years because of the risk of head injury. According to research published in the *British Journal of Sports Medicine*, the risk of concussion in children and adolescents playing rugby union and rugby league is significant, and tackles are responsible for 87 per cent of concussions in youth rugby.

The risk is particularly significant in children because they are more likely to experience concussion from a head injury and take longer to recover. Young players are also at greater risk of a potentially fatal condition called 'second impact syndrome', where a player sustains a second head injury before they have fully recovered from the first.

Unlike some other sports, headgear does not seem to provide much protection from brain injury in rugby players.

This means it comes down to changing the rules to protect the most vulnerable players.

Several nations have taken steps to protect children from rugby-related concussion. Because the main risk is from tackling, these changes have come mostly in the form of banning tackling in younger age groups.

In England, there is no tackling in rugby for under-9s. In New Zealand it's banned for players who are under 8; in Canada, under-11s.

A more practical approach would be to have competition groupings based on weight rather than age, given the wide range of sizes and developmental stages of children and adolescents. This would avoid a small-for-their-age child being tackled by much bigger boys of the same age.

In February 2018, Rugby Union became the first major contact sport in Australia to bring in comprehensive weight and height grading for juniors (under-10s to under-15s), allowing them to develop skills and experience against players of a similar size.

While some sports bring an inherent risk of multiple head injuries over time, traumatic brain injury more often happens as a single event.

Of course, accidents can and do happen. Many of life's great activities and adventures bring with them some degree of risk. However, it is the anticipation of a potential traumatic brain injury and the actions people take to avoid injury that can protect them from a disaster.

Skiing and snowboarding

When you think about whooshing down a steep mountain among trees and rocks and chairlift pylons at great speed, the

risk of falling or landing badly seems obvious. But years ago, skiers didn't wear protective helmets.

Several tragic high-profile skiing deaths, including those of Sonny Bono and Natasha Richardson, raised awareness of the risk of brain injury in snow sports and more people started to wear helmets.

Once, if you wore a helmet you were unusual. Now it is unusual to see a skier without one.

Research tells us that about 10 million people engage in these sports worldwide each year. Head injuries are still the leading cause of deaths in skiing and snowboarding. Overall, about one in five head injuries is severe enough to cause loss of consciousness or clinical signs of concussion.

There was some concern that wearing helmets might encourage skiers and snowboarders to be more reckless, and make them inclined to take more risks, but research has shown that has not happened.

The general consensus, based on evidence and common sense, is that helmets decrease the risk of a traumatic brain injury and also reduce the severity of head injuries compared to skiers and snowboarders who do not wear helmets.

Cycling

There is an ongoing debate between cyclists who accept that wearing a helmet is a good idea, and the more libertarian view that wearing a helmet should be a choice.

I have heard the arguments against compulsory wearing of helmets. One such argument is that forcing people to wear a helmet discourages them from jumping on a bike, and so reduces the public health benefit of exercise.

I don't think any of the arguments against compulsory helmets outweigh the simple fact that helmets are the single

most important piece of safety equipment for a cyclist. Stripped down to the simplest terms, if you fall off your bike or are knocked over by a car and hit your head, a well-designed and fitted helmet will give you some protection against brain injury. Without a helmet, you have no protection.

Traffic accidents consistently show that the majority of fatal injuries sustained by cyclists in a crash involve head injuries.

An Australian study of emergency department admissions found that between 2008 and 2010, non-helmet wearers were five times more likely to develop intracranial bleeding or suffer a skull fracture due to falling from a bicycle compared with helmet wearers.

It is certainly the view of the medical profession that bike helmets should be worn, and should be compulsory to reduce the risk of traumatic brain injury.

Obviously there are issues of big picture planning for cycling safety, such as building infrastructure in cities that separates cyclists from traffic and from pedestrians, particularly for people who commute by bicycle.

KEEPING YOUR BRAIN YOUNG BY PREVENTING BRAIN INJURY

If you are aiming to keep your brain fit for the future, it is essential to take whatever measures you can to protect yourself from brain injury.

My message to parents is to discourage your children from taking up boxing and similar sports (like mixed martial arts and kickboxing), which target injury to the head. You really need to think carefully about your child's choice of sport, and consider the most appropriate sport for your child's physical abilities, developmental stage, size and strength. This can be

really difficult in cultures where contact sports are celebrated and expected of children and adolescents.

It helps to introduce young people to sports that do not have a contact element and have a lower risk of head injury. As a mother and a grandmother, I acknowledge that this can be a challenge. Fortunately, my son Carl was more interested in sailing, surfing and swimming than in one of the football codes. Time will tell if my grandsons are keen to play contact sports, but at age three, Billy was already working on his golf swing.

Many of the other recommendations for preventing brain injury are obvious, and relate to foreseeable and avoidable accidents. I am going to list them anyway, even if they are obvious, because they form a reminder of the potential risks:

- Always wear a seatbelt when you are driving or a passenger in a car.
- Make sure children are secured in a properly fitted safety seat or booster.
- Child-proof your house to prevent risk of falls. This includes safety guards on high windows and barriers on stairways.
- Wear a helmet when you are riding a bicycle.
- Wear a helmet when you are skiing or snowboarding or in other sports where helmets are recommended.
- Wear all the safety equipment recommended for the sport you are playing.
- Never drive, cycle or engage in risky sports under the influence of alcohol or other drugs that can impair reaction times.

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Brain Cancer

The purpose of this book is to get you thinking about the many factors that influence your brain health from conception to old age, with the aim of maintaining optimal brain function throughout your life.

Brain cancer is a tragic disease with a relatively low survival rate, and despite a great amount of research into possible prevention or cure, it continues to baffle us.

Brain cancer can affect anyone at any age. It was once a disease of elderly people, but now childhood cases are also on the rise. Nobody knows why.

This and many other questions need to be answered if we are to make progress in treating this potentially devastating form of cancer.

Although there is no known way to prevent brain cancer, I thought it was essential to devote a section of the book to this topic.

Have you ever had a splitting headache and thought to yourself: ‘I hope this isn’t a brain tumour’? You’re not alone. It is a common fear of patients I see in general practice who have unexplained neurological symptoms such as worsening headaches.

Of course, very few headaches turn out to be brain cancer, but for those who are diagnosed with this devastating and life-threatening condition, the journey is rough.

In rare cases, a brain tumour can look like dementia. Symptoms may appear as intellectual decline, trouble finding the right words, using the wrong words, poor concentration, disorientation in a familiar environment, difficulty with performing routine tasks and social withdrawal. There may also be other warning signs, such as a change of personality or having falls.

One reason brain scans are part of the routine testing of a patient with recent onset of memory loss or cognitive difficulty is to rule out the possibility of a benign brain tumour or a brain cancer.

Brain cancer is mysterious for a number of reasons. We don't know what causes it. We can't prevent something if we don't know the cause, and we can't cure a disease we don't yet fully understand.

The risk factors for brain cancer include exposure to ionising radiation (X-rays and gamma rays). Genetics may also play a role. Researchers tell me that through examining the genetic structure of dozens of different tumours, they have discovered that every single tumour is unique. Even if the mutation is on the same gene, it will be in a different part of the gene.

One encouraging new direction for research and treatment involves immunotherapy, triggering the body's own immune system to fight the cancer.

RED FLAGS FOR A POSSIBLE BRAIN CANCER

As we have seen, the brain is a complex organ that governs all of the body's processes, so the symptoms of brain cancer will

depend on the position of the tumour in the brain, the size of the tumour and its rate of growth. Some possible signs include:

- severe headaches or a change in usual headache pattern, possibly accompanied by nausea and vomiting
- weakness or lack of coordination in one side of the body
- seizures
- a change of personality or thinking processes
- memory loss
- trouble with vision or speech
- persistent dizziness
- hormone dysfunction.

Some of the signs of a brain cancer mimic harmless or easily manageable conditions, but any of these symptoms should be discussed with your doctor. Headaches could be related to muscle tension in your neck, or a migraine. Dizziness could be a problem with your inner ear or low blood pressure. If there is a genuine concern about the symptoms, your doctor will arrange for an magnetic resonance imaging (MRI) scan.

BRAIN CANCER

In Australia in 2020, 1879 people were diagnosed with brain cancer and approximately 1518 die from the disease every year.

The current five-year survival rate is 22 per cent.

The most common brain cancers are called gliomas. There are a number of types of brain cancer, and the terms you might hear include: astrocytoma, glioblastoma multiforme (GBM), medulloblastoma, ependymoma and oligodendroglioma.

Primary brain cancer is different to secondary cancers in the brain from another source. Some patients mistakenly think they have brain cancer when they have a metastasis or secondary cancer from a primary cancer somewhere else in the body. These brain tumours are more common than primary brain cancers, and are named after the location where they began (such as lung, bowel, breast or skin). In some cases, surgery or radiotherapy can be done to treat brain secondaries.

IS THERE ANYTHING YOU CAN DO TO REDUCE YOUR RISK?

There is not enough evidence to give dogmatic advice about how you might reduce your risk of brain cancer. There is, however, at least some circumstantial evidence to inform decisions you might make.

Exposure to medical radiation

Exposure to medical radiation is the only risk factor for brain cancer that we can really state with confidence. CT scans, X-rays and radiotherapy treatments to the head increase the risk of future brain cancer.

X-rays and CT scans are very important in diagnosing and monitoring some medical conditions and treatments. However, it is important to avoid radiation where there is no genuine medical need. If you are recommended for a head or neck X-ray or CT scan, ask your doctor these questions:

- Is this test really necessary?
- Will the result of this test change the treatment or the outcome at this time?
- Is there an option that does not involve radiation, such as ultrasound or MRI scanning?

Mobile phone use

The question about whether mobile phone use causes brain cancer just won’t go away. The suspicion arose because mobile phones emit non-ionising radiation, which can be absorbed by adjacent tissues. This has not yet translated to any proof of a link between mobile phone use and brain cancer.

That said, the electromagnetic fields produced by mobile phones are classified by the International Agency for Research on Cancer as ‘possibly carcinogenic to humans’ based on limited evidence of a possible increase in risk for brain tumours among mobile phone users, and inadequate evidence for other types of cancer.

While there is a lot of international research activity in this area, the jury is still out on whether there is a definite causal link between mobile phone use and brain cancer. In the meantime, what do you do? The devastating consequences of brain cancer are significant enough to justify doing what you can to reduce your (theoretical) risk from mobile phone use.

This risk is theoretically greater in children because their brains are still developing, but again, a definite causal link has not been established. Because of conflicting information regarding risk in children, the World Health Organization (WHO) recommends limiting mobile phone use and promotes the use of a hands-free headset for both adults and children.

The American Cancer Society also recommends a range of measures to lower exposure to radiofrequency (RF) waves from mobile phones, and some of the suggestions included below are drawn from them.

Until we know for sure, my advice is:

- Follow the WHO recommendations and keep children’s use of mobile phones to a minimum, and preferably on speaker.
- If you have a landline with a cordless home phone with a base connected by wires to the telephone, this is not a mobile phone, and it operates at about 1/600 of the power of a mobile phone. So use a mobile phone only for short conversations or when a landline is not available.
- Text instead of talking on a mobile.

- Use a hands-free device, speaker mode or corded or cordless earpieces to move the antenna away from your head. Bluetooth earpieces emit a small amount of radiation, but much less than mobile phones.

Environmental toxin load

Exposure to solvents, pesticides, oil products, rubber or vinyl chloride may increase the risk of developing brain cancer. Although there is not yet scientific evidence that supports this possible link, the brain development of children is so sensitive that we have to act on the possibility that there could be a link. My advice is to check your home and workplace and other places where you spend time to reduce or eliminate exposure to environmental toxins for you and your family where you can.

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Depression and Anxiety

> ‘I don’t like standing near the edge of a platform when an express train is passing through. I like to stand back and, if possible, get a pillar between me and the train. I don’t like to stand by the side of a ship and look down into the water. A second’s action would end everything. A few drops of desperation. And yet I don’t want to go out of the world at all in such moments.’
>
> – Winston Churchill

Sir Winston Churchill was thought to have suffered the effects of depression, a condition he called ‘the black dog’. At times he would take to his bed for months, unable to concentrate, his mind devoid of ideas, his energy and his appetite gone. When he was not in that state, he was said to have had abundant energy, slept little and worked and talked incessantly. There have been suggestions that he may have had a form of bipolar disorder.

Depression will affect at least one in seven people in their lifetime. One of the great challenges of psychiatry and psychology is to unravel the mechanisms underlying depression and, by developing a better understanding of what

is going on in the brain, determine the most effective ways to treat the condition.

Three quarters of people who experience depression will have a recurrence, and it can continue to relapse into a chronic condition. It is important to get effective treatment as early as possible.

Anxiety and depression often occur together, and anxiety is also a risk factor for later depression.

SYMPTOMS OF DEPRESSION

Each person's experience of depression is quite individual, just as each person is unique, but there are common features. Depression is not just being sad, although the feeling of sadness is common to all people who are suffering from depression.

People experiencing depression may not experience joy in things that they usually enjoy, a symptom we call anhedonia. It can be an effort to have social contact with friends and family. They may feel tired, overwhelmed, frustrated or short-tempered a lot of the time, and may find it difficult to concentrate on work or to find meaning in their activities. Making decisions becomes difficult. Sleep is disrupted, and sufferers often wake in the early hours and are unable to get back to sleep.

Depression brings with it a sense of bleakness and hopelessness that, in its most severe form, can see sufferers considering or planning their own exit from life.

In some cases, there is a trigger for depression. An earlier traumatic event or situation such as sexual abuse might later trigger depression. Adverse life events may also be a factor, such as the loss of a job, financial distress, a family rift, chronic pain or disability, or the death of someone important to you.

There may not be a trigger at all. One comment I sometimes hear from people who have been diagnosed with depression is that they feel they don't 'deserve' to be depressed, that they have a wonderful partner and children, a comfortable house and financial security, yet they feel sad all the time.

SYMPTOMS OF ANXIETY DISORDER

There are many descriptive words for anxiety. Anxiety is a feeling of nervousness, fear, dread, worry, panic. Anxiety is intended to be a protective mechanism to deal with perceived threats.

With anxiety disorders, the anxiety may be provoked by a sense of insecurity or uncertainty, worrying that something bad might happen so that even if there is no actual physical threat, your body reacts as if there is one. Your pulse rate quickens as your heart pumps faster. You might become short of breath, break out in a sweat, your mouth becomes dry, you feel like you are going to throw up, your hands tremble. Chronic anxiety can make you chronically tired and irritable, have trouble concentrating and have difficulty sleeping. Your muscles feel tense and you get headaches.

SO WHAT'S HAPPENING IN THE BRAIN?

During an episode of anxiety, the key parts of the brain that become excessively activated are parts of the limbic system, the amygdala and the hypothalamus.

The cerebral cortex senses signs of danger and the thinking and decision-making functions assess the threat of danger and what is the best course of action. Meanwhile in the limbic system, the amygdala is processing the emotional elements and mounts a rapid response to perceived danger. The amygdala communicates the sense of danger to the

hypothalamus with messages to send out stress hormones that signal to the body to mount the fight or flight mechanisms, raising the heart rate, increasing muscle tension and so on. You may think of this as an almost instantaneous reflex reaction, ‘acting on instinct’ before your cerebral cortex has had a chance to make a plan.

The amygdala is also interconnected with parts of the brain that form memories. So if an event triggers a memory of a threatening situation, the amygdala uses that information to create a rapid emergency-type response.

An anxiety disorder can occur with or without depression, and depression can occur with or without anxiety, but they commonly occur together.

WHAT’S HAPPENING IN THE BRAIN IN DEPRESSION?

The question of what’s happening in the brain in depression is a complex one. Chemical imbalances in the brain certainly play a part but there are likely to be a variety of different imbalances in different individuals. There is also a genetic component that increases vulnerability to depression. Brain-imaging techniques are helping us to track the parts of the brain that regulate mood and emotion. There is evidence that, in the long term, depression may cause changes to the physical structures in the brain. Through advances in neuroimaging techniques such as MRI, PET and fMRI, we have been able to see changes in brain structure that might relate to the symptoms of depression.

This involves multiple brain regions including the structures in the limbic system. The limbic system consists of a group of interconnected brain structures and includes the amygdala, hippocampus and cingulate gyrus. It is responsible for behavioural and emotional responses necessary for

survival. These are the areas of the brain that seem to be involved in depression. The hippocampus and the amygdala have been shown to be decreased in volume in people with depression.

Reduced hippocampal volume is associated with longer, prolonged (even lifetime) depression, and repeated stress during recurrent depressive episodes may result in cumulative hippocampal injury reflected in volume loss of the hippocampus.

Studies to date have shown that depression is associated with structural changes in the hippocampus, thalamus, amygdala, and frontal and prefrontal cortices, with large volume reductions in the anterior cingulate and orbitofrontal cortex and moderate reductions in the hippocampus, the putamen and the caudate.

Interestingly, clinical improvement is believed to be associated with reversal of structural changes – patients who experience remission have larger hippocampal volumes compared with patients who have not experienced remission. At this stage, these structural changes are observations; more studies are being done to learn more about the relationship between hippocampal volume and depression.

Damage to the neural connections between some regions of the brain can result in depression. For example, a traumatic head injury or multiple tiny areas of damage due to disrupted blood flow in the brain can disrupt connections and lead to depression. Evidence suggests that stress hormones play an important role in the development of psychiatric disorders like depression and anxiety, as well as having direct effects on serotonin-related pathways. Serotonin is the principal neurotransmitter implicated in depression, and this is why antidepressant medications are largely aimed at modulating serotonin.

Over the years, the prevailing view about depression has been that it resulted from a deficiency of the neurotransmitters serotonin or noradrenaline. Antidepressant medications 'selective serotonin reuptake inhibitors' or SSRIs were developed, aimed at increasing the availability of these neurotransmitters around synapses. However, this is not the whole story, which explains the often-disappointing effects of antidepressant medications, especially in mild to moderate depression, and the abundant side effects.

Dopamine is a neurotransmitter that is intimately associated with the ability to experience pleasure and motivation. Dysfunction of dopamine transmission in the reward circuit is associated with symptoms such as the inability to experience pleasure, difficulty concentrating, apathy and dysphoria (disturbed mood).

Noradrenaline is associated with the fight or flight response and is another neurotransmitter implicated in regulation of emotion, with depleted levels in depression. Chronic stress can cause noradrenaline levels to fall. Antidepressant medications called serotonin-noradrenaline reuptake inhibitors (SNRIs) may be prescribed to relieve symptoms of depression. They work by inhibiting the reuptake of serotonin and noradrenaline by neurons, and as a result make more of these neurotransmitters available for use by neurons.

In reality, it is likely that many chemicals are involved in depression, both inside and around the outside of neurons and in multiple parts of the brain, in determining your mood and perceptions of the world.

Research is focussing on identifying the genes that increase vulnerability to depression and that will help to guide specific and more targeted drug treatments.

THE ROLE OF THE GUT

We know that the Brain–Gut Microbiome Axis (the complex and fascinating two-way interaction between the brain, the gut and its microbiome through the nervous system, endocrine system and immune system) has a significant influence on brain function, including cognition and moods.

Evidence is emerging that the gut and its microbiome have a strong association with mental wellbeing. We do not yet fully understand the mechanism. Future possibilities include using probiotics to influence mental health.

We know that people with inflammatory diseases are more likely to experience depression, and that one in five people with inflammatory bowel disease have sleep disturbances and other symptoms of depression.

Stressful events can alter the microbial composition and diversity of the gut flora leading to depressive symptoms.

We have a long way to go in understanding which gut microbiome patterns are related to depression, and it is an active area of clinical research to define these patterns and to work out the best ways to manipulate the gut flora to change its interaction with the brain and thereby to relieve depression and other mental health problems. Of course, there are many variables when it comes to the experience of depression. Your history of stressors, your genetics, your personal coping strategies and resources, and your close social supports will all have an influence on your vulnerability to depression and its clinical course.

TREATMENTS

The treatment of mental health conditions like depression has always been challenging. Treatment needs to be individualised based on each person’s early life experiences, their personal

preferences, the likelihood that a therapy will be effective, the availability and affordability of therapies, and the severity of the symptoms.

Early and persistent intervention is important because bouts of longer-lasting depression can result in persisting dysfunction in memory, executive function, attention, mood and emotional regulation.

Talk therapies

Treatment of depression and anxiety needs to be comprehensive and integrative. It is not enough to prescribe an antidepressant and expect that to solve the problem. Talk therapies are the starting point. These techniques aim to explore the possible triggers, to guide the person with depression or anxiety into an understanding of any underlying issues and to help them develop the skills to think differently. We know that treatment processes such as cognitive behaviour therapy (CBT) can themselves create lasting changes in emotional states and in brain function. The specific changes in the brain brought about by psychological therapies are still in the process of being mapped.

Mindfulness and meditation

Mindfulness and meditation are important practices in the treatment of depression. Research shows that after practising mindfulness, the grey matter in your brain's amygdala – a region known for its role in stress, fear and anxiety – can become smaller.

A study known as the PREVENT trial showed that a mindfulness-based psychological therapy called mindfulness based cognitive therapy (MBCT) was as effective as antidepressant medication in preventing further relapses in recurrent depression.

Exercise

We know that regular exercise helps to relieve mild to moderate depression. The greatest improvements are achieved through rhythmic, aerobic exercises, using large muscle groups (jogging, swimming, cycling, walking), at moderate and low intensity.

Yoga is a part of the Indian Ayurvedic tradition. It may involve a single activity or a combination of activities including relaxation (*shava asana*), physical postures (*asana*), breathing regulation techniques (*pranayama*) and meditation (*dhyana*).

Yoga practice has been shown to help to manage depression and to relieve depression symptoms. It also improves flexibility, reduces muscular aches and pains, reduces breathing and heart rate, lowers blood pressure and cortisol levels, and helps with the management of stress and anxiety.

Spirituality

Having an active search for meaning, including having a supportive and positive religious or spiritual dimension to one's life, appears to be protective against mental health problems. It can also help you to recover more quickly or to cope better if mental health problems do arise.

Medication

Depression and anxiety are complex multifactorial mental health issues. Various types of antidepressant medication are available. It is not always possible to pick the right antidepressant medication first time, and until we are able to match an individual's particular genetic type or chemical imbalance with a medication targeted to that specific

imbalance or gene type, in clinical practice there is a need to trial the medication most likely to help, and then to monitor for effectiveness and side effects. Stopping medication or changing doses should only be done under careful medical supervision.

The evidence shows us that antidepressant medications are not particularly effective for mild to moderate depression, but are more effective for severe depression. Evidence about the effectiveness of antidepressant medications has been conflicting and controversial. Here's what we know:

- Psychological therapies such as cognitive behaviour therapy and interpersonal therapy are as effective as antidepressants for mild to moderate depression and should be tried first before medication is considered.
- Antidepressants are effective in severe and chronic depression, but probably not in mild to moderate cases.
- Exercise and stress management also make a difference to all grades of depression.
- Different medications suit different people. We do not yet have a sure-fire way of selecting the right medication first time for each individual.
- Side effects are common. Some side effects are temporary, some are not.
- If you plan to stop taking an antidepressant, it should be gradually reduced over several weeks under medical supervision to avoid withdrawal effects or relapse.

Anxiety-relieving medications in the benzodiazepine class have come under intense scrutiny in recent years. They provide short-term symptomatic relief of anxiety symptoms but have a strong tendency to cause dependence and so are not suitable for long-term management of anxiety.

NUTRITION, HERBS AND SUPPLEMENTS

Nutrition is important to brain health and optimal function, and therefore also to mood stability. Correcting diet is the first step (see chapter 24: Brain Food).

Supplements may be necessary to overcome deficiencies and for their therapeutic effect. Some specific nutritional supplements show promise as therapeutic agents that should be considered in depression, but a nutritionally rich diet is far more beneficial than a poor diet boosted with nutritional supplements.

Folate: It has been estimated that 15 to 38 per cent of depressed people also have a folate deficiency. Low dietary folate, low folate levels in blood and a MTHFR C677T gene type (see page 230) are all independently associated with increased risk of depression. There is evidence of a reduced response to the commonly prescribed antidepressant fluoxetine (Prozac) with declining folate levels. Preliminary studies have also shown folate to be useful in the treatment of major depressive disorders. Food sources include tomato juice, green beans, broccoli, spinach, asparagus, okra, black-eyed peas, lentils, and navy, pinto and garbanzo beans.

SAMe (s-adenosyl-L-methionine): SAMe may raise levels of the neurotransmitter dopamine. SAMe is superior to placebo, as effective as tricyclic antidepressants, and better tolerated in the treatment of depressive disorders, but may have significant side effects. SAMe is not be taken without medical supervision. The body usually manufactures all the SAMe it needs from the amino acid methionine, which is found in ordinary dietary sources such as meat, soybeans, eggs, seeds and lentils.

Foods high in B vitamins, particularly B6, have long been thought to help with prevention of depression. Foods rich in a

range of B vitamins include potatoes, bananas, lentils, chillies, tempeh, liver, turkey, spinach, broccoli, mushrooms and tuna.

5-HTP (5-hydroxytryptophan): This is an amino acid that is used to make serotonin and melatonin, and can enhance mood and sleep. Foods that contain the amino acid tryptophan can help raise levels of 5-HTP. Such foods include red meat (beef, pork, lamb and wild game), poultry (chicken and turkey) and seafood (tuna, salmon, halibut and shrimp), as well as cottage cheese, Swiss cheese, peanuts, cashews and avocados. Vitamin C assists in the production of 5-HTP and is an excellent antioxidant. You have to be careful because combining 5-HTP with antidepressant medication may cause a severe reaction.

HERBAL MEDICINES

People with anxiety and depression commonly self-prescribe herbal medicines to relieve their symptoms based on advice from friends, or their own internet research about what might help. Herbs can interact with pharmaceutical medicines so it is important to get advice from a practitioner who is trained in this area.

One of the most commonly prescribed herbs for countering depression is St John's wort.

A Cochrane Review found that St John's wort extracts work better than placebo in patients with major depression with fewer side effects than pharmaceutical antidepressants. Due to the low incidence of side effects it is not unreasonable to start with a therapeutic trial. St John's wort is a well-tolerated medicine with few side effects; however, drug interactions are possible, so talk to your GP or pharmacist if you are considering this herbal medicine.

Many herbs relieve anxiety. One review reported that the commonly used traditional herbs with varying levels of

evidence for alleviating anxiety include: kava (*Piper methysticum*), chamomile (*Matricaria recutita*), valerian (*Valeriana officinalis*) (often combined with lemon balm (*Melissa officinalis*) or with St John's wort (*Hypericum perforatum*), passionflower (*Passiflora incarnata*), rhodiola (*Rhodiola rosea*), *Bacopa monneiri*, *Centella asiatica*, *Withania somnifera*, and *Ziziphus jujuba var. spinosa*.

If you want to use herbal medicines to manage depression or anxiety, make sure you have professional advice on doses and combinations, and that your medical advisors are aware of what you are taking.

Repetitive transcranial magnetic stimulation (TMS)

Transcranial Magnetic Stimulation (TMS) is a relatively new non-drug treatment for major depression. TMS is an evidence-based treatment that has the potential to relieve symptoms and avoid antidepressants. It is also free of the adverse effects of electroconvulsive therapy (ECT), such as reduced memory and concentration.

TMS uses pulses of magnetic fields over carefully selected areas of the brain that are responsible for depression. There has been clinical experience with this technology in the United States and Europe over the past decade, allowing researchers to gather evidence of its effectiveness. It was approved for use in Australia in 2007, but has not been widely available. It is also endorsed by the Australian and New Zealand College of Psychiatrists.

This treatment is not free of side effects, which might include mild headache, lightheadedness and scalp pain. It is not covered by Medicare.

The usual treatment protocol is one session three to five times a week for four to six weeks.

Electroconvulsive Therapy (ECT)

Who can forget the scene in the 1975 movie *One Flew Over the Cuckoo's Nest* when Jack Nicholson's character undergoes electroconvulsive therapy (ECT) without anaesthetic, being held down by medical attendants as he has a medically-induced seizure.

ECT is still used today for the treatment of medication-resistant and life-threatening depression, but it is not delivered in the way it is portrayed in the movie. It is delivered in controlled doses under general anaesthetic and muscle paralysis, with the induced seizure activity being seen only on an electroencephalogram (EEG) or brain-wave monitor.

Why ECT works is still unclear. It is thought that the electric currents alter brain chemistry but the details are sketchy.

What is even more unclear is why anyone in the medical profession thought to try doing it in the first place.

It has some significant side effects, including headaches and confusion and, more worryingly, memory loss. That said, in severe unremitting cases of depression it may be a life-saving measure.

> If you know someone who's depressed, please resolve never to ask them why. Depression isn't a straightforward response to a bad situation; depression just is, like the weather.
>
> Try to understand the blackness, lethargy, hopelessness, and loneliness they're going through. Be there for them when they come through the other side. It's hard to be a friend to someone who's depressed, but it is one of the kindest, noblest, and best things you will ever do.
>
> – Stephen Fry

Resources:

Lifeline 13 11 14

Beyond Blue 1300 22 46 36 or www.beyondblue.org.au/about-us/contact-us

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Dementia

‘person woman man camera TV’

– President Donald Trump, 2020

Imagine for a moment that you are facing older age. You may have been university educated, had a successful career, raised your children and experienced the joy of grandchildren. You have faced life’s challenges and are looking forward to a long retirement with travel, family, friends, and volunteer work for causes you care about.

Then one day you realise that you have started forgetting people’s names, just occasionally at first. Your partner tells you that you have been repeating stories, apparently unaware that you have already had that conversation. You can’t remember where you put your car keys. At first you think you’re just being distracted and brush it off. Gradually, however, you realise that something is not right.

As time goes by you become embarrassed and distressed by the fact that you can’t recall information you know you ‘should’ be able to recall. You can’t find your way home from a familiar place. You make mistakes with your household paperwork.

Concerned family members try to suggest having a medical check-up because you don't seem yourself lately. You see your GP, who does a screening test. The results suggest there is a problem with your short-term memory, and your GP recommends that you see a specialist. By now you are really anxious and uncertain, and becoming distressed about what this might mean for your future.

Then the day comes when your fears are realised: the specialist tells you that tests show that you have Alzheimer's disease. Suddenly you are discussing prognosis and time frames and living with dementia and future planning for care. The specialist tells you that there is a medication to increase the amount of the neurotransmitter acetylcholine in your brain. It may slow your decline, but there is no cure.

You try to process the shock and worry about what that means for you and those closest to you.

Dementia is sometimes called 'the long goodbye', because the person diagnosed with dementia gradually becomes detached from their previous daily life.

From the perspective of loved ones, dementia is the gradual loss of the person they knew, both mentally and physically. It is a difficult adjustment that requires a lot of support.

In an interview on Fox News with medical reporter Dr Marc Siegel in July 2020, President Donald Trump famously repeated the words 'person woman man camera TV' several times to demonstrate that he had undergone a basic screening test for cognitive impairment, saying that his doctors had found his performance 'amazing'. It takes a bit more than that to 'amaze' us doctors, but it is nonetheless a good idea to undergo an assessment for cognitive impairment if there are concerns about your thinking or judgement.

The initial screening test used by general practitioners is called the Mini Mental State Exam, or MMSE, which involves a series of 30 simple questions and tasks. One of those tasks is to repeat a sequence of random words and then later recall them, hence the 'person woman man camera TV' example.

If your test makes cognitive impairment unlikely, you can focus on your general health and, more specifically, on all the things you can do to support your brain health.

The most important reason for confirming mild cognitive impairment is my reason for writing this book – because it is so important to recognise, diagnose and identify any reversible or treatable causes, and intervene at an early stage wherever possible.

If a cognitive impairment is found to be the early signs of a progressive condition that currently cannot be cured, again, it is important to know what you are dealing with so you can take action to slow the progression and put in place support structures and services to meet your needs and plan for the future.

When I ask middle-aged people what their greatest concern is about ageing, losing their cognitive ability is often right up the top of the list. It is a particularly potent fear for anyone who has had a close family member or friend suffer from cognitive impairment or dementia. Brain health is key to independence in older age.

It is worth spending a little time understanding the meaning of the terms we hear used to refer to loss of cognitive ability. For example, there is a difference between cognitive impairment and dementia, and between the different types of dementia.

COGNITIVE IMPAIRMENT

Cognitive impairment or cognitive dysfunction are broad terms that include many areas of brain function, such as memory, learning, mental flexibility, attention and executive function.

Mild cognitive impairment (MCI) is a state between normal cognition or thinking ability, where there is still the ability to function normally, and dementia.

There are cognitive changes that can occur as part of the ageing process, but these are not the same as MCI or early dementia.

Both mild cognitive impairment and mild dementia are relatively common with advancing age. Just how common? After the age of 70, numerous studies tell us that approximately 14 per cent of people have cognitive impairment warranting a diagnosis of dementia, and about the same number have cognitive impairment that does not meet the definition of dementia.

Dementia is diagnosed when cognitive impairment or cognitive dysfunction has become severe enough to compromise a person's ability to perform their work, or manage social situations or their usual daily tasks.

In both mild cognitive impairment and mild dementia there will be signs such as trouble remembering names or events or learning new things, difficulty concentrating or organising daily life. Making the distinction between these two problems is a matter for a specialist to assess.

The main aspect that will determine whether the diagnosis is mild cognitive impairment or mild dementia is that in mild dementia, more than one area of cognition is involved, and in dementia there is substantial interference with daily life.

DEMENTIA

‘In 2019, there [are] an estimated 447,115 Australians living with dementia. Without a medical breakthrough, the number of people with dementia is expected to increase to 589,807 by 2028 and 1,076,129 by 2058.’ These sobering statistics about this debilitating condition come from Dementia Australia.

Dementia is not one single disease. The term dementia refers to a deterioration of intellectual capacity and personality changes caused by damage to neurons in the brain. The common features of the condition we call dementia include:

- loss of memory affecting daily functioning
- reduced intellectual ability
- difficulty with communication and social skills
- impaired judgement
- difficulty performing familiar tasks like shopping, managing a household, paying bills, dressing and other forms of self-care.

Age is the biggest risk factor, but advancing age is not the only thing that increases the likelihood of developing one of the types of dementia.

Many of the risk factors for some types of dementia are modifiable, meaning that you can change your behaviour or habits in order to manage areas of risk and make a difference to the rate of progress or outcome of the disease.

RISK FACTORS FOR DEMENTIA

Identified risk factors for dementia include:

- advancing age
- mild cognitive impairment
- family history of dementia
- history of smoking or excessive alcohol consumption
- high cholesterol
- cardiovascular disease
- cerebrovascular disease (including stroke)

- diabetes mellitus, or midlife obesity
- use of anticholinergic medications (see chapter 6: Medications)
- Apolipoprotein e4 genotype
- lower education level.

Some, though not all, of these risk factors are things you can do something about.

Having a family history of Alzheimer's disease increases the risk of developing the disease. However, it is important to understand that many people with a family history of Alzheimer's disease do not go on to develop the disease, and many people with no family history do.

For example, people with the Apolipoprotein e4 genotype have a higher risk of developing Alzheimer's disease, but the majority of people with that genotype do not develop the disease. To add to the uncertainty, a genetic test will identify if you have the gene, but results cannot predict whether you will develop Alzheimer's disease (see chapter 3: DNA Predictions of Dementia). It is important to see the risk in perspective, scary as it is.

Other forms of dementia can also have an inherited risk component, such as Huntington's disease.

Diabetes increases the risk of vascular dementia and Alzheimer's disease, so I cannot stress enough the importance of early diagnosis, expert management and careful control of blood sugar levels, and other cardiovascular risk factors. (See chapter 11: Glucose.)

Some components of mild cognitive impairment may be treatable. This means it is important to recognise it, distinguish it from early or evolving dementia, diagnose any underlying cause as well as any other health issues, and do what you can to intervene or provide the best possible healthcare and social support.

If you suspect that you or someone close to you has early signs of dementia, the first step is to see your GP for a full medical assessment. Some medical conditions, such as depression, may mimic the early signs of dementia. Your GP is likely to arrange a referral for specialist neuropsychological assessment and imaging such as a brain MRI.

Depending on the diagnosis and how early in the disease process it is, there may be actions you can take to stop or slow the progression, remembering that cognitive impairment and dementia are inextricably linked to the functions and dysfunctions of your whole body.

Some of the more common types of dementia include:

- Alzheimer's disease
- vascular dementia
- Lewy body dementia
- frontotemporal dementia
- alcohol-related dementia.

ALZHEIMER'S DISEASE

Alzheimer's disease is the most common form of dementia.

The early signs of Alzheimer's disease usually include difficulty remembering the details of recent conversations, names or events. Depression and apathy, irritability, disorganisation, impaired judgement and difficulty making decisions are also frequent features in the early stages of Alzheimer's.

Some causes of Alzheimer's disease have a known genetic influence. There are so-called risk genes, such as Apolipoprotein e4, the presence of which indicates an increased risk of dementia, but does not mean that developing dementia is inevitable.

Then there are the so-called deterministic genes:

- amyloid precursor protein (APP)
- presenilin-1 (PS-1)
- presenilin-2 (PS-2).

The presence of one of these deterministic genes means that the person will inevitably develop dementia.

What is happening in the brain?

I will attempt to give you a simple explanation of our current knowledge of the pathophysiology of Alzheimer's disease. This is an evolving area of knowledge, and while science has discovered many pieces of the dementia puzzle, the keys to its causes and possible cures remain elusive. There is still some deliberation about whether the changes seen in the brain of a person with Alzheimer's disease are the cause or the result of the disease.

To begin with, it seems that there is an initial injury or insult to the brain. This is in the form of inflammation in the presence of exposure to toxins and a deficiency of nutrients needed to maintain brain function.

The confluence of factors triggers a protective response, the formation of clumps or plaques of beta-amyloid. There is a failure of microglial cells to clear away inflammatory debris, including beta-amyloid plaque.

This in turn may trigger the formation of neurofibrillary tangles of tau protein inside neurons. Normal tau protein is found in neurons in the brain and forms a part of structures called microtubules, which are responsible for transporting nutrients and other substances from one part of the brain to another.

In a number of neurodegenerative brain diseases, including Alzheimer's disease, tau proteins detach from microtubules and collect with other tau proteins, forming threads that turn into tangles which block the neuron's transport system. This in turn damages the communication between neurons. In the case of Alzheimer's disease, it appears that the abnormal tau protein accumulates in the parts of the brain responsible for memory.

Accumulation of abnormal tau tangles may continue, even if beta-amyloid plaque is removed. There is a corresponding reduction of the neurotransmitter acetylcholine in the brain. Ultimately, there is disruption of the connections between neurons, the widespread death of neurons, and shrinkage of some areas of the brain.

At a tipping point, the progression to Alzheimer's disease becomes inevitable.

The Holy Grail of Alzheimer's research is to find some way to prevent a person from reaching that tipping point, or even to reverse the disease once it has been diagnosed.

Disappointingly, the development of drugs to target the formation of amyloid plaque has so far not produced any results.

Neurologist Dr Dale Bredesen and his team at University of California Los Angeles (UCLA) published reports of an evidence-based program for reversing cognitive decline in some people with early Alzheimer's disease and its precursors, MCI (mild cognitive impairment) and SCI (subjective cognitive impairment). They reported on a number of personalised interventions that showed not only reversal of cognitive decline but also recovery of lost hippocampal volume. (Personalised interventions mean that treatment is based on each individual's health, condition, level of cognitive impairment and lifestyle.) They achieved these improvements

with a comprehensive approach to nutritional, metabolic and other lifestyle factors.

Large-scale trials are needed to fully assess the results of these interventions. Studies of comprehensive programs with multiple personalised interventions are difficult, although not impossible, to design.

Given the devastating implications of unchecked cognitive decline, making changes to the way you live and any habits that are contributing to that decline becomes urgent.

That is the purpose behind this book – to have you thinking about brain health as early in your life as possible, preferably before the onset of any cognitive decline, and to realise that, based on our current understanding of Alzheimer's disease, there may be no second chances.

Advancing age is the major risk factor for Alzheimer's disease, but it is not the only risk factor, so it is important to understand some of the lifestyle factors that may reduce the risk of Alzheimer's disease developing, or reduce its severity.

As discussed on page 181, with Alzheimer's disease commonly have other changes in the brain, particularly vascular changes. Alzheimer's disease is directly associated with cardiovascular risk factors and cerebral small vessel disease (CSVD).

Alzheimer's disease and cardiovascular diseases share a common risk factor: elevated blood levels of homocysteine, an amino acid, caused by inadequate dietary intakes of vitamins B2, B6, B9 (folate) and B12. Elevated homocysteine is a strong independent risk factor for Alzheimer's disease; people with the highest homocysteine levels have been found to have almost double the risk of dementia.

One study found that, compared with people with normal levels of both vitamins, subjects with low levels of B12 or folate had double the risk of developing Alzheimer's disease.

Multivitamins reliably lower homocysteine in most if not all cases; they are the only ‘therapy’.

So there is crossover between Alzheimer’s disease and vascular dementia, and addressing cardiovascular risk factors will provide some benefit, optimising blood flow, and oxygen and nutrient delivery to the brain.

As things stand, there is no cure for Alzheimer’s disease and despite substantial research efforts, medication can at best help reduce some of the symptoms, such as memory loss and confusion.

The difficult truth is that in over a decade, more than 100 medications have been tested and only three brought to market, with minimal effectiveness.

There are two main medications approved for use in Alzheimer’s disease: donepezil (Aricept) and memantine. Donepezil is a cholinesterase inhibitor. It is designed to stop cholinesterase (an enzyme) from destroying the neurotransmitter acetylcholine (see chapter 1: How Your Brain Works). While this makes more acetylcholine available, it does not have an effect on the underlying disease. In addition, the brain can respond by making more of the cholinesterase. Memantine inhibits the neurotransmitter glutamate, and is usually not prescribed until later in the course of the disease.

Neither of these drugs influences the underlying pathology, so unless there is some intervention, the disease continues to progress regardless.

At this stage, medication is at best only minimally effective in delaying the progression of dementia once the process has begun. This makes it all the more important for you to do whatever you can to protect your brain function throughout life.

POSSIBLE ALZHEIMER’S CURE?

Researchers from Tel Aviv University, Israel, are working on a nasal vaccine that could reverse Alzheimer's disease and possibly other neurodegenerative diseases.

The vaccine research is based on naturally occurring micro-organisms (live viruses) called bacteriophages.

In mice tests the nasal spray proved highly effective at dissolving beta-amyloid plaque and improved cognition (shown by improved ability to run mazes and other tasks) and increased sense of smell. M13 virus could also dissolve the tau tangles found in Alzheimer's and the amyloid plaque associated with other diseases, including alpha-synuclein (a neuronal protein that regulates synaptic vesicle neurotransmitter release) in Parkinson's disease.

There is a long way to go to prove safety and effectiveness in humans, but it is cause for hope.

VASCULAR DEMENTIA

Vascular dementia is the second most common form of dementia diagnosed after Alzheimer's disease.

Some people have both vascular dementia and Alzheimer's disease. The term vascular refers to blood vessels.

Blood vessels supply all tissues of the body with oxygen and nutrients. If there is disease of the blood vessels, that blood supply is threatened. The tissues of the brain are nourished by a complex network of small blood vessels. The condition cerebral small vessel disease (CSVD) causes a range of different types of pathology in the brain due to disease in these small vessels. The diseased blood vessels become narrowed, resulting in low oxygen supply and ischaemia and infarction (tissue death), disruption of the blood–brain barrier, inflammation and possible microbleeds.

The brain does not have a lymphatic system, but it has the glymphatic system. The glymphatic system is a waste clearance system in the brain that works mainly during sleep to clear the brain of waste products, including amyloid and tau proteins. It also distributes glucose, lipids, amino acids and

neurotransmitters. It is thought that failure of glymphatic function to clear waste products is as an important factor in the development of CSVD.

CSVD is a significant finding because in addition to being the second most common cause of dementia, it more than doubles the risk of a recurrent stroke, contributes to almost half of all dementia cases, and causes more than a quarter of ischaemic strokes. It is also associated with apathy and the mood disorder known as vascular depression.

It is important to note too that Alzheimer's disease and vascular dementia can be present in the same person. The significance of this is that the vascular component may be able to be modified, affecting the rate of cognitive decline.

Vascular dementia becomes more common with age, along with other chronic health conditions. In the case of CSVD, it is present in 20 per cent of people under 75, but in 65 per cent of people aged over 75.

Diagnosing early-stage vascular dementia is challenging. An elderly patient may present to their doctor with unexplained dizziness or unsteadiness. They may have noticed problems with memory or concentration.

More commonly, changes may be seen incidentally on an MRI scan of the brain, or on an MRI scan that was arranged to investigate headache, dizziness or cognitive impairment, or another neurological symptom.

An MRI may show up changes reported as 'white matter hyperintensities'. If these changes are noted in an MRI brain report, they are significant. They are associated with cognitive impairment, and their presence triples the risk of stroke and doubles the risk of dementia.

The risk factors for CSVD are pretty much the same as for cardiovascular disease:

- a family history of vascular (blood-vessel) disease,
- high cholesterol,
- hypertension (high blood pressure),
- smoking,
- diabetes and
- sleep apnoea.

Elevated homocysteine levels are an independent risk factor for vascular cognitive impairment and dementia, causing dementia because elevated homocysteine causes vascular damage. Low folate and vitamin B12 levels result in elevated homocysteine. For this reason, it is important to maintain adequate intake of folate and vitamin B12. While the evidence has not yet shown that lowering homocysteine using B vitamins has a protective effect against dementia, it is a safe and simple strategy.

Your regular medical check-ups should include testing for diabetes and cholesterol. Elevated LDL or 'bad cholesterol' needs to be treated with diet and exercise, and possibly medication, to lower cholesterol.

Elevated blood sugar or insulin resistance also needs to be rigorously managed (see chapter 11: Glucose). The mainstays of treatment are physical activity and dietary changes.

If high blood pressure is suspected, or detected at a medical visit, you will most likely be referred for 24-hour ambulatory blood-pressure monitoring. This involves wearing a blood-pressure cuff and recording device for 24 hours, giving us a real-time, real-life measurement of your blood pressure during your usual daily routines.

Obviously, stopping smoking is not negotiable.

If sleep apnoea is suspected, we arrange for a sleep assessment. If the diagnosis of sleep apnoea is confirmed, then

we arrange a continuous positive airways pressure (CPAP) machine to be worn at night to keep your breathing regular.

Risk factors tend to overlap and interlink, too. Risk factors for sleep apnoea include being overweight or obese, smoking and excessive alcohol intake. I have seen many patients start out with a CPAP machine, and they have been able to stop using it once they have reached their healthy weight range and stopped smoking.

A supervised exercise and rehabilitation program is important for general health and for avoiding falls.

Adopting a holistic approach, it is also essential to check for osteoporosis because of the risk of falls due to unsteadiness. A fall with osteoporosis brings a greater risk of a hip fracture.

The importance of identifying CSVD and early-stage vascular dementia is that its progression can be slowed with rigorous attention to risk management.

LEWY BODY DEMENTIA

In Lewy body dementia, abnormal spherical structures called Lewy bodies are deposited inside neurons in parts of the brain responsible for memory and movement. Lewy bodies are made of an abnormal protein called alpha-synuclein.

Along with the Parkinson-like movement disorder (tremors, stiffness and slowed movements) increasing the risk of falls, people with Lewy body dementia may come in and out of a confused state and have difficulty concentrating. They may ‘see things’ – that is, have delusions (psychosis) or hallucinations due to decreased levels of the neurotransmitter acetylcholine in the temporal and parietal cortex.

Dopamine levels also decrease resulting in depressed mood, and problems with memory, motivation and

concentration.

Lewy body dementia may appear as Parkinson's disease or dementia with Lewy bodies. It may be difficult to differentiate from Parkinson's disease because people with Parkinson's can develop dementia similar to that seen in Lewy body dementia.

The latest expert advice set an arbitrary '12-month rule' to differentiate Lewy body dementia from Parkinson's disease with dementia. If the person has had Parkinson's disease symptoms for 12 months or longer before any cognitive impairment is noticed, then the disorder is most likely Parkinson's disease with dementia. If the dementia develops in less than 12 months, then the disorder is Lewy body disease. In most cases of Lewy body dementia, the dementia precedes the motor signs.

Lewy body dementia also shares many common features with Alzheimer's disease. It can occur in addition to and alongside the changes of Alzheimer's disease or vascular dementia.

Treatment is aimed at easing symptoms and maintaining function for as long as possible.

There are some pharmacological options:

- Cholinesterase inhibitors used in Alzheimer's disease: rivastigmine, galantamine and donepezil to help with cognitive impairment.
- Carbidopa-levodopa used in Parkinson's disease for the similar movement disorders of Lewy body disease. Unfortunately these medications can trigger hallucinations, delusions and confusion, so they are used with caution.
- Other drugs sometimes used include SSRI antidepressants or antipsychotics.

The progression of the disease is fairly rapid, and life expectancy is five to eight years after diagnosis.

FRONTOTEMPORAL DEMENTIA

The frontal and temporal lobes of the brain are responsible for personality, social behaviour, judgement, self-control and language expression.

In frontotemporal dementia, we see shrinkage in parts of the frontal and temporal lobes. The damage to brain cells in these parts of the brain is thought to be caused by accumulation of abnormal proteins tau and TDP-43.

Changes in these parts of the brain cause a loss of their normal structure and function and result in:

- change in personality
- socially inappropriate behaviour, including loss of inhibition
- poor self-care and personal hygiene
- mood changes
- poor judgement and inability to reason or plan
- repetitive compulsive behaviour
- difficulty recognising familiar objects or people
- difficulty with speech and language expression, including reading, spelling and language comprehension.

The main early signs of frontotemporal dementia are changes in personality, behaviour and emotional regulation, rather than the memory loss you see in other forms of dementia. There may also be a loss of language ability.

Anyone showing these signs should be referred to a specialist such as a neurologist, a psychiatrist with a special interest in dementia or a geriatrician for a full assessment.

ALCOHOL-RELATED DEMENTIA

Alcohol-related dementia is most likely a combination of a direct toxic effect of alcohol on brain cells over time, and a result of alcohol-related vitamin deficiencies, particularly thiamine.

If brain damage is evident but the symptoms fall short of a dementia diagnosis, this may also be referred to as alcohol-related brain damage.

Where thiamine deficiency due to chronic excessive alcohol is an underlying cause, you will see it referred to in the medical textbooks as Wernicke's encephalopathy, Korsakoff's syndrome or Wernicke–Korsakoff syndrome. Although these three conditions have a common cause, there are differences between them.

Wernicke's encephalopathy is an acute form of alcohol-related brain damage caused by undernutrition and particularly thiamine deficiency. I have seen this syndrome in clinical practice. The condition was first described back in 1881 by Carl Wernicke. Sufferers will experience confusion along with double vision or jerking eye movements, poor balance and loss of coordination with a staggering gait.

The symptoms can come on quite rapidly. They must be treated as an emergency, preferably within hours of onset, with injections of high doses of thiamine, because the symptoms can be reversed if you catch it early.

If treatment is delayed, the person may die or only partially recover.

Korsakoff's syndrome was described back in 1887 by Russian neuropsychiatrist Sergei Korsakoff. This condition develops more gradually, and may follow Wernicke's encephalopathy as an irreversible residual condition. The areas of the brain responsible for short-term memory are affected.

People with Korsakoff's syndrome suffer an irreversible severe amnesia, may make up stories to cover their memory

loss (a symptom called confabulation) and may experience hallucinations. In a person who has developed Korsakoff's syndrome, the memory loss is largely irreversible. If they continue to drink alcohol and do not address the underlying nutritional deficiencies, the condition becomes progressive.

As alcohol-related dementia develops, it can be recognised by changes in personality, problems with short-term memory and learning, difficulty with balance, personality changes, and impaired judgement and social skills.

The treatment for Wernicke–Korsakoff syndrome and alcohol-related brain damage is complete abstinence from alcohol forever, along with a healthy diet and vitamin supplementation.

A brain affected by alcohol will need nutritional support including the following micronutrients, with professional advice on doses:

- B vitamins: vitamin B1 (thiamin), vitamin B2 (riboflavin), vitamin B3 (niacin), pantothenic acid, vitamin B6 (pyridoxine), vitamin B12, vitamin B9 (folate)
- calcium
- chromium to assist blood sugar balance by facilitating the action of insulin. Refined grains and simple sugars cause chromium loss.
- iron (check first for deficiency and to exclude overload condition haemochromatosis)
- magnesium
- manganese
- omega-3 fatty acids from food (fish, flaxseed oil) or supplements
- potassium
- vitamin C

- zinc.

How much alcohol does it take?

There is no ‘safe’ level of alcohol consumption and it is not possible to pick who is going to develop alcohol-related brain damage. The recommendation is for a maximum of two drinks a day, with a couple of alcohol-free days a week. However, males who habitually drink more than six standard alcoholic drinks a day for many years, and women who drink more than four (equivalent to half a bottle of wine) a day, are at increased risk of developing alcohol-related dementia.

This can all be confusing, given the occasional media reports that drinking alcohol can be ‘good for your brain’. However, this has been disputed by a review of evidence, and is not a reason to take up drinking if you are a non-drinker.

Alcohol-related dementia is at least partly reversible in the early stages if the condition is recognised, alcohol consumption stops, and nutritional deficits are corrected with diet and supplements.

PROTECTING YOUR BRAIN AGAINST COGNITIVE IMPAIRMENT

We do not yet know how to prevent or slow the progression of some forms of dementia, but there are positive lifestyle changes that will help to protect your brain health from some forms of cognitive impairment. These changes will improve your general wellbeing, too. Perhaps the most obvious lifestyle risk factor is smoking, which we know causes damage to blood vessels, including the blood vessels in the brain, contributing to the development of cerebrovascular disease, or damage to the blood vessels that supply the brain. These are the changes that lead to vascular dementia and that can complicate other forms of cognitive impairment and dementia.

It is also important to check whether any medications or the other dementia mimics (see chapter 16: The Dementia Mimics) might be creating the appearance of cognitive impairment.

Reversible or treatable causes of cognitive impairment include taking anticholinergic medications, taking multiple medications with potential to affect brain function, depression, underactive thyroid, urinary tract infection, increased calcium levels, benign brain tumour, normal pressure hydrocephalus and sleep apnoea.

You can also address risk factors to slow the progression of damage to the brain's sensitive structures and functions. Controlling high blood pressure, quitting smoking, controlling the elevated blood sugar of diabetes and fixing nutritional deficiencies are some of the measures you and your doctor can take to slow, stop or reverse the progression of mild cognitive impairment.

For more detailed advice about how you can adjust your diet to improve your brain health, see chapter 24: Brain Food.

Engaging in activities that stimulate your thinking, and taking on new challenges and skills with a commitment to lifelong learning will help to keep your brain functioning optimally. Across populations, it has been shown that there is less cognitive decline in people who have higher levels of engagement in intellectual activity, read, play board games, play a musical instrument or dance.

If you are in a risk group for dementia, there are some principles to follow which will need to be personalised with the supervision of health professionals. These are:

- Optimise nutrition with a healthy wholefoods diet rich in nutrients and micronutrients that we know are essential to brain function. Include fish frequently in your diet.

- Consider micronutrients essential to brain function, including selenium, antioxidant vitamins C and E, transition metals (such as iron and zinc), vitamin D, B-complex vitamins, and omega-3 fatty acids, as well as lean sources of protein, and supplement where necessary under professional supervision.
- Maintain hydration by drinking water.
- Consider a gluten-free or low-gluten diet. This is particularly important if you are shown to be gluten sensitive.
- Don't smoke, as mentioned previously.
- Don't overuse alcohol.
- Maintain good oral health and hygiene (gums and teeth).
- Avoid refined sugar in your diet.
- Achieve and maintain healthy weight.
- Check your insulin level, reduce insulin resistance and maintain optimal blood glucose levels.
- Exercise daily.
- Ensure adequate vitamin D levels through regular sun exposure and/or supplementation.
- Stimulate your brain to increase your cognitive reserve.
- Get enough quality sleep.
- Review your lifestyle to reduce sources of stress.

WHY DIAGNOSE PROGRESSIVE DEMENTIA?

There can be a dilemma about identifying progressive forms of dementia such as Alzheimer's disease or Lewy body dementia, when they are currently considered to be progressive and incurable. I say 'currently' because I believe that in the

coming years we will unravel the puzzle of dementia and find ways of treating, if not curing, the various forms of the disease.

The advantage of a dementia diagnosis at this time in history is that it gives you an idea of what you can do right now to maintain brain function for as long as possible. It also enables you to make some predictions about what you can expect, take steps to put in place whatever supportive measures you might need and make plans for the future.

You may take this time to make sure your legal and financial matters are in order and to be clear about your wishes. It is also important to have a realistic picture of what lies ahead so that you and your support people can make plans for short- and medium-term life goals, planning for the type of care and support you are likely to need, and optimising your physical and mental health.

Resources:

For detailed or specialised advice on different types of dementia and for dementia care support, visit:

Dementia Australia: 1800 100 500

www.dementia.org.au

www.ncbi.nlm.nih.gov/pmc/articles/PMC4221920/#R46

21

Parkinson's Disease

I remember back in 1985, the first *Back to the Future* movie was released. At the time, the star of the movie, Michael J Fox, was 24 years old. Nobody could have predicted that, only five years later, at the age of 29, he would be diagnosed with young onset Parkinson's disease. In what must have been a feat of great courage and determination, he continued his acting career and became an advocate and a source of inspiration for others with the disease, setting up a foundation in his name to support efforts to find a cure.

I remember being shocked that someone so young could be diagnosed with Parkinson's disease, because our medical training taught us to look for this diagnosis in much older people. Indeed, the condition is rare in young adults (although one in ten will be diagnosed before the age of 45), and typically it develops in people in their sixties and beyond. It is estimated to affect ten million people worldwide, and affects men more often than women.

Parkinson's disease is a movement disorder, a neurodegenerative disease of the area of the brain called the substantia nigra. Loss of pigmentation in the substantia nigra in the midbrain and the appearance of Lewy bodies leads to

the death of the cells responsible for producing the neurotransmitter dopamine.

There is no specific test for Parkinson's disease so it is a clinical diagnosis, meaning it is diagnosed by medical examination and assessing symptoms and clinical signs, along with full medical assessment, including neurological examination. While a brain MRI will not be diagnostic, it is arranged to rule out other causes of symptoms.

SYMPTOMS AND SIGNS OF PARKINSON'S DISEASE

At first the symptoms of Parkinson's disease are mild and subtle, and affect one side of the body. Over time, the symptoms become more pronounced and affect other parts of the body.

A slowing of all movements (bradykinesia) is one of the cardinal signs of Parkinson's disease. This leads to difficulty walking. The characteristic feature is difficulty getting started, and then small shuffling steps without arms swinging. Even blinking becomes slower.

A tremor also develops. The resting tremor of Parkinson's disease is described using the illustrative term 'pill-rolling tremor', because it gives the appearance that there is a pill or other small object being rolled between the thumb and index finger. The tremor characteristically starts in one hand.

Loss of facial expression can be one of the earliest signs of Parkinson's – the person looks 'stony-faced', showing little or no facial expression.

Muscle stiffness can also occur in any part of the body. In medical testing we refer to this as 'cogwheel rigidity'. In a clinical examination, when the doctor bends a patient's arm up and down at the elbow, there is a 'stop-start' motion rather

than a smooth gliding motion. There can also be muscle stiffness in any muscle groups in the body, which can be painful.

Fine motor control can also be affected. This can show up as a change of handwriting, where the writing becomes very small.

Speech can become soft or slurred and lose the usual intonations and inflections.

The sufferer may also develop an unstable posture. The posture of Parkinson's disease is described as stooped. Balance problems also develop, with a risk of falls.

The majority of people with Parkinson's disease also suffer from non-motor difficulties such as cognitive impairment, autonomic dysfunction, sensory dysfunction and disordered sleep.

Autonomic dysfunction symptoms involve sexual dysfunction, swallowing and gut disorders, bowel and bladder abnormalities, sleep disturbances, and derangements of cardiovascular regulation, particularly a sudden drop in blood pressure when you stand up from a sitting or lying position.

Cognitive impairment in Parkinson's disease can vary in severity from mild cognitive impairment to dementia. This can show up as difficulty planning and organising or problem-solving, difficulty with memory and attention, and trouble finding the right words. We know that the majority of people with Parkinson's disease develop dementia in the late stages of the disease. The treatment of cognitive impairment and dementia in Parkinson's disease is frustratingly limited, but research efforts continue to look for answers.

About half of people with Parkinson's disease suffer from depression. This is related to the effect of dopamine on mood as well as movement. About 40 per cent of people with Parkinson's disease also suffer from anxiety. A component of

this mood change is likely to be related to feelings about the diagnosis and progressive deterioration in physical ability.

There is no known cause of Parkinson's disease, so there is no known way of preventing it. A family history of the disease increases your risk, and some gene variations have been identified that can contribute to the cause.

There are theories about some of the factors that might trigger the development of Parkinson's disease. A combination of factors are considered likely to be factors in triggering Parkinson's disease in an individual, including genetic and environmental factors such as:

- illicit drug taking with amphetamine-like stimulant drugs.
- pollution.
- medications. For example, more than one year of antidepressant, anxiolytic or hypnotic drugs combined with a family history of Parkinson's has been linked with significantly increased risk of developing the disease, but a cause-and-effect relationship has not been established.
- heavy metals. Many studies have linked Parkinson's disease to the neurotoxic effects of some heavy metals, including chronic exposure to manganese, copper and lead.
- exposure to pesticides. Epidemiological evidence indicates that exposure to pesticides (particularly organophosphates, carbamates, pyrethroids and organochlorides) may also play a significant role in triggering Parkinson's disease.

There has been some fascinating new thinking about the role of the gut microbiome in the early development of Parkinson's disease, with gut disturbances such as constipation evident in some patients up to a decade before the appearance of motor symptoms.

Repeated traumatic brain injury has also been cited as a cause of Parkinson's disease. Boxer Muhammad Ali was an

example. There has also been the more recent recognition of traumatic brain injury in football players, increasing the risk of later developing Parkinson's disease. See chapter 17: Brain Injury for more about the importance of preventing brain injury.

TREATMENT

There are currently two main treatments to help control the symptoms of Parkinson's disease for a period of time: medication and deep brain stimulation.

Medication

The mainstay of treatment is levodopa replacement therapy, combined with carbidopa to reduce side effects from the levodopa. Levodopa is the most common medication prescribed for Parkinson's disease, and the combination with carbidopa is currently the most effective treatment of the symptoms. It is an amino acid precursor of dopamine. A precursor is a substance that is transformed into another substance through a metabolic reaction. Carbidopa inhibits the enzyme that turns levodopa into dopamine, so combining it with levodopa also allows more levodopa to reach the brain from the bloodstream. Taken on its own, levodopa can cause nausea and vomiting. It is taken with carbidopa to limit this side effect. Other side effects include drowsiness, low blood pressure and hallucinations. As the disease progresses, higher doses of levodopa may be needed to control symptoms. The aim of medication is to control symptoms because there is currently no treatment that can reverse the effects of Parkinson's disease.

You may have heard about 'on' and 'off' times. 'On' times are when medication is working well and symptoms are well controlled. 'Off' times happen when medication is wearing off

before the next dose is due. This can happen multiple times a day. Prescribing the right medication at the right doses and at the appropriate stage of the disease requires individualised advice from a neurologist with expertise in movement disorders. Dopamine agonists are a group of drugs that imitate the action of dopamine in the brain. They are not as potent as levodopa and carbidopa, and can be used instead of, or in addition to them or other Parkinson's medications. They may be used to smooth the 'on–off' effect you can get with levodopa. There are other less commonly prescribed groups of medications, too. Prescribing the right medication at the right doses and at the appropriate stage of the disease requires individualised advice from a neurologist with expertise in movement disorders. Over time, medication doses may be changed, medications switched or added.

Deep brain stimulation

If medication stops working, or if symptoms do not respond to available medications, deep brain stimulation is considered. Deep brain stimulation involves implanting a battery-operated neurostimulator device to deliver electrical stimulation to specific parts of the brain responsible for controlling movement, blocking abnormal signals that lead to abnormal movement such as tremors. Deep brain stimulation is not without risk, but it can provide improved quality of life for several years in people with advanced Parkinson's disease.

WHAT ELSE HELPS?

Exercise

Regular exercise benefits physical functioning, quality of life, strength, balance and gait speed in people with Parkinson's disease. In particular, dancing and aerobic exercise have positive benefits.

Acupuncture

A meta-analysis has shown that acupuncture in Parkinson's disease is more effective in relieving the symptoms than no treatment or conventional treatment alone, so acupuncture can be considered as a combination treatment with conventional medical treatment for patients with Parkinson's disease.

Herbs and supplements

Mucuna pruriens

The Ayurvedic herb *Mucuna pruriens* or 'velvet bean' is a natural source of levodopa and is the traditional herb used in Ayurvedic medicine to treat Parkinson's disease.

The pharmaceutical preparation HP-200, which contains *Mucuna pruriens* combined with coenzyme Q10 and nicotine adenine dinucleotide, has been shown to be more effective than conventional levodopa in treating Parkinson's in animal studies. Unlike synthetic levodopa, HP-200 was found to significantly restore endogenous levodopa, dopamine, noradrenaline and serotonin in the substantia nigra, suggesting that it has both neurorestorative and neuroprotective effects. If added to pharmaceutical levodopa, it could result in too much levodopa or inconsistent symptom control. This should only be taken with expert advice from a qualified healthcare practitioner.

Coenzyme Q10

Coenzyme Q10 or CoQ10 is an antioxidant that helps cells to utilise oxygen for energy.

Low plasma, platelet and cerebral cortex levels of coenzyme Q10 in patients with Parkinson's has been shown in several studies. However, the evidence for improvement of motor symptoms in Parkinson's disease with supplementation with CoQ10 is lacking.

Vitamin E, vitamin C and betacarotene

Oxidative stress is increased in the substantia nigra of people with Parkinson's disease, and this is suspected to play a role in the cause of the disease. A meta-analysis of these antioxidants has revealed that dietary intake of vitamin E may have a neuroprotective effect, reducing the risk of Parkinson's disease.

A more recent study in 2017 looked at antioxidant intake and concluded that intake of dietary vitamin E and beta-carotene was associated with a lower risk of Parkinson's disease.

This provides an important incentive to include foods that are rich in vitamin E (for example, vegetable oils, nuts, seeds and green leafy vegetables) and betacarotene (for example, carrots, sweet potato, kale, spinach, broccoli, red and yellow peppers) in your diet. For more about this, see chapter 24: Brain Food.

Vitamin D

There is a high prevalence of vitamin D deficiency in people with Parkinson's disease. There are vitamin D receptors in the substantia nigra. One of the most consistent findings in the medical literature is that low levels of vitamin D are correlated with worse motor symptom severity in Parkinson's disease. The association between vitamin D and non-motor symptoms is less clear.

While the evidence of the exact relationship between vitamin D and Parkinson's disease remains inconclusive, the best advice is to test vitamin D levels and ensure they are in the normal range through a combination of sun exposure and vitamin supplementation.

Folate and vitamin B12

People with Parkinson's treated with levodopa have been found to have significantly lower serum levels of folate and vitamin B12.

Interestingly, those patients with Parkinson's and depression have significantly lower folate levels, whereas those with Parkinson's and cognitive impairment have lower levels of vitamin B12.

Elevated levels of homocysteine can be lowered with vitamin B12 and folate. This can be of particular importance in people with Parkinson's disease, who are at risk of cardiovascular diseases, cognitive impairment or dementia.

Adequate dietary intake of vitamin B6 has also been shown to reduce the risk of developing Parkinson's disease.

Magnesium

Magnesium deficiency has been associated with neuronal degeneration in the substantia nigra, and this is thought to contribute to the development of Parkinson's disease. Animal studies have shown that magnesium might protect against this, but further human clinical trials are needed.

Zinc

People with Parkinson's disease show significantly reduced zinc levels compared with those who do not have the disease. It is difficult to extrapolate the available evidence to a recommendation, except to say that adequate dietary zinc is essential to brain function.

Diet

Avoid fad diets that restrict food groups. A wide variety of foods will give you the best chance of incorporating all the nutrients your brain needs for protection.

Where possible, choose organic pesticide-free food. A diet high in fruit, vegetables, legumes, whole grains, nuts, fish and poultry combined with low saturated fat, low refined sugar and moderate alcohol consumption is protective against Parkinson's. Higher intake of polyunsaturated fatty acids may reduce the risk of Parkinson's disease. In contrast, a typical Western diet, which is high in animal and saturated fats, may be associated with an increased risk of Parkinson's.

Make sure you incorporate foods that are high in antioxidants, including brightly coloured fruit and vegetables. In particular, the polyphenols in fruit such as blueberries have been shown to improve neuronal signal conduction and communication.

PART 3

WHAT CAN SUPPORT YOUR BRAIN

22

Train Your Brain

Brain training uses a variety of methods to reinforce or build your memory and cognitive skills. Educational toys, exercises and games for children are designed to build memory and language, pattern recognition and problem-solving skills.

In my school days we had memory joggers or mnemonics to help us remember the colours of the rainbow: 'Roy Of York Got Bashed In Venice' – Red Orange Yellow Green Blue Indigo Violet – was a bit of a favourite. I'm sure many school groups had their own version of this. These mnemonics are a form of brain training, a highly effective way of enhancing memory performance.

> The top participants of the annual World Memory Championships regularly demonstrate the ability to memorize hundreds of words, digits or other abstract information units within minutes. Surprisingly, such memory skills do not seem to be associated with extraordinary brain anatomy or general cognitive superiority, but are acquired through deliberate training in mnemonic strategies.

We took this form of memory enhancement or brain training through to medical school where we would have mnemonics handed down to us by older students, or develop our own to

help us remember complex lists such as the periodic table of elements or the branches of a nerve. Some of these mnemonics are devised by people with an eye to popular culture and a sense of humour, like this one for the complications of a heart attack using the *Star Wars* villain 'Darth Vader':

- **D**eath
- **A**rrhythmia
- **R**upture (free ventricular wall/ventricular septum/papillary muscles)
- **T**amponade
- **H**eart failure (acute or chronic)
- **V**alve disease
- **A**neurysm of ventricle
- **D**ressler's syndrome
- thrombo**E**mbolism (mural thrombus)
- **R**ecurrence/mitral **R**egurgitation.

The premise of brain training relies on the principle of neuroplasticity (see chapter 2: Neuroplasticity) or brain plasticity. Neuroplasticity is the capacity of brain cells to modify and adapt their structure and function throughout our lives in response to external experiences and internal body processes. We believe that neuroplasticity is maintained to some extent into old age.

We know that the benefits of neuroplasticity are the sum total of all the actions and habits we put into action, from nutrition to exercise, social interactions to reading and learning new skills. As one example, aerobic exercise has been shown to encourage increased neurogenesis in humans.

Some brain functions that do decline with advancing age include processing speed, short-term memory and decision-

making. The aim of brain training is to halt that decline.

Brain training is an ongoing process of using the skills you have gathered over the years and challenging yourself with new skills to master. It is important to engage a variety of methods of stimulating your thinking and memory skills.

For effective brain training you need novelty, focused attention and a challenge. Learning music is an example of a pursuit that can enhance brain activity. It certainly presents a challenge. It is a complex and multisensory form of brain enrichment, and has a positive influence on neuroplasticity in several regions of the brain because it requires integration of audio and visual input, as well as appreciation of abstract rules.

Find a new and challenging activity that you can practise regularly. This might be taking a course, a creative pursuit such as taking art lessons, learning a musical instrument, learning a new language, or playing a variety of problem-solving and memory-testing games on digital devices.

BRAIN-TRAINING APPS

Since the development of innumerable brain-training apps for smartphones and digital devices, the brain health digital boom has become its own segment of the IT industry. Brain-training programs target various aspects of brain function, including attention, concentration, memory, creativity and problem-solving.

The saying goes that practice makes perfect. We can expect that practising a brain-training exercise will result in you performing better at that particular exercise. What we cannot say is whether those specific skills will transfer to your daily life.

Why are these apps so popular?

Brain-training apps have several obvious attractions, aside from entertainment. They are convenient, accessible and affordable. Smartphone apps for brain training are marketed with the promise of preserving or improving your brain function. The idea is that skills gained or enhanced by brain-training exercises will transfer to day-to-day cognitive tasks.

So could using a brain-training app make you smarter, or preserve your brain function? Could it reduce your risk of cognitive decline or dementia? If so, which apps and what elements of brain function can benefit?

A number of studies have shown that video game training in older adults does have a positive effect on reaction times, attention, memory and global cognition.

We don't really know exactly which games or apps are likely to be most effective in enhancing cognition, and despite their widespread use, there have been no large-scale studies comparing the efficacy of brain-training apps at different ages and different cognitive abilities.

There are now a number of scientifically conducted studies of the use of smartphone brain-training apps for cognitive training of older people with promising results for the improvement of working memory and reasoning skills.

The reality is that there is not a lot of scientific research to demonstrate if, how or what amount of any particular brain-training apps might enhance brain function. It is important to point out that the absence of evidence is very different to there being evidence of no benefit. And in fact, there is a lot of evidence that engaging your brain regularly in different ways will support and incrementally enhance your brain health.

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Brain and Exercise: More than Endorphins

In my long career in health communication, I have always looked for ways to motivate people to incorporate into their everyday habits lifestyle measures that have a positive effect on their health. Importantly, this always includes regular exercise.

In the 1970s, a group of chemicals called peptides was discovered in the brain and central nervous system. Scientists found that these naturally occurring neurotransmitters acted on painkilling receptors in the brain, inhibiting the transmission of pain signals using a similar mechanism to opioid drugs. They were also found to produce a euphoric effect, similar to that of a mind-altering drug, but without the adverse effects.

Research into the way these neurotransmitters were released found that pain was not the only trigger. A number of other human activities released them, including meditation and vigorous aerobic physical exercise, explaining the positive feeling also known as the runner's high.

The term endorphins eventually came into popular use, and became a very useful motivator, encouraging people to exercise so they could experience that 'rush'.

But the endorphin surge is not the only effect that exercise has on the brain.

Could exercise also be one of the keys to keeping your brain young? The answer is an unequivocal yes! Regular exercise can change your brain structure and function in ways that protect your ability to think and remember.

EXERCISE CAN:

- protect you from developing depression, and relieve existing depression
- improve attention, learning and memory
- help you focus and concentrate
- improve executive function
- reduce risk of stroke
- delay age-related mental decline, dementia and Alzheimer's disease.

Exercise is a stimulus for brain plasticity or neuroplasticity. Exercise increases growth factors in the brain that facilitate new neuronal connections.

The effect starts early. A recent analysis of the scientific literature found a positive relation between physical activity and cognitive performance in school-age children (aged 4–18 years) in perceptual skills, intelligence quotient, achievement, verbal tests, mathematic tests, memory, and developmental level/academic readiness. This is a strong case for early intervention to encourage physical activity in children.

But how does exercise achieve all this?

CIRCULATION

Exercise improves overall brain health in the same way that it improves all other aspects of your physical health. The health of your body tissues relies on the delivery of nutrients to your cells and the removal of by-products and toxins via the circulation of blood. This means your brain depends on

healthy circulation to perform its essential functions efficiently.

Check your carotid pulse before and during exercise. To do this, place your index and middle fingers on your neck to the side of your trachea (windpipe). You will feel the pulsation of blood flowing up to your brain. The carotid artery is the main blood vessel delivering oxygenated blood from your heart to your brain. You will notice when you exercise that your pulse becomes faster and stronger, increasing the supply of oxygen-rich blood to your brain. The small vessels in the brain distribute oxygen-rich blood to the brain structures. Cognitive tasks need increased energy delivered by increasing blood flow to those areas of the brain engaged in that task.

Regular exercise reduces the risk of chronic diseases such as coronary artery disease and stroke, type 2 diabetes and osteoporosis. It lowers blood pressure, reduces and alleviates depression, and reduces the risk of some cancers and cancer recurrence.

The risk factors for heart disease and vascular dementia are similar, and they include physical inactivity. Increasing physical activity increases blood flow to the brain as well as the blood flow in the small vessels in the brain supplying brain tissue, and improves cognitive function.

Taking a holistic view, of course, in reducing risk factors for conditions like diabetes, hypertension and cardiovascular disease, exercise also contributes to reducing neurodegeneration and preserving brain function.

NEUROTRANSMITTERS

Exercise has a positive effect on your brain function almost immediately, improving your mood, concentration and focus – and these benefits persist for several hours after an exercise session. This positive effect is due to an increased level of

neurotransmitters like dopamine, serotonin and noradrenaline. The increased production of neurotransmitters strengthens the communication between neurons in the brain. Those connections between neurons are known as the synapses, or synaptic connections.

For several hours after an exercise session, a range of brain functions improve, including attention, working memory, problem solving and decision-making.

Then there is the ‘endorphin effect’. Even when your muscles are screaming for mercy, it is that mood-lifting and pain-modifying effect of endorphins that sees you coming back for more.

Regular aerobic exercise over several months starts to give you longer term benefits.

Regular physical activity results in long-term increases in the neurotransmitters responsible for lifting mood. Over time, exercise can improve both your cardiovascular fitness and your brain function, and protect your brain from a range of conditions. It does this by enhancing your brain’s actual form, physiology and function.

NEUROGENESIS

Neuroscientists have shown that aerobic exercise increases the numbers of neurons (brain cells) in the hippocampus, which increases its volume. This increase in the numbers of neurons in the hippocampus is called neurogenesis, and it improves your capacity for learning and long-term memory. Research has shown us that the capacity for neurogenesis in the hippocampus persists throughout adult life.

Regular physical activity has been shown to have a similar effect of increasing the volume of the prefrontal cortex.

The effect of exercise on these two areas of the brain is particularly relevant because the hippocampus and the prefrontal cortex are the areas of the brain most affected by the cognitive decline of ageing, and by neurodegenerative conditions such as Alzheimer's disease, which are characterised by a marked reduction in the number of neurons in the hippocampus. This decline might be partly relieved by the increased neurogenesis resulting from aerobic activity.

Other forms of exercise such as resistance training or strength training have not been shown to have this same effect. That said, resistance training improves hypertension (high blood pressure), cholesterol levels, and insulin and glucose regulation, so it is likely that these forms of exercise will also contribute to brain health.

A sedentary lifestyle contributing to weight gain in midlife and later life is associated with reduced brain tissue volume and associated cognitive decline. This may also be explained by lower levels of physical activity and increased inflammation associated with obesity.

ANGIOGENESIS

An increased number of neurons and increased brain volume needs to be accompanied by an increase in nutrients delivered to that area of the brain. New blood vessel growth sprouting from existing blood vessels is known as angiogenesis and this process can continue into older age. Angiogenesis is improved by exercise and this in turn increases blood supply to the brain. This is one of the mechanisms that explains how exercise improves brain function.

REDUCING INFLAMMATION

The brain health benefits of exercise come directly from the brain's ability to reduce insulin resistance and inflammation,

and stimulate the release of growth factors.

Evidence indicates that chronic inflammation is associated with age-related decline in brain health.

We also know that systemic inflammation increases with age, and that older brains are more vulnerable to the effects of inflammation. For example, inflammation can impair growth factor signalling in the brain.

We know that one of the most effective and easily accessible antidotes to inflammation is exercise. Maintaining a healthy weight also helps to reduce inflammation. One recent study reported that significant weight loss was associated with decreased levels of central nervous system inflammation and increased brain activity.

Along with exercise and weight loss, there are also nutritional ways to reduce inflammation. This can be achieved with a diet rich in plant foods, and the inclusion of omega-3 fatty acids. (See chapter 24: Brain Food.)

SLEEP

Regular exercise enhances sleep quality. If you have ever been through a period of sleep deprivation, such as having a new baby or going through a stressful or anxious period in your life, you will know that lack of sleep affects your ability to think clearly and to make good decisions.

By enhancing sleep, exercise can help maintain healthy brain function. (See chapter 28: Sleep.)

HOW MUCH EXERCISE?

One of the most common questions I am asked is ‘How much exercise do I need to do?’

There is the minimum, and there is the ideal. The minimum amount of exercise needed to achieve the effect you want as an adult is 30 minutes a day, five to six times a week. Ideal, on the other hand, looks more like an hour a day, most days. The intensity will differ from person to person depending on your age, your current level of fitness and your medical condition. Low to moderate intensity aerobic exercise appears to provide the greatest benefit.

The most recent data on physical activity suggests that most people have a lot of room for improvement. The Australian National Health Survey 2017–18 showed that:

> Just over 1 in 2 adults (55%) did not participate in sufficient physical activity in 2017–18. Women were more likely than men to be insufficiently active (59 per cent compared to 50 per cent). The rate of insufficient physical activity generally increases with increasing age … Among 18–24 year olds, 41 per cent of men and 48 per cent of women were insufficiently active. For those aged 65 and over, 69 per cent of men and 75 per cent of women were insufficiently active.

'Insufficient physical activity' was defined by the survey as:

- Adults aged 18–64 who did not complete 150 minutes of moderate to vigorous physical activity across five or more days in the last week
- Adults aged 65 and over who did not complete at least 30 minutes of physical activity per day on five or more days in the last week.

If 30 to 60 minutes a day seems daunting to you, see it as an aspirational goal and start with what you can manage and build up as your level of fitness allows. Even starting with 10 minutes once or twice a day is 10 or 20 minutes more than you were doing.

WHAT TYPE OF EXERCISE?

As we have seen, aerobic exercise is necessary to increase your heart rate and the volume of blood pumped through your body. It has also been shown to increase the number of neurons and the volume in parts of the brain that are critical for improving and maintaining brain function.

How you achieve that is largely a matter of preference. Walking is the form of exercise most commonly studied. However, the type of exercise that suits someone else may not suit you at all. Most importantly, you need to choose forms of exercise that you enjoy, and that you are likely to continue. Often I find that rediscovering forms of exercise from your youth works well, like swimming or cycling or tennis, because the body memories are there.

Exercise can be either formal or opportunistic. Examples of formal exercise include a planned walk or a run, swimming laps, going to a gym class or a dance class, or team sports. Opportunistic exercise, on the other hand, is when you are faced with the choice of taking the lift or the stairs, and you decide to take the stairs. Or when you walk or cycle to the local shops instead of taking the car, if that is practical.

Having an exercise buddy can be a great motivator on the days you don't necessarily feel like it. Having a standing arrangement makes you more likely to turn up. In addition, you can motivate each other, and company can make it more fun. I also suggest that if reluctant starters are going for walks on their own and finding it boring, they could take a device and listen to music as a distraction.

Yoga originated in India around 2000 years ago and is known to help brain function in similar ways to aerobic exercise. Studies have demonstrated a positive effect of yoga practice on the structure and/or function of the hippocampus, amygdala, prefrontal cortex and cingulate cortex.

Tai chi originated in China and it is well recognised for its health benefits in improving muscle strength and balance, and in stress management. The positive impact of tai chi on brain function is being increasingly recognised.

Tai chi has been shown to improve executive function in older adults without significant cognitive impairment, improving skills in areas such as multitasking, managing time and making decisions. In people with mild cognitive impairment, tai chi slowed the progress of dementia more than other types of exercise and improved cognitive function similarly to other types of exercise or cognitive training.

Until we have more evidence about the specific exercises for brain health, the advice for maintaining general physical health applies. That means a diverse combination of different aerobic, resistance and mind-body practices.

Exercise can improve and maintain learning and memory, reduce the risk of neurodegenerative diseases and delay age-related cognitive decline. Even though we do not yet know how to prevent conditions like Alzheimer's disease, it appears that regular exercise can help to preserve your existing cognitive function for longer.

24

Brain Food

You are what you eat. It's such a cliché that it is easy to overlook the central truth in this old saying. Every part of your body depends on the fuel you give it to operate efficiently, and this in turn depends on how well the cells of your body are able to digest the food and use those essential nutrients.

The brain is no exception. Your brain works around the clock, whether you are asleep or awake. What you eat provides the fuel and the essential ingredients for the brain to perform all of its functions, from thinking to learning, forming memories, moving your limbs, forming your facial expressions, playing a musical instrument, singing, talking, communicating with your gut and so much more.

I work with a lot of patients who have gut and food issues, so I am very aware that many people have problems with digestion, food intolerances and allergies. (See chapter 15: Your Brain and Your Gut.) This can make it difficult to include certain foods in their diet. Some people choose to restrict some food groups from their diet because they do not like the taste or texture of those foods. Others restrict their diet because they are convinced that they have a health problem relating to food, and they are attempting an unsupervised elimination diet in order to work out how to feel better.

Some people simply don't know what to include in their diet to achieve optimal wellbeing.

The risk of any dietary limitation, or of being unable to digest some foods, is that you may suffer micronutrient deficiencies that will affect the performance of your brain.

You need to make an extra effort to provide your brain with all the right nutrients to continue its operations. Ideally, that can be achieved with the right combination of whole foods, but in reality, many people will need supplementation in the short, medium or long term (see chapter 25: Herbs and Supplements for Brain Health).

The link between your nutrition and your brain health begins during your mother's pregnancy. This is when the structure of your brain and its connections are established, as neurons grow and form connections with adjoining neurons.

Breastfeeding by a well-nourished mother is also important for early brain development. Where breastfeeding is not possible, babies need a suitable high-quality infant formula.

As a child progresses through infancy and foods are gradually introduced, parents need to be particularly mindful that their child is getting all the essentials for this dynamic period of brain development. During this time, their child is developing the connections that will govern how they think, learn, remember, experience and understand the world, as well as developing impulse control and regulation of moods and emotions. The first three years after birth are a particularly crucial window for anatomical and functional development of the brain.

Through adult life and into old age, nutrition continues to be a fundamental consideration for brain health.

Let's explore the nutrients essential for brain growth and development and the maintenance of brain health, and some examples of the foods where they can be found.

CHOLINE

Choline is important for the structure of every cell. It is crucial to early brain development, especially the ‘memory centre’ in the hippocampus. In 1998 the National Academy of Sciences in the USA issued a report identifying choline as a required nutrient for humans, and set recommended daily intake amounts.

In the brain and nervous system, choline is needed to produce acetylcholine, the important neurotransmitter for cognition, attention, memory, mood and muscle control. In the peripheral nervous system, acetylcholine is found in all motor neurons, and it is what these motor neurons release to make muscles contract.

Studies have shown that maternal choline levels are depleted during pregnancy and that lack of choline in the diet during pregnancy and breastfeeding can have a lifelong impact on the child’s brain.

People with Alzheimer’s disease have lower levels of the enzyme that converts choline into acetylcholine in the brain.

Choline is naturally present in some foods, including meat, poultry, eggs, wheat germ and dairy. Other food sources include cruciferous vegetables (such as cabbage, cauliflower, broccoli, brussels sprouts, bok choy) and soybeans. Other dietary sources of choline include whole grains, some nuts and seeds.

POLYUNSATURATED FATTY ACIDS (PUFAS)

Polyunsaturated fatty acids (PUFAs) play a hugely important role in brain development and brain health. They have an anti-inflammatory role in resolving inflammation in the brain. The critical period for PUFAs in early brain development spans from the beginning of the third trimester of pregnancy to two

years of age, during the stage of maturing of neurons, creation of synapses, myelination of nerve fibres and expansion of grey matter. Neurons incorporate PUFAs into their cell membranes.

Dietary intake of PUFAs is essential to maintain adequate levels in cell membranes. There are two types of PUFAs: omega-3 fatty acids and omega-6 fatty acids. These are most easily found in fatty fish and fish oils, but they can also be found in some other oils, and many foods are also fortified with them.

There are three main omega-3 fatty acids: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Linoleic acid (LA) and arachidonic acid (ARA) are two of the main omega-6 fatty acids.

ARA and DHA are the most abundant PUFAs in the brain.

ALA and LA must be obtained from your diet. ALA can be converted to EPA and DHA, but in practical terms they need to come from diet or supplements.

In most contemporary Western diets, there is a preponderance of omega-6 fatty acids. Ideally, the balance needs to shift back to more omega-3s.

The richest sources of EPA and DHA are fish, especially oily fish. LA and ALA are found mainly in vegetables, oils, and seeds such as chia, linseed and flaxseed. ARA is found in meat and eggs.

IODINE

Iodine is a trace element and it is a component of thyroid hormones. Iodine is essential for brain development during pregnancy and in early childhood. Iodine deficiency is the most common cause of preventable intellectual disability in the world. Mild to moderate iodine deficiency in pregnancy

has also been associated with attention deficit hyperactivity disorder (ADHD) in children. The prevention of iodine deficiency in pregnancy and during breastfeeding is so important to foetal brain development that iodine is included in pregnancy/breastfeeding supplements.

Seaweed (in the form of kelp, nori, kombu and wakame) is an excellent source of iodine, as are seafood and eggs (mostly in the yolk). For most people, iodine-enriched foods are the main source – for example, iodised salt and enriched grains.

Iodine is present in some fruit and vegetables, but the content varies depending on the iodine content of the soils where the produce is grown.

IRON

In early life, iron is essential for developing brain structures, neurotransmitter systems and the myelination of brain cells. Throughout life, iron is essential for normal neurological function.

When we are medically monitoring a woman during pregnancy, we watch her iron levels carefully. There is a greater demand for iron during pregnancy, and deficiency is common. Where there is a deficiency this must be corrected as quickly as possible to make sure there is adequate iron for the foetus's development. Toddlers and adolescent girls are also at risk of iron deficiency. It is crucial to detect iron deficiency in early life because the neurodevelopmental consequences of uncorrected iron deficiency in infancy and childhood may be irreversible.

In adults, iron deficiency can cause fatigue, brain fog, trouble concentrating, and other cognitive disturbances and behavioural and mood alterations such as irritability. Where there is iron deficiency, iron supplementation improves cognitive function.

Importantly, iron overload can have a toxic effect on the brain. This can happen with the genetic iron overload disorder haemochromatosis, or if there is excessive supplementation of iron. This highlights the reason it is so important to test iron levels before embarking on supplementation.

Meat is the most obvious food source of iron. Plant sources include green leafy vegetables such as spinach, tofu, tempeh, chickpeas, beans and lentils, fortified wholegrain cereals and breads, nuts, pumpkin seeds and baked potatoes (skin on).

PROTEIN

Protein is necessary for growth and development. It is also necessary for maintenance of brain health at all ages. The amount of daily protein you need depends on your age, gender and your level of physical activity. Research has found that a child's physical growth rate before 12 months of age significantly predicts the child's intelligence quotient (IQ) at age nine years.

At all ages, protein is needed in the production of key neurotransmitters and to support cognition. The research on the link between dietary protein intake and cognitive function has been limited and inconsistent. It is reasonable to advise you to make sure there are high quality food sources of protein in your daily diet. This is particularly important if your diet is vegan. Protein can be found in meat, poultry, seafood, dairy, beans and peas, eggs, soy products, nuts and seeds.

VITAMIN A

The human body converts betacarotene into vitamin A (retinol). Vitamin A and its derivatives are involved in the modulation of neuroplasticity, including hippocampal neurogenesis, neuronal survival and synaptic plasticity. Adequate levels are needed for brain development and

maintenance of brain health. Excess levels from supplementation should be avoided in early pregnancy because it can cause birth defects.

Food sources of vitamin A and/or betacarotene include dairy products, liver, fish, dark green leafy vegetables such as spinach, fortified cereals and orange/yellow vegetables such as carrots and sweet potato.

VITAMIN B6 (PYRIDOXINE)

Vitamin B6 is absorbed through the jejunum in the small intestine, then transported to the liver, where it is converted to pyridoxal 5-phosphate (P5P). It is then available to other body tissues.

Vitamin B6 is necessary for cognitive development in children and for brain function at all ages. It helps the body to synthesise the neurotransmitters serotonin, dopamine, GABA and noradrenaline and the hormone melatonin.

Groups at risk of low vitamin B6 include women, smokers, people who are alcohol dependent, teenagers and people who have gut problems that cause difficulty absorbing food.

Low vitamin B6 affects the brain, causing symptoms such as irritability, lethargy, confusion, lowered seizure threshold, and electroencephalogram (EEG) abnormalities showing abnormal brain-wave patterns. Even a mild deficiency can cause a reduction in serotonin and GABA synthesis, causing disordered sleep and behaviour changes.

Excess vitamin B6 should also be avoided because it can cause sensory neuropathy, with tingling in the hands and feet, numbness, muscle weakness and twitching, and impeded coordination of body movements.

Some food sources of vitamin B6 are fish, organ meats, legumes, nuts, eggs, bananas and potatoes.

VITAMIN B12

Because plants do not synthesise vitamin B12 and the food sources are animal products, people following a vegan diet are most likely to suffer vitamin B12 deficiency. Vegans need regular blood tests to check their B12 levels and must supplement where necessary. Vitamin B12 deficiency can also be the result of failure to absorb vitamin B12 from the gut. Elderly people are particularly at risk of this.

There is also a disorder called pernicious anaemia, which results from the inability to produce the protein 'intrinsic factor' in the stomach lining, and impairs the uptake of vitamin B12. This means the body is unable to make enough normal red blood cells, resulting in anaemia, or is unable to operate the brain and nervous system efficiently.

Vitamin B12 is involved in synthesising the proteins in the myelin sheath and nerve cells.

One study found a doubled risk of Alzheimer's disease in people with low levels of vitamin B12 and folate over a three-year period.

Nerve damage caused by vitamin B12 deficiency causes symptoms such as tingling and numbness in the hands and feet, muscle weakness, vision disturbance, depression, confusion, cognitive impairment, peripheral neuropathy and demyelination of the corticospinal tract and dorsal columns.

Vitamin B12 is found in foods of animal origin including meat, seafood, egg yolk and dairy.

FOLATE (VITAMIN B9)

Folate is one of the B-group vitamins, also known as B9. It is essential in making DNA and RNA genetic material, and is also needed for cell division.

Folate works with vitamin B12 and vitamin B6 in controlling levels of the amino acid homocysteine in the blood. It also helps iron to function in the body.

Folate is so important to the development of a foetus that every woman planning a pregnancy is advised to take a folate supplement in addition to dietary sources of folate for three months before conceiving, and throughout the pregnancy. Folate supplementation during pregnancy helps prevent the risk of severe brain and spinal cord defects in babies. (See chapter 4: A Head Start.) It is also necessary for maintenance of brain health.

Folate deficiency is common in elderly people, especially institutionalised elderly people. The most common causes are dietary deficiency of fresh fruit, vegetables and fortified cereals, or poor absorption from the gut.

The absorption of folate is inhibited by chronic excessive alcohol consumption. Low folate contributes to high homocysteine levels, and there is an association between low folate/high homocysteine and cardiovascular disease and dementia.

MTHFR (METHYLENETETRAHYDROFOLATE REDUCTASE) GENE MUTATION

MTHFR deficiency is a common genetic variant that results from poor metabolism of **folate** (also called vitamin B9), due to a lack of working enzyme called **MTHFR**.

Folate deficiency causes homocysteine levels to rise. This in turn increases the risk of cardiovascular disease.

People with this gene type need to opt for a supplement that contains the most bioavailable form of **folate**—methylfolate—which can help your body absorb the vitamin more efficiently.

The signs of folate deficiency include fatigue, anaemia, headache, hair loss, nausea and diarrhoea, insomnia, peripheral neuropathy and cognitive decline. (See chapter 16: The Dementia Mimics.)

There is an association between low blood levels of folate and depression. This is thought to be linked to high homocysteine levels. In addition, people with low levels of folate might not respond as well to antidepressant treatment as people with normal folate levels. Folate supplements, particularly those that contain methylfolate (5-methyl-THF), might make SSRI antidepressant medications more effective.

The best food sources of folate are dark green leafy vegetables such as spinach, asparagus, broccoli, sprouts, mushrooms, legumes such as chickpeas, fruit, nuts, fortified cereals, breads and organ meats.

VITAMIN D

By far the best source of vitamin D is sunshine. Vitamin D3 is produced in the body as a result of conversion of a cholesterol-based substance, 7-dehydrocholesterol, which is produced in the sebaceous glands of the skin. Exposure to sunlight converts 7-dehydrocholesterol into vitamin D3 (also called cholecalciferol) over a two- to three-day period.

Unfortunately, the successful public health messages to ‘slip, slop and slap’ to prevent skin cancer have brought an unintended consequence: vitamin D deficiency. It is almost impossible to get adequate vitamin D from diet alone.

Short periods of sun exposure while avoiding sunburn is considered the most effective way to maintain adequate vitamin D levels.

Some groups of people are particularly at risk of vitamin D deficiency, including the elderly, people who are institutionalised, people who cover most or all of their skin and do not get adequate sun exposure, people with dark skin tones and pregnant women. These groups are most likely to need supplementation.

In general practice we certainly see a lot of people with vitamin D deficiency. It is very important to correct this and maintain adequate levels to prevent the consequences of long-term vitamin D deficiency, which include osteoporosis, muscle weakness, muscle and bone pain, impaired immunity and impaired glucose metabolism.

In the brain and cerebrospinal fluid, vitamin D is needed to activate and deactivate the enzymes that are involved in neurotransmitter synthesis, including acetylcholine and the catecholamines, as well as nerve growth (‘neurotropic’) factors, and contributes to brain detoxification.

You can’t eat sunshine, but there are some foods containing vitamin D. The flesh of oily fish such as salmon, tuna and sardines contain vitamin D, as do beef, cod liver oil, butter, eggs and products fortified with vitamin D, such as fortified milk. Naturally occurring vitamin D2 (also called ergocalciferol) is found only in mushrooms.

FLAVONOIDS

Flavonoids are naturally occurring bioactive pigments found widely in plant-based foods. Flavonoids are what give fruit like berries their vibrant colours: the blue in blueberries, the red in strawberries. They have been shown to improve memory, learning and cognitive function.

Dietary flavonoids have a number of neuroprotective qualities. They have the potential to protect neurons against injury induced by neurotoxins, they can suppress neuroinflammation, and they have the potential to promote memory, learning and cognitive function.

There is also evidence to suggest that flavonoids may be capable of preventing many forms of cerebrovascular disease, including those associated with stroke and dementia.

Further, evidence shows that higher long-term dietary intakes of flavonoids are associated with lower risks of Alzheimer's disease and related dementias.

Flavonoids are present in tea, berries, citrus fruit, apples, legumes, red wine, soy products and dark chocolate.

ZINC

Zinc plays an essential role in regulating communication between cells in the brain. It also has an important role in the immune system.

Deficiency of zinc during pregnancy and breastfeeding is associated with congenital abnormalities of the baby's nervous system. In children, insufficient levels of zinc have been associated with poorer learning ability, apathy, lethargy and poor intellectual development.

Zinc deficiency in the brain in adults can lead to depression, loss of enjoyment, lethargy and irritability. One interesting sign of zinc deficiency is loss of taste sensation.

Zinc is best absorbed from animal sources, and intake can be impeded by natural chemicals called phytates in grains. This makes vegans more prone to zinc deficiency.

Excess alcohol consumption increases the risk of zinc deficiency.

The best sources of zinc are seafood (particularly oysters and shellfish), eggs and meat. Zinc is also found in wholegrains, soy foods such as tofu and miso, mushrooms, pumpkin seeds, dairy products, nuts and green beans.

THE BASICS OF BRAIN FOOD

A healthy balanced diet of wholefoods forms the basis of the fuel your brain needs to perform all its functions. It may be

difficult to incorporate all these nutrients into a diet. Some parents will find it very challenging to ensure their children get the foods they need, especially if they are fussy eaters, or if the family is vegan.

The quantity of food is also important for brain health. Excess calories can reduce synaptic plasticity[32,102] and increase the vulnerability of brain cells to damage.

Just as there are dietary components that enhance and support brain health, there are also some ingredients and types of diets to avoid or limit because they can harm your brain health. A diet high in refined sugar is one example. In chapter 11: Glucose we saw the effect of impaired glucose metabolism on brain function. High dietary sugar increases brain inflammation, leading to brain tissue injury, and increases oxidative stress, impairing brain function. A diet high in sugar can also worsen depression.

IS THERE A PERFECT BRAIN FOOD DIET?

There are some eating patterns that appear to provide particular health benefits for the populations that follow those ways of eating. Any eating plan needs to take into consideration cultural factors, individual taste preferences, medical conditions such as food allergies or diabetes, and food availability.

You can start by eliminating the dietary ingredients that you know will have a negative impact on your health, and introduce a wide variety of the foods that promote brain health.

Then look at each of the nutrients I have listed and make sure you include in your usual eating plan foods that provide those fundamental elements. This may mean shopping differently, and stocking your fridge and pantry with foods that at first might be unfamiliar to you. You may need to look for

some new recipes that incorporate foods, herbs and spices that you have not used before.

It can be very exciting to trial new recipes and incorporate the ones you like best into your ‘go-to’ list of meals. I often find that I can start with a basic recipe like a vegan curry and then experiment with different beans or legumes, introduce some new spices or add different-coloured vegetables to introduce extra variety.

Over time, you can develop your own bespoke diet that suits your taste, helps your brain work and meets any other criteria you may want to include.

In terms of existing cultural or medically studied diets, there are some that have been shown to confer particular benefits for brain health: the Mediterranean diet, the DASH diet and the MIND diet.

The Mediterranean diet

I mention the Mediterranean diet first because it has received the most attention from research and is generally considered to be a model of healthy eating. Populations that culturally follow a Mediterranean-style diet have some of the longest life spans and lowest incidence of chronic disease compared with other parts of the world.

The Mediterranean diet reduces the risk of heart disease, metabolic syndrome, diabetes and some cancers. Research has also shown that adhering to a Mediterranean diet has a beneficial effect on the brain and mental health, including a reduction in symptoms of depression. The Mediterranean diet has been associated with slower cognitive decline, a reduced risk of developing mild cognitive impairment and reduced conversion of mild cognitive impairment to Alzheimer’s disease.

This diet generally follows a pattern of an abundance of plant-based foods, with high vegetable and fruit intake, particularly green leafy vegetables, nuts, seeds, legumes and lentils, wholegrains and seafood. Extra-virgin olive oil is the main source of healthy fat. There is minimal red meat or processed sugars.

Another feature of the Mediterranean lifestyle is a healthy amount of exposure to the sun, providing vitamin D. Some foods also contain a little vitamin D, such as mushrooms, eggs and oily fish.

Wine is included, but in small amounts, and only with meals.

The DASH diet

The DASH diet (Dietary Approaches to Stop Hypertension) was developed by the US National Institutes of Health to prevent and control high blood pressure. Hypertension is a risk factor not only for heart disease but also for dementia.

This diet emphasises abundant fruit, vegetables, low-fat dairy, whole grains, lean meat, nuts and beans.

The MIND diet

The MIND diet is a hybrid of the Mediterranean diet and the DASH diet. It was introduced in 2015 by Dr Martha Clare Morris, a leading expert in nutritional epidemiology at Rush University Medical Center, Chicago.

Like other brain-healthy diets, it recommends eliminating processed foods. The MIND diet emphasises plant-based foods, especially green leafy vegetables. We know that vegetables are important for brain health, and green leafy vegetables like kale, spinach and lettuce have been specifically shown to lower the risk of cognitive decline and dementia.

One serving a day of green leafy vegetables, along with other vegetables, will help to keep your brain young.

Fruit also provides important nutrients. In particular, the MIND diet recommends berries such as blueberries and strawberries, which provide important nutrients such as flavonoids to enhance brain health. Eating lots of berries reduces the rate of cognitive decline.

If you want to snack, nuts are ideal. Choose the dry-roasted or raw types, and avoid the processed, added-salt type. If you enjoy nut butters, check the ingredients and make sure there are no hidden extras.

As with the Mediterranean diet, olive oil is the go-to oil for cooking and adding to salads.

The MIND diet also recommends reducing the amount of meat that you eat. Most families don't think too much about how to make vegetables interesting. This is where a good vegetarian recipe collection comes in handy. Remember that soybeans, lentils and other beans can provide protein.

Poultry is also a brain-healthy source of protein. And of course fish is an important source of protein, and should be eaten at least once a week.

The MIND diet was associated with a slower decline in global cognition: the equivalent of being 7.5 years younger in age cognitively.

Probiotic foods

As discussed in chapter 15: Your Brain and Your Gut, the brain and gut are connected and are in constant communication. We call this relationship the Brain–Gut Microbiome Axis. The gut produces many of the same neurotransmitters as the brain, such as serotonin, dopamine and GABA. It is estimated that around 90 per cent of the

body's serotonin is made in the gut. The combination of microbes in your gut microbiome will have a definite effect on your moods and the way your brain is able to operate.

Current thinking is that your gut microbiota is largely established by the age of three years, by which time it is similar to that of adults, and is considered to be optimal when it contains a diverse range of flora in a balanced, stable environment. Throughout life it will be positively and negatively influenced by diet, geographic location, environmental conditions and exposure to chemicals such as antibiotics.

Probiotics are able to restore the composition and function of a disturbed gut microbiome, resulting in prevention or relief of gut inflammation and other intestinal or systemic diseases. Different strains of probiotics have different actions.

The right combination of probiotics has been shown to improve cognition and moods, and lower stress and anxiety.

Research is still ongoing to determine which probiotics and which microbiome combinations have a positive effect on brain health. While that knowledge is growing, it is important to include probiotic foods in your regular diet. The probiotic foods you choose will depend on your personal preferences and also on cultural factors.

Common examples of fermented foods that naturally contain probiotics, or foods that have probiotics added to them, include yoghurt, kefir, kombucha, sauerkraut, pickles, miso, tempeh, kimchi, and sourdough bread.

TIMING OF EATING

The fundamental ingredients in your diet form the basis of what your brain needs in order to function. In recent years there has also been a lot of interest in the timing of eating and its effect on aspects of health, such as weight management,

glucose metabolism, inflammatory conditions, cardiovascular disease and, of course, brain function.

Intermittent fasting is a repeated regular cycle of dietary restriction, inducing an altered metabolic state. This altered metabolic state triggers a metabolic switch from glucose-based to ketone-based energy, with increased stress resistance, increased longevity, and a decreased incidence of chronic health problems such as hypertension, obesity, insulin resistance, high cholesterol and inflammation.

A few intermittent-fasting protocols have been developed and studied. The most well known of these are the 5:2 diet, the 16:8 diet and alternate-day fasting. These are considered to be eating strategies or eating patterns, rather than diets.

The 5:2 pattern involves eating healthily for five days a week, and then kilojoule restricting for two days a week.

The 16:8 pattern involves eating during an eight-hour window only, and not eating for the other 16 hours each day.

Intermittent fasting creates an environment where your cells and body systems are challenged and put under a form of stress by being deprived of food regularly for periods of time. This has been shown to help bodies change and adapt, becoming more efficient and resilient and better able to function.

During fasting, cells activate pathways that enhance intrinsic defences against oxidative and metabolic stress, and those that remove or repair damaged molecules. During the period when you are eating, cells engage in tissue-specific processes of growth and plasticity.

Research has shown that intermittent fasting can help with weight loss and blood glucose metabolism.

Intermittent fasting and brain health

Fasting has the potential to improve cognition, slow age-related cognitive decline, slow neurodegeneration, and reduce brain damage and enhance functional recovery after stroke by regulating inflammatory responses within the brain.

Clinical trials on humans have shown some very promising findings:

- In a clinical trial, older adults on a short-term regimen of caloric restriction had improved verbal memory.
- In a study involving overweight adults with mild cognitive impairment, 12 months of caloric restriction led to improvements in verbal memory, executive function and global cognition.
- A large multicentre clinical trial showed that two years of daily caloric restriction led to a significant improvement in working memory.

As we know, the brain is responsible for governing moods, and research shows that intermittent fasting may help to improve mood, and reduce anxiety and depression.

Is intermittent fasting right for me?

Some people find the routine of IF very straightforward and easy to achieve, while others need more flexibility. Some people should avoid intermittent fasting, such as those who have a history of disordered eating, are underweight, are aged under 18 or elderly, have established diabetes, are on some prescription medications or are pregnant or breastfeeding. Your doctor or a dietician will help you decide if intermittent fasting is right for you. You can also find out more in *16:8 Intermittent Fasting* by Jaime Rose Chambers (2019).

BRAIN FOOD FOR BRAIN HEALTH

The common features of diets that have been shown to benefit brain health are high amounts of fruit, vegetables, fish and legumes and low amounts of processed foods, red meat, sweets and sugars. Here are some tips to help you determine the best diet for your brain health:

- Follow the principles of ‘mindful eating’.
- Work out the foods you need to combine in your diet to get all of the nutrients your brain needs.
- Make sure there are two serves of fruit and five serves of vegetables in your diet every day.
- Check for sources of protein, iron, and essential vitamins and minerals in your diet.
- Make a plan for what you will eat over the next few days.
- Make a plan for regular fresh food shopping and stocking of your pantry so you can follow your eating plan.
- Eliminate preservatives, artificial colourings and flavourings, refined sugar, and processed and packaged foods from your diet, your fridge and your pantry.
- Minimise simple carbohydrates (sugars, bread, white rice).
- See a dietician if you need individual advice or if you have special dietary or medical needs.

The right dietary combination of nutrients, kilojoule content and eating pattern, with appropriate supplementation where necessary, has the potential to enhance your cognitive abilities and protect your brain from damage, promote repair and counteract some of the effects of ageing.

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Herbs and Supplements for Brain Health

It is tempting to look for a ‘quick fix’ for brain health, some pill or combination of pills that will improve or preserve your cognitive function.

So great is our collective concern about declining cognition, a recent survey found that about 25 per cent of adults over age 50 take a supplement to improve their brain health.

Your brain needs a constant supply of the essential micronutrients in order to perform all of its cellular functions, to produce and activate neurotransmitters, and to conduct all of the complex neurological and metabolic functions necessary for the brain to operate optimally.

Mainstream medical dogma has long held that you can’t take a supplement to avert or treat dementia, and it is true that there is no known cure for established conditions like Alzheimer’s disease. However, understanding of the brain’s nutritional needs is advancing rapidly, and there is growing evidence that nutrition and, yes, nutritional supplements and herbs/plant chemicals can play specific roles in maintaining and enhancing brain function. There is also evidence that you

can ward off dementia or slow its progress by providing some specific nutrients to your brain in the right quantities and combinations.

The function of the brain is so complex, it will be the subject of ongoing discovery for many years to come. This means the recommendations for nutrients, either in food or in supplement form, will evolve along with our understanding of the brain's complex biochemistry.

Of course, you can't expect a supplement to provide all the answers. Lifestyle measures such as nutrition, exercise, intellectual stimulation, environmental enrichment and avoiding brain toxins are all extremely important in keeping your brain young and healthy.

When it comes to nutrition, there is evidence that certain eating patterns and particular foods and ingredients are essential to maintain or improve cognitive function. Your diet is fundamental, but it may not be able to supply everything you need in optimal quantities at every age.

For various reasons, you may not be getting all the nutrients your brain needs to maintain optimal function, even if your diet seems 'healthy'. This might be because you are not able to eat all of the right foods, you have a problem with absorption of nutrients from your digestive system, or you have a medical problem or medication that creates a nutrient depletion. In these cases, dietary modification along with supplementation will need to be a part of your approach.

As discussed on page 137, iron is one of the common nutrients we know affects the brain and nervous system. Deficiency of iron is common. It is easy to test for iron levels in the blood, and the more accurate reflection of iron stores in the body is ferritin.

There are two types of iron in food: haem and non-haem iron. Haem iron is only found in meat, chicken and fish, and is

easily absorbed.

Non-haem iron is also found in plant foods, such as tofu, legumes, wholegrain cereals, eggs, seeds and green leafy vegetables such as spinach, but it is not absorbed as well by the body. Iron can be lost from the gut through conditions such as colitis, or lost during menstrual bleeding. If you are found to have a low iron level, your doctor will need to investigate the cause.

Iron is easy to supplement, and the results are evident as iron levels are restored.

There are other particular supplements with a credible or proven chance of maintaining or improving brain function. For some, like vitamin B12, folate or selenium, we have tests to detect deficiency and monitor progress. Other micronutrients such as Coenzyme Q10 are not so simple to test for.

Additionally, we know that as people get older, they are increasingly likely to be taking one or more prescribed medicines for chronic disease. Many medications are known to cause specific micronutrient deficiencies.

The major culprits are drugs prescribed to reduce stomach acid, diuretics, laxatives, benzodiazepines, some antibiotics, some antidepressants, statins for cholesterol lowering and some epilepsy drugs. If you are taking any of these, you need to check whether you can get all of the extra nutrients you need through changes in diet, or whether you need to take a supplement to cover any likely deficiencies. (See chapter 6: Medications.)

There are also herbal treatments that may have been used in traditional medicine for centuries to enhance cognitive function. Beyond nutritional support, herbs and supplements can have quasi-pharmacological effects. There are variable levels of scientific evidence for their use.

The purpose of this chapter is to give you some background information on some of the supplements and herbal therapies likely to have a beneficial effect on brain function, so that you can have an informed discussion with your healthcare practitioners.

A NOTE ABOUT SELF-PRESCRIBING

Self-prescribing or self-medication is a part of the spectrum of self-management, and is usually described as the use of substances, including medications, supplements, alcohol and comfort food, to maintain wellbeing, relieve symptoms or manage health problems.

Many people see multiple healthcare practitioners for health maintenance and management of health problems. You might have been prescribed some medicines, therapies, herbs and supplements by one professional. You might also buy some things over the counter that you read about in a magazine or online, or that a friend told you about.

If this sounds like you, the dangers are obvious. People who want to integrate different types of therapies and mix them up with pharmaceutical or conventional medical treatments without good knowledge place themselves at risk of potentially serious consequences. A haphazard approach to combining herbs and supplements with pharmaceutical products has the potential to be ineffective or even dangerous.

Accurate information is a huge asset in taking control of your health, but there is no shortage of places to get unreliable information: crazy internet sites with unfounded conspiracy theories, friends of friends, or people purporting to have special knowledge of health without any training, experience or professional responsibility.

It is very important not to try putting together a combination of herbs and supplements yourself without expert

advice on your individual situation that takes into account your medical condition(s), age, and other supplements and medications which might interact.

What I am proposing here is a plan devised in consultation with your GP, other medical specialists and other trained health professionals, as well as informing yourself and working out the specific role that selected herbs and supplements will play in the overall plan to maintain or improve your brain health.

HERBS AND SUPPLEMENTS FOR BRAIN HEALTH

Acetyl-L-carnitine

Acetyl-L-carnitine is an amino acid that occurs naturally in the brain and liver. The liver and kidneys produce enough carnitine from the amino acids lysine and methionine to meet daily needs.

There are also several dietary sources of this important nutrient. The best sources are animal products like red meat, fish, poultry and milk. Dairy products contain L-carnitine primarily in the whey fraction.

Acetyl-L-carnitine has neuroprotective effects, and has been shown to improve depressed mood, reaction time and cognitive impairment in a range of contexts, such as ageing, dementia and traumatic brain injury.

The properties of acetyl-L-carnitine that are thought to be beneficial in dementia include activity at cholinergic neurons stimulating the synthesis of acetylcholine, membrane stabilisation and enhancing mitochondrial function.

Studies suggests that supplements of acetyl-L-carnitine may improve mental function and reduce deterioration in older adults with mild cognitive impairment and Alzheimer’s

disease. The daily dose in the studies varied from 1.5–3.0 g per day. Research result have been inconsistent, however, so it is difficult to make a definitive clinical recommendation.

Acetyl-L-carnitine can be used in conjunction with pharmaceutical antidepressant medications and with dementia drugs.

Ashwagandha

Ashwagandha, also known as *Withania somnifera* or Indian ginseng, is an Ayurvedic herb in the class of adaptogens, substances that help the body cope with stress. It is widely used for treating people with physical or emotional exhaustion and during periods of convalescence. Ashwagandha has antioxidant properties.

Animal studies have confirmed that Ashwagandha enhances memory via a cholinergic effect (increased acetylcholine receptor capacity). It has also been shown in animal studies to have a neuroprotective effect, including protection from neuronal injury in Parkinson's disease and promotion of dendrite formation.

Most of the evidence for the effectiveness of Ashwagandha in humans is through traditional experience. A 2017 pilot study of 50 adults found that Ashwagandha root extract was effective in enhancing both immediate and general memory in people with mild cognitive impairment, as well as improving executive function, attention and information-processing speed.

Bacopa monnieri (Brahmi)

Bacopa monnieri has been used for thousands of years in Avurvedic medicine as a 'brain tonic' for enhancing memory, intellect, cognitive ability and learning capacity. Brahmi is the Sanskrit name for *Bacopa monnieri*.

It has been extensively studied, and the possible mechanisms for its effects include anti-inflammatory, antioxidant, metal chelation, amyloid and cholinergic effects. It is also used to treat anxiety, nervous exhaustion and insomnia.

Bacopa monnieri has been shown in animal models of Alzheimer's disease to reduce beta-amyloid levels when it is administered before beta-amyloid deposition.

Two Australian studies, one in generally well people aged 18–60 years and one in people aged 40–65 years, showed that *Bacopa monnieri* led to improved brain function, and better retention and recall of information.

As with many herbal medicines, it can take time to see an effect. In the case of *Bacopa monnieri*, 12 weeks of regular use is needed before cognitive benefits are likely to be seen.

Choline

You can produce some choline in your liver, but not enough for your body's needs, so you need to obtain some from your diet. Choline is naturally present in many foods, such as meat, poultry, fish, dairy products, eggs, cruciferous vegetables and some beans, nuts, seeds and whole grains (see chapter 24: Brain Food). It is also available as a supplement.

Choline is essential for early brain development. It is necessary in the production of the important neurotransmitter acetylcholine, which is involved in memory, mood and muscle control.

Choline deficiency is rarely diagnosed because we do not test for it. However, it is known that choline deficiency can cause muscle damage, liver damage and non-alcoholic fatty liver disease. In a diet that is deficient in folate, the need for choline increases.

We know that excessive and long-term alcohol consumption produces disruption in neuronal synaptic connectivity and apoptosis. Excessive and long-term alcohol consumption also has a potent effect on choline metabolism in the left prefrontal cortex in the brain.

Alzheimer's disease sufferers have been found to have a lack of the enzyme responsible for converting choline into acetylcholine within the brain.

Some small trials have shown that choline supplements improve cognitive performance in adults. However, systematic reviews have not shown clear improvements in cognitive performance in healthy adults using choline supplements. Other studies have looked at supplementing with choline-rich lecithin in people with Alzheimer's disease or Parkinson's disease, but have not found a clear benefit. More evidence would be needed before being able to make a strong recommendation.

Coenzyme Q10 (CoQ10)

As described on page 204, and in further detail here, Coenzyme Q10 is a compound present in mitochondria of every cell in the body. Mitochondria are the tiny 'organelles' within cells that are responsible for energy production. CoQ10 is a key component of energy production in the mitochondria. Its active form is also known as ubiquinol.

CoQ10 is naturally produced in the liver, but its levels decrease as we age and may be low in people with some cancers, diabetes, heart conditions and Parkinson's disease. It is also produced by beneficial *E. coli* bacteria in the gut, so dysbiosis (altered gut microbiome) conditions resulting in low *E. coli* levels may result in low CoQ10 levels.

Cholesterol lowering medications (statins) interfere with the production of CoQ10 and can result in lower CoQ10

levels.

CoQ10 has attracted a lot of research and clinical attention for its potential in treating cardiovascular diseases, chronic fatigue and neurodegenerative diseases.

We need to focus on its effect on the brain and central nervous system, and its use and potential as a supplement to assist healthy brain function.

Oxidative damage and inflammation and mitochondrial dysfunction are thought to be contributing factors in ageing and the development of brain diseases such as Parkinson's disease. The brain is thought to be particularly susceptible to oxidative damage because of its high consumption of oxygen. Free radicals can cause damage to DNA, protein and membrane lipids in the brain, leading to the death of important neurological structures.

There is circumstantial evidence that CoQ10 can help limit the damage done by these disease processes. We know that CoQ10 protects neuronal cells from oxidative damage, possibly reducing the action of harmful substances that can lead to brain diseases such as Alzheimer's disease and Parkinson's disease.

Deficiencies in CoQ10 in brain cells are common in people with Alzheimer's disease, but there is currently no clinical evidence showing that supplementation slows the progression of the disease.

A 2002 study of CoQ10 and Parkinson's disease showed that CoQ10 appears to slow the progressive deterioration of function in Parkinson's disease. Less disability developed in study subjects assigned to CoQ10 than in those assigned to placebo, and the benefit was greatest in subjects receiving the highest dosage. Researchers found that CoQ10 was safe and well tolerated at dosages of up to 1200 mg per day. However,

other studies have failed to show a benefit. It is safe and easy to take, but it is not routinely recommended.

An Australian trial investigating the effects of CoQ10 supplements on cognition in healthy elderly people is underway. CoQ10 is thought to have the potential to improve brain function in healthy elderly people because of its known beneficial effects on mitochondrial function, vascular function and oxidative stress.

Omega-3 fatty acids

Fatty acids are major components of the brain, particularly in the neuronal cell membranes and the myelin sheath. There are many excellent reasons for including omega-3 fatty acids in your diet, and to supplement if you are unable to eat seafood.

There are three types of omega-3 fatty acids. The first two are EPA (eicosapentanoic acid), DHA (docosahexaenoic acid), which are mostly found in fatty fish.

Then there is ALA (alpha-linolenic acid), which is found in green leafy vegetables, vegetable oils, nuts and seeds, and is commonly taken as a flaxseed oil supplement for its high ALA content.

Your body converts ALA into DHA and EPA, but only in small amounts, so the best way of getting more EPA and DHA is to eat more fish, at least twice a week. However, some people do not like seafood or are allergic to it. In these cases, supplementation is necessary.

With regard to brain function, low levels of omega-3 have been found in people with attention deficit hyperactivity disorder (ADHD), learning deficits, depression and dementia.

Fish oil, with its components of EPA and DHA, has a powerful anti-inflammatory and anti-oxidant effect, which suggests there could be a protective effect on the brain.

In people who are healthy and have normal thinking and learning ability, we cannot say for sure whether omega-3s will prevent the onset of cognitive impairment. The evidence points to diets containing fish at least once a week being more beneficial for brain function than supplementation.

RECOMMENDATION: eat at least two meals of fatty fish per week and include ALA-rich plant foods.

Ginkgo biloba

Ginkgo biloba is one of the world's oldest living tree species, and its leaves and seeds have been used as a medicine for many centuries. Indeed, the individual trees can live for over a thousand years.

I remember visiting Xian in China a few years ago and being struck by the appearance of trees with brilliant golden yellow foliage. I was told they were ginkgo trees. There is one in the park near my home in Sydney, and every year in autumn it sheds its leaves, creating a beautiful golden carpet.

The leaf is quite distinctive. It is flat and shaped like a fan with a groove down the middle.

The most commonly studied standardised formulation is EGb761. It is widely prescribed in traditional Chinese medicine, and ginkgo is one of the most widely used herbal medicines in Europe and the United States of America.

Ginkgo biloba leaf extract is a complex herbal medicine with many active constituents. It has neuroprotective and mitochondrial protective effects, and has been used traditionally to improve brain function both in healthy people and in people with memory impairment.

However, an eight-year trial called the GEM study, published in 2009 in the *Journal of the American Medical Association*, questioned the effectiveness of ginkgo in

preventing cognitive decline. They found that it was not effective in reducing the development of dementia and Alzheimer's disease in older people. This study did have limitations, however. The age of the subjects (72–96 years, at an average of 79 years at the beginning of the trial) was quite advanced. This age group is not typical of the age of either healthy people or those with mild cognitive impairment who use ginkgo biloba for protecting or improving their cognitive performance.

Studies over the years have supported the traditional use, with controlled clinical trials showing that ginkgo increased short-term memory, concentration and time to process mental tasks.

The effects are not seen overnight. Like many herbal medicines, it takes time, around one to three months, to see initial results. And of course, research will continue to contribute knowledge and understanding of this herbal medicine and its effects on brain function.

B vitamins including folic acid (vitamin B9), vitamin B6 and vitamin B12

It was Australians Professor Fiona Stanley and Professor Carol Bower who made the crucial discovery of the link between maternal folate intake and the risk of neural tube defects such as spina bifida in babies. This led to a universal recommendation for pregnant women to take folate supplements, in addition to any dietary intake, to make sure their folate levels are adequate before conception and during pregnancy.

Folic acid or folate is essential for foetal development of the brain and nervous system, and it continues to be an essential nutrient in brain function throughout life.

The incidence of folate deficiency increases in older age, and there is epidemiological evidence of an association between low folate levels and dementia. There are also other risk factors for folate deficiency, including gut problems causing malabsorption of nutrients, some medications (see chapter 6: Medications) such as PPI acid-lowering medication and the oral contraceptive pill (especially higher dose versions), and excess alcohol consumption.

Evidence shows that correcting folate deficiency with supplementation may improve brain function in people with Alzheimer's disease and other forms of dementia, and also depression.

Various randomised trials and meta-analyses have shown a significant reduction in the relative risk of stroke with the use of vitamin B12, vitamin B9 (folic acid) and vitamin B6. Supplementing vitamin B12 (methylcobalamin), folic acid and vitamin B6 (pyridoxine) is important for people in the early stages of late onset Alzheimer's disease.

Vitamin B12

One of the conditions that mimics dementia (see chapter 16: The Dementia Mimics) is vitamin B12 deficiency. This deficiency can occur either as a result of inadequate dietary B12 (often seen in vegetarians or vegans), or poor absorption in conditions such as pernicious anaemia.

Inadequate vitamin B12 intake may cause cognitive deficits and even dementia. In people with dementia, a deficiency of vitamin B12 can make the condition look worse than it is. If someone has a form of dementia, supplementing with vitamin B12 will not cure the dementia, just the component of it that was made worse by the vitamin B12 deficiency.

It follows that to protect your brain, you need to make sure you have healthy levels of vitamin B12, either through diet or supplementing, or both.

One study revealed that the cognitive pattern of B12 deficiency showed some important differences to that of Alzheimer's disease. The group of older people who improved initially had more deficits in concentration, visuo-spatial performance and executive functions. They did not show language problems and ideomotor apraxia (the inability to correctly imitate hand gestures), which were present in the second group (the people who did not improve with B12 supplementation). Their memory pattern was also different. These findings suggested that vitamin B12 deficiency may cause a reversible mimic of dementia in elderly patients that may be differentiated from that of Alzheimer's disease.

Homocysteine and MTHFR

Vitamin B6, vitamin B12 and folate all reduce high plasma levels of the amino acid homocysteine. Elevated homocysteine is a known risk factor for cardiovascular disease, cerebrovascular disease and peripheral vascular disease, poor memory and cognitive impairment.

High homocysteine is also a strong and independent risk factor for cognitive loss and Alzheimer's disease. Homocysteine levels can be assessed with a blood test.

Keeping your homocysteine levels at a healthy low means maintaining adequate levels of vitamin B6, vitamin B12 and folate in their active forms:

- active vitamin B6 = pyridoxal-5-phosphate (P5P)
- active vitamin B12 = methylcobalamin
- active vitamin B9 (folate) = methylfolate.

Homocysteine can also be affected by ageing, physical inactivity, smoking, obesity, dietary deficiency, thyroid disease, diabetes, high cholesterol and some medications. This means that lifestyle factors such as exercise and diet, maintaining a healthy weight and not smoking are essential in modifying this risk factor.

MTHFR (methylene tetrahydrofolate reductase) is an enzyme that breaks down homocysteine. The MTHFR enzyme's production is directed by the MTHFR gene. The enzyme converts a portion of folate and folic acid into folinic acid. Folinic acid is then converted into the active form methylfolate.

The MTHFR gene can mutate, interfering with the ability of the enzyme to function normally, or at all. You inherit one MTHFR gene from each parent. Mutations can affect one or both of the genes. There are two common MTHFR gene variants: C677T and A1298C.

The mutation can lead to high levels of homocysteine in the blood, which can have health consequences, including birth abnormalities and mental health disorders such as depression, anxiety and attention deficit hyperactivity disorder. There may be an increased risk of some types of cancer, cardiovascular disease and cerebrovascular disease, abnormal blood clotting, and nervous system problems such as peripheral neuropathy and ataxia (poor coordination).

In the context of MTHFR mutations, high homocysteine is often associated with cerebrovascular small-vessel disease that shows up on brain scans. Cerebral small vessel disease (CSVD) has a crucial role in lacunar stroke and brain haemorrhages and is a leading cause of cognitive decline and functional loss in elderly people.

While a cause–effect link between MTHFR gene mutations and Alzheimer's disease is yet to be made, elevated

blood levels of homocysteine in elderly people is a treatable risk factor for cerebrovascular disease and dementia, and usually responds to careful treatment with supplements of B vitamins, including B6, B12 and methyl-folate under expert healthcare supervision.

Centella asiatica

Also known as gotu kola, Indian pennywort, pegaga and mandukaparni, centella asiatica is a herb that has been used for thousands of years in Avurvedic traditional medicine and other traditional medicine systems as a ‘brain tonic’ to improve mental clarity, focus and attention. It is also used as a herbal medicine in Europe. It is deemed to be a very safe herb with minimal to no side effects.

It has antioxidant, neuroprotective and neuroregenerative properties.

A systematic review found that centella asiatica could improve alertness and relieve anger. The review did not find strong evidence for overall cognitive improvement, but there was a positive benefit for working memory.

Magnesium

Magnesium is involved in over 300 enzyme reactions. It is needed in energy metabolism, insulin and glucose metabolism, protein synthesis, fatty acid synthesis and breakdown, muscle contraction, and for almost all hormonal reactions.

Magnesium is critically essential for brain function. Concerningly, magnesium deficiency is common. In fact, recent data from the Australian Bureau of Statistics Health Survey reveals that about a third of adult Australians don’t get enough magnesium.

Knowing this, in clinical practice I always keep magnesium deficiency and supplementation in mind in a range of clinical conditions. The signs I look out for include loss of appetite, nausea, vomiting, fatigue and weakness. More severe levels of magnesium deficiency can lead to numbness, tingling, muscle twitches and cramps, and abnormal heart rhythms.

Severe magnesium deficiency can result in disruption of other minerals, specifically causing low calcium or potassium levels, which cannot be corrected until the magnesium level is corrected.

Alcohol, caffeine and excess salt intake can also affect your magnesium levels, as well as gut malabsorption and excessive protracted stress.

You will find magnesium in foods such as wholegrain cereals, green leafy vegetables, legumes, soybeans, nuts, dried fruit, animal protein and seafood.

Magnesium plays an essential role in brain and neuromuscular function. It is required for the production of neurotransmitters. For example, the synthesis of dopamine requires magnesium. Magnesium helps to maintain normal levels of the excitatory neurotransmitter glutamate and it also supports the calming effect of GABA. Overstimulation by unnecessarily excessive levels of excitatory neurotransmitters can kill brain cells so magnesium protects against this. Among its many other functions, magnesium is also essential for the regulation of muscular contraction, blood pressure, insulin metabolism, heart function, nerve transmission and the action of nerves to make muscles work.

It is thought that in early Alzheimer’s disease, magnesium levels are low in the hippocampus, where memory is consolidated. More research is needed to confirm this, however.

Epidemiological research has noted an association between magnesium deficiency and Parkinson's disease.

Some forms of magnesium are not able to enter the cerebrospinal fluid (CSF). Magnesium in the form of magnesium threonate has been shown to cross over into the CSF, and may have a neuroprotective effect.

You can have a blood test to check for magnesium levels. The most useful test is the red blood cell magnesium level (RBC Mg).

Resveratrol

Resveratrol has been studied for its health benefits, such as anti-cancer, anti-inflammatory and brain protective effects. Resveratrol is present in foods such as grapes, red wine, mulberries, peanuts and rhubarb.

The presence of resveratrol in red wine is a fact celebrated by wine lovers. This is not a reason to take it up, but if you like an occasional glass of red, it's a bonus to know that there is an association with neuroprotection.

The neuroprotective effects of resveratrol in neurological diseases such as Alzheimer's and Parkinson's diseases are related to the protection of the brain's neurons against oxidative damage and toxicity, inflammation and to the prevention of neuronal death. It inhibits beta-amyloid protein aggregation.

There is some initial evidence that supplementing with resveratrol improves memory performance, in association with improved glucose metabolism and increased functional connectivity in the hippocampus in older adults.

St John's wort (hypericum)

St John's wort is one of the most commonly used herbal medicines. In particular, it is prescribed for its antidepressant effect related to the inhibition of serotonin reuptake. It also has an effect on various neurotransmitter systems affecting the levels of serotonin, noradrenaline and dopamine in the brain.

A promising area of use for the herb is in the moderation of brain-derived neuroptrophic factor (BDNF), which assists the brain to regulate plasticity, enhancing brain survival and growth.

It is also useful in the treatment of premenstrual syndrome, obsessive-compulsive disorder, and for managing some psychological menopausal and perimenopausal symptoms.

This herb is not to be taken with some regular medications, including antidepressants, so it is best to check with your practitioner before taking it.

Selenium

Selenium is a micronutrient essential to maintaining health. It supports your immune defences, your thyroid gland and cardiovascular function, and has a role in the prevention of cancer.

Selenium works as an antioxidant with glutathione to mop up free radicals. These are the molecules that cause damage to the structure and function of cells in the body, including brain cells, and the resulting oxidative stress is thought to be one of the mechanisms underlying several neurodegenerative diseases.

Selenium deficiency is seen in some areas of the world where the soil is deficient in selenium. We also know that selenium levels decline with age. Borderline low or deficient selenium concentrations might be associated with age-related declines in brain function, possibly due to decreases in selenium's antioxidant activity.

Reduction in selenium has been shown to be associated with cognitive impairment. A 2004 study described a direct correlation between the reduced selenium plasma concentration and the decline of cognitive function in people with Alzheimer's disease compared to healthy people. The main food sources of selenium are grains, cereals, seafood, meat, cruciferous vegetables (mainly broccoli) and brazil nuts.

You can test for selenium with a blood test. It is important not to take selenium in supplement form unless your selenium level is proven to be low. Even then, food is the preferable source. Selenium is contained in small quantities in some multivitamin and mineral preparations or antioxidant combinations. It is also available as a supplement to correct deficiency under the advice of a qualified healthcare practitioner. We don't know whether selenium supplements are able to help prevent or treat cognitive decline.

Older people should know their selenium levels and take action to correct deficiency, by dietary correction and/or supervised supplementation. It is important not to exceed 600 micrograms per day from dietary or supplement sources to avoid selenium toxicity.

Skullcap (Baical skullcap)

Skullcap is a herb used in traditional Chinese medicine to treat a range of conditions, including chronic inflammatory conditions.

One of its components, baicalin, has been shown to have neuroprotective properties in the brain by promoting neurogenesis and inhibiting neuronal apoptosis (programmed cell death). It has also been shown to have antidepressant and anti-anxiety properties (by stimulating GABA), and to improve cognitive performance.

Turmeric

Turmeric is a yellow spice used in cooking, and has been used in India as a herbal medicine for centuries. It is a member of the ginger family. Curcumin is a compound found in turmeric that is known to have powerful antioxidant, anti-inflammatory, anti-cancer and neuroprotective properties. It is now being suggested that curcumin has an anti-amyloid accumulation effect in the brain.

Many forms of curcumin are not well absorbed from the gut and do not easily cross the blood–brain barrier. Absorption is improved if it is taken with black pepper because of a compound contained in the pepper called piperine.

A small study at UCLA showed that curcumin supplements taken over 18 months improved memory and mood in 40 people between the ages of 51 and 84 with mild, age-related memory loss. The study found that memory improved by 28 per cent in the participants who took curcumin, but not in those who took the placebo.

As discussed in chapter 20: Dementia, in Alzheimer's disease a peptide called beta-amyloid aggregates and forms deposits known as amyloid plaques around neurons in the hippocampus and cerebral cortex. We also see the accumulation in cells of neurofibrillary tangles formed by tau protein, and subsequent neuronal loss.

FDDNP-PET scans performed on people in the study of curcumin before and after treatment suggested that behavioural and cognitive benefits were associated with decreases in plaque and tangle accumulation in brain regions affecting mood and memory.

This was a small and relatively short-term study. Larger studies over a longer period of time would be needed to determine what role curcumin might have in preventing or

delaying cognitive decline. There is a lot of interest in the potential for curcumin to be used clinically for this purpose.

Vitamin C

Vitamin C (ascorbate) has many functions essential to health. It is probably best known for its antioxidant effect.

It also has a role to play in the synthesis of neurotransmitters, and is needed to produce serotonin.

You need to include vitamin C in your diet because your body is not able to synthesise it for you. Deficiency to the point of scurvy is uncommon in Western countries, but marginal deficiency is more common. This may be more common in elderly people who are isolated or institutionalised, people with chronic alcoholism and tobacco smokers.

Observational studies have reported lower vitamin C levels in people with Alzheimer's disease compared to cognitively healthy subjects, and found better cognitive function or lower risk of cognitive impairment with higher plasma vitamin C.

While vitamin C is essential for brain health, the science does not seem to support supplementing vitamin C in people with adequate levels.

The recommendation is to make sure that you do have adequate levels of vitamin C in your diet and to supplement where this is not possible. You can achieve adequate levels by making sure you eat a variety of fresh fruit and vegetables each day, including citrus fruit, berries, kiwi fruit, capsicum, tomato and spinach.

Vitamin D3

Vitamin D is an essential micronutrient. It is important for developing and maintaining strong bones, muscles and a

functioning immune system, and is essential for normal brain development and function.

There are receptors for vitamin D throughout the central nervous system, including neurons and glial cells. A deficiency of vitamin D has the potential to impair cognitive ability.

Vitamin D protects neurons and reduces inflammation, and may have a role in detoxification processes in the brain. It activates and deactivates enzymes in the brain that are involved in neurotransmitter synthesis and nerve growth.

Even in a country like Australia, where we like to see ourselves as being all about the great outdoors, a lot of people spend most or nearly all of their time indoors. I commonly see people who get up before sunrise, exercise indoors at the gym, get dressed for work, and don't return home until after the sun has set. They may get some time outdoors on weekends, but they are so concerned about skin cancer that they avoid any sun exposure and cover up with sun protection. The sun protection message can go too far. Our bodies need regular sun exposure (without sunburn) to maintain adequate vitamin D levels.

Vitamin D deficiency is a particular risk for people who spend little time outdoors or who do not expose their skin to the sun when they are outdoors. People with darker skin are more likely to have a deficiency. Some conditions such as coeliac disease and inflammatory bowel disease affect vitamin D absorption, as well as some medications (prednisone, diabetes medication and some blood pressure medication).

Low circulating levels of vitamin D may also be associated with a higher risk of multiple sclerosis and there may be an association with the onset of Parkinson's disease.

A deficiency of vitamin D can have serious health consequences, including an impact on brain function, although

the exact relationship is not yet clear.

A study at the University of Cambridge, England, found that low serum 25-hydroxyvitamin D in older people is associated with an increased risk of cognitive impairment. The lower the vitamin D level, the greater the effect on their cognitive test results. The researchers raised the question of whether ‘vitamin D supplementation is a cost-effective and safe way of reducing the incidence of cognitive impairment in the growing elderly population around the world’.

Another study at the University of Manchester also in England found that people with lower vitamin D levels exhibited slower information-processing speed.

There is a small amount of vitamin D in some foods, such as fish and eggs, but it is nearly impossible to get adequate vitamin D from your diet, so either regular exposure of your skin to sunlight, or a dietary supplement is necessary to maintain your levels.

How much is enough? It is important to know if your vitamin D level is adequate, especially if you rarely get out in the sun. Your vitamin D levels can be checked with a blood test.

If you have a significant Vitamin D deficiency, you will need to supplement with vitamin D tablets, capsules or drops. You will need professional advice about the right dose to correct a deficiency. The range will vary from 2000IU to 5000IU or more a day for several weeks, then a maintenance dose of 1000–2000IU daily to avoid a future deficiency, if regular sun exposure is not achievable. Between 10 and 20 minutes per day of sun exposure two to three times a week to the arms, legs and torso, is needed for maintenance. This can be more difficult in the cooler months.

Vitamin E

Vitamin E is an antioxidant with anti-inflammatory and neuroprotective properties. It is thought to protect brain health by reducing oxidative stress, and is essential in maintaining the integrity of cell membranes.

Severe vitamin E deficiency can result in neurological complications, including ataxia (loss of coordination), peripheral neuropathy (damage to the nerves in your extremities), myopathy (muscle weakness) and loss of vision.

Dietary sources include vegetable oils, nuts, seeds, avocados and green leafy vegetables.

Levels of vitamin E in Alzheimer's disease patients are lower than in people without dementia.

Vitamin E may be useful in Alzheimer's disease sufferers who are lacking in this nutrient. The success of vitamin E supplementation may be down to the form given, but also to genetic and lifestyle factors – smoking being the most detrimental. Studies suggest that there is some benefit to reducing cognitive decline, but that it may not be useful in treatment.

Zinc

Zinc is present in brain tissue and in synaptic vesicles, where it plays an important role in neurotransmission mediated by glutamate and GABA. It has a critical role in regulating communication between brain cells.

Zinc has general neuroprotective properties and zinc deficiency impairs neurological and cognitive function and has general neuroprotective properties. Zinc is involved in neurogenesis in the hippocampus. One sign of zinc deficiency is a loss of taste and lack of appetite.

Dietary sources of zinc include meat, poultry, shellfish, eggs, miso, tofu, beans, nuts and wholegrains. Vegetarians and

vegans are more likely to be deficient in zinc, both because there is less zinc in a vegan diet and because absorption of zinc is impaired in the gut by phytates in grains, and may need to supplement to avoid zinc deficiency.

Souvenaid™

There is a combination supplement called Souvenaid™, which I am including here because it is recommended by a number of geriatricians who see my elderly patients with mild dementia. Souvenaid contains the active ingredients docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), uridine monophosphate, choline, vitamins B12, B6, C, E and folic acid, phospholipids and selenium.

This combination was chosen because concentrations of these nutrients in plasma and cerebrospinal fluid around the brain were known to be lower in patients with Alzheimer's disease, and the ingredients were known to have various neuroprotective qualities.

A 2017 study published in *The Lancet* journal found some promising results. Over 300 people with very early stage Alzheimer's disease were studied in the trial. Half received the Souvenaid and half were given a placebo that looked and tasted the same, but did not contain the active ingredients. After two years, the subjects' dementia progression and brain structure were reassessed. People taking the Souvenaid had slightly less brain shrinkage (particularly the hippocampus) on MRI scans. There was 26 per cent less reduction in the volume of the hippocampus volume in the active group.

There was also a small improvement in memory, with some evidence of a beneficial effect at the 'cognitive-functional level' with skills like managing financial transactions or remembering major events.

MEDICINES CAUSING NUTRIENT DEPLETION

If you are taking a medication that impacts on the absorption of nutrients from your digestive system, you may need to anticipate this and take a supplement to avoid or correct the deficiency. Where the problem is absorption, adjusting your diet is unlikely to be enough. I looked at some of the most likely nutrient depletions in chapter 6: Medications. Here is that list again, with recommendations for supplementation. This is not an exhaustive list, but it will provide you with some awareness and guidance on how to protect yourself and what supplements to consider. If you are prescribed one of these medications, I suggest discussing doses and combinations of supplements, as well as a review of medications, with your healthcare advisors.

- Oral contraceptives (birth control pills): B vitamins, vitamin C, magnesium, selenium and zinc
- Hormone replacement therapy: vitamin B6, vitamin B12, folate and magnesium
- Anti-diabetes drug (metformin): folate, vitamin B12, coenzyme Q10
- Anti-inflammatory (examples: ibuprofen, aspirin): iron, vitamin C
- Oral diabetes medication: vitamin B12, folate. Reducing blood glucose imbalance is a protective factor in the reduction of cognitive decline.
- Indigestion and anti-ulcer drugs (H2 antagonists and proton pump inhibitors) used to lower stomach acid: vitamin B12, folate, vitamin D, and magnesium, calcium, iron and zinc
- Statins (cholesterol-lowering drugs): coenzyme Q10
- Diuretics (fluid tablets): B vitamins, magnesium, zinc and potassium

- Beta-blockers: coenzyme Q10, melatonin
- Digoxin: calcium, magnesium, phosphorus, vitamin B1 and potassium
- SSRI antidepressants: folate
- Antipsychotics: vitamin B2 (riboflavin)
- Benzodiazepines: calcium, endogenous melatonin
- Antibiotics: many antibiotics can deplete B vitamins. Also, while gut flora are not strictly nutrients, depletion of the important bacteria in your gut can affect the absorption and metabolism of some important nutrients. A probiotic is essential if you are taking or have recently taken a course of antibiotics.

RECOMMENDATION

This chapter is not an exhaustive list of all of the herbs and supplements that may provide a protective or supportive role in brain health. Make sure you correct your nutrition by introducing brain-healthy foods and eliminating brain-unhealthy foods. As their name suggests, supplements supplement an optimal diet for brain health. But that is not all that they do. They also have a role as therapeutic agents.

There are a number of supplements that have been shown to have a benefit or a potential benefit to brain health. Over time, the evidence will grow, and it will become clearer which supplements are most beneficial to achieving particular outcomes such as brain development, mood stabilising or prevention of cognitive decline. For example, the evidence for folate supplementation before and during pregnancy is now universally accepted and recommended.

On the other hand, we know that B vitamins, antioxidants and omega-3 fatty acids are necessary for brain health, but it is not established beyond doubt that supplements over and above

dietary correction will improve memory or protect against age-related cognitive decline.

As with all areas of medicine, we have to rely on clinical experience and the best available evidence, and make decisions accordingly.

It is important not to self-prescribe. Not all health practitioners (and I include doctors in this) have expertise in prescribing herbs or supplements, so I recommend that you seek expert advice from a health professional with experience in prescribing supplements for brain health. This is particularly important if you are taking any medications likely to interact with a supplement.

26

Brain and Connectedness

The year 2020 was an extraordinary and unexpected experiment in the importance of connectedness. When the COVID-19 pandemic was declared, and there was no vaccine and no cure, the only protection we had against the virus was to stay away from other people. We were forced to view even our closest friends and family as potentially, unknowingly, lethal to us.

People everywhere were told they had to lock down their household. Grandparents were told it was too dangerous to see their grandchildren.

Employees of many workplaces began to work from home. Offices and retail stores emptied.

Restaurants and cafes closed.

Teachers spent weeks working to set up remote learning as children were home-schooled.

Public transport was empty.

Laws were passed to restrict movements and limit social interactions.

Gyms closed.

Events were cancelled.

Theatres went dark.

The only legal excuses for leaving home were for activities like daily exercise, essential shopping and medical appointments.

These were extraordinary times.

An interesting element of this unprecedented time was the almost universal compulsion to embrace all manner of virtual online platforms, all in a bid to maintain connections.

University tutorials went to platforms like Zoom.

Special laws were passed to allow local councils to meet online.

Doctors began doing telehealth consultations. The government moved faster than I have ever seen them move to allow Medicare rebates for remote consults by video or phone.

Grandparents had to resort to watching their grandchildren play on FaceTime.

Friends caught up over FaceTime or Zoom wine and cheese evenings.

Churches and synagogues started live-streaming religious services.

People found inventive, creative ways to achieve physical distancing while still establishing personal and social connections.

The World Health Organization, which had started referring to the importance of ‘social isolation’, changed its terminology to ‘physical distancing’. This made sense, because in fact, people made every effort to minimise the loss of their social connectedness.

As the weeks and months ground on, the experience continued to reinforce for me, more than ever, the existential necessity of positive human contact.

Connectedness is the connection we feel to other people, to community and our social institutions. Humans need social connections. Connections with partners, family, friends, school, university, workplace, clubs, faith groups and community groups.

The opposite of connectedness is isolation. Social isolation or a sense of loneliness has been assessed to be a health risk equivalent to smoking 15 cigarettes a day, and is considered to be one of the major life stressors.

There are many times in our lives when our situations change significantly. In my own life there have been times when social connections have been disrupted: leaving school to go to university, where I knew nobody, for example. Being a young mother who didn't know anyone with children was a lonely and at times depressing part of my life. I tried several different playgroups until I found a group of mothers who shared some common interests. Parent groups are very important in helping new parents cope with social isolation.

Separation or divorce can fracture your friendship group – sometimes friends of a couple polarise, and social connections are severed.

Changing jobs or retiring bring change that can disrupt the day-to-day social connections that come with a shared workplace.

Becoming widowed or reaching an advanced age are other high-risk times for social isolation.

Our brains need social connectedness too. Social isolation is a known risk factor for cognitive decline and dementia. As a doctor, I often identify social isolation as one of the key issues

that needs to be addressed when people present with apparent depression.

Connectedness is essential to early brain development, and to avoiding depression, sleep problems, poor heart function and impaired immunity at every stage of life. Social isolation has also been linked to accelerated cognitive decline.

The impact of social connections on brain development starts in our earliest days of life, and those experiences shape the actual structure of the brain. Many of the early signs of development that we look for in a newborn baby are indicators of social interaction, like the ‘fixing and following’ of a face by a baby’s eyes, or the responsive smile of a baby at around six weeks of age.

Different types of play and stimulating social interactions encourage healthy brain development too. The development of the brain’s structure and function in those areas that govern motor, sensory, thinking, language and self-regulation skills, as well as social skills such as collaboration, are all enhanced by providing children with opportunities for different types of play.

We know that infants who are deprived of quality social interactions in early life, children exposed to war, physical and sexual abuse, chronic poverty, abandonment, domestic violence and other adverse environmental influences have developmental difficulties related to abnormal brain development.

Children raised in institutions are more likely than children raised in functional loving families to have impaired cognition.

A study of Romanian children investigated whether there was any demonstrable difference in the brain development of children raised in orphanages with little social interaction compared with a control group of children raised in loving, supportive homes within the same culture.

Researchers compared the brains of ‘typically developing Romanian children’ to children previously in institutions who were moved to high quality foster care. This was known as the Bucharest Early Intervention Project.

Structural MRI scans showed that orphaned and abandoned children with histories of institutional rearing and very limited stimulation and social interaction had significantly smaller cortical grey matter volume than children who had never been institutionalised. The cortical white matter part of the brain was no different for children placed in foster care than never-institutionalised children, but was significantly smaller for children not randomised to foster care. The researchers concluded that the increase in white matter among children moved to an improved home environment compared with children who remained in institutional care suggests the potential for developmental ‘catch up’ in the brain’s white matter growth, even after extreme environmental deprivation.

Children placed in a quality foster care environment at a younger age showed greater improvement.

ADOLESCENCE

The ‘teenage brain’ is a source of fascination and no small measure of frustration for parents, teachers and psychologists.

Risk-taking behaviour, failing to think through the consequences of actions, impulsivity and miscommunicating emotions are all features of the teenage brain.

Of course, there is enormous individual variation in personality types, genetic factors, environmental factors and hormonal influences governing behaviours in adolescence.

Just as the internet can be a lifeline for people who are physically isolated, it can also be a danger to the social and emotional development of a vulnerable teenager.

The development of the teenage brain occurs at the same time as an adolescent has increasing opportunities for autonomy, in turn providing more opportunities for risk and danger.

Adolescence is also a time of immense growth in understanding of your own identity, and self-consciousness, and comprehension of other people's actions and motivations.

It is important to understand that acquiring skills like thinking before you act is a developmental stage as important as learning to walk and talk as an infant.

Health behaviours and social environment continue to shape brain development through adolescence. This is a crucial time in life for understanding social interactions, developing decision-making skills, and responding to peer influence to take risks and push limits.

Adolescence is also a risk period for the development of mental health disorders such as depression, anxiety and psychosis, and we know that many are associated with social dysfunction.

Neuroimaging techniques such as MRI and functional MRI developed in the past two decades have transformed our understanding of what happens to the structure and function of a developing brain.

Brains continue to develop and remodel through adolescence and well into adulthood. The amygdala develops early and is the part of the brain responsible for impulses, emotions and aggression. The adolescent brain is more likely to rely on the amygdala for immediate reactions. As it matures, it brings greater sensitivity to social cues, social hierarchies and physical appearance, and greater emotional regulation.

The prefrontal cortex is about higher-order thinking. It is the part of the brain responsible for reasoning, decision-

making, impulse control, problem-solving, planning and thinking about the consequences of your actions. Changes in the prefrontal cortex occur more slowly, and continue into the mid-twenties and beyond.

The wiring connections between brain cells and the protective myelin sheath around nerve cells also continue to develop through adolescence.

I have often heard young people say they don't want to study mathematics or science at school because they don't think they will ever use, say, calculus or chemistry in their lives. Of course they will use that knowledge to make sense of the world, but the point is that the brain training and structural brain-forming those exercises provide enhances brain development and thinking processes.

Similarly, along with ensuring enough sleep, providing a wide range of educational experiences, regular exercise and nutrition, and avoiding brain toxins, the quality of social experiences in adolescence helps to continue the development of parts of the brain responsible for understanding the minds, motivations, needs, goals and behaviour of other people (called 'mentalising') and governing social interactions.

When we think about the impact of social connections on the development of the adolescent brain, we need to think also of how the so-called teenage brain affects social competence and social connections with friends, family members, teachers and the wider community.

Encouraging healthy adolescent social development is a challenge for parents, but helping adolescents develop positive supportive friendships is essential to healthy brain development. As a parent, you can't protect your child from every bad experience, and it may also be by experiencing negative friendships that young people learn about themselves and what they need (and don't need) emotionally.

Young people also learn about social relationships from observing and interacting with their parents and parents' friends.

Adolescent friendships are a transition from parental relationships to future independent adult relationships.

Through these friendships, adolescents learn valuable social values such as showing care for others, communicating feelings, developing trust and solving problems together. They may also learn what they need to avoid in a relationship.

So, what can parents and the community do to ensure that this essential part of adolescents' brain structure and wiring, particularly in the amygdala and prefrontal cortex, develops in a healthy way for their future?

Adolescence is a time for encouraging personal interests and passions. In addition to engaging in school activities, involvement in a range of extracurricular activities, sports and the arts in safe supervised environments will help build interpersonal skills and community engagement.

As outside friendships become more dominant, it is important to foster ongoing connection with family members of different ages.

The COVID-19 lockdowns reinforced how important online social connections are, but those interactions can also be distressing or risky for a young person, and internet safety is an important conversation. Parents need to be aware of the potential for dangerous online interactions and know how to manage that risk. This will involve making a plan for internet safety and, particularly for younger adolescents, monitoring their online activity.

Parents need to be on the lookout for signs of depression, anxiety or other mental health problems in adolescents, and set a good example of healthy behaviours (abstaining from

alcohol and smoking, demonstrating non-violence and non-judgemental communication).

It is wise for parents to get to know their child's friends and their parents. Communicating regularly with friends' parents is a useful exchange of information that may alert a parent to any concerns within the school year group or wider friendship group.

GETTING OLDER

Social connections are no less important in the older years than they are in the early developmental years.

Social isolation can be life-threatening. One study found that men who had experienced a heart attack were three times as likely to die from their heart disease in the following six months if they were socially isolated.

Research also tells us that older people who are more socially engaged and have larger social networks tend to have a higher level of cognitive function.

We also know that social and productive activities such as games, work and social outings are protective against death and cognitive decline in the elderly.

When I was a member of Parliament, I visited a project called the Men's Shed in eastern Sydney. This is a government initiative to reduce the number of men who are at risk from preventable health issues that result from social isolation. Several of the men I spoke with joined the group after they had divorced or become widowed. Several had sought out the project after they retired from high-pressure jobs and found they had no connections outside their workplace. They all relied on their regular visits to the Men's Shed for social connections and to be involved in meaningful community projects.

Of course, life events can get in the way of established social connections: retirement, the loss of a partner through death, separation or divorce, limited mobility due to illness or disability.

These can all contribute to a contraction of social networks, making it more likely that people become less socially engaged as they age.

While connectedness is important to brain health at every age, as you get older you need to find some new ways to maintain those social connections that are essential to brain health.

RECOMMENDATIONS

Here are my recommendations to maintain and build meaningful social connections in order to support your brain health through your life:

- Put effort into the relationships or social activities that give you the most enjoyment.
- If you have time on your hands and you feel isolated, volunteer. Pick a community organisation that needs help and offer your time and expertise.
- If you find yourself without social connections, reach out. Think about your interests and the types of people you would like to have as friends. You may need to try a few different groups until you find one that suits you. This may mean joining a sporting club or a social group.
- If you have trouble getting around, see if there is someone who can help you with transport. Many local councils have community transport assistance available for people with mobility problems.
- Cultivate a group of friends of different ages and from different backgrounds, and make sure you have regular

positive contact with them.

- Think of the people in your life who are important to you, and to whom you are important, and try to communicate with them at least once a week, face to face when possible.
- Whether or not you are in a committed relationship, develop other important friendships.
- Try taking on new interests or learning new skills in a group.
- Join an organised club, sign up for a course that interests you or get politically active.
- If you have difficulty making initial connections, reach out to others with common interests on social media.

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Relationships

In chapter 26: Brain and Connectedness, we talked about the importance of social connectedness for brain development and maintenance of brain health at all life stages, from infancy through to old age.

Taking that a step further, what effects do more intense personal relationships have on your brain?

What about falling in and out of love?

Some relationships take you on an emotional rollercoaster. A close and supportive love relationship can be the scaffolding you need to cope with the stresses and challenges of life. Conversely, a toxic or abusive personal relationship can damage your emotional health.

If you are lucky enough to really fall in love once or twice in your life, you will know the feeling of euphoria it generates. For centuries, poets and songwriters have sought to capture the essence of love in words and music.

Before we had an understanding of the role of neurotransmitters, love was thought to be generated from the heart. But no, love is orchestrated by the brain. It seems almost brutal to try to boil it down to an analysis of the brain

chemicals that generate such a complicated physical and emotional phenomenon, but here goes anyway!

Many scientists have tried to reach an understanding of love, this most fundamental of human conditions. Dr Helen Fisher and a team of scientists at Rutgers published a paper in 1997 in which they deduced that romantic love can be broken down into three categories: lust, attraction and attachment. Further, they found that each of these stages has its own set of responsible neurotransmitters.

Lust, or the sex drive, is mainly associated with oestrogen produced in the ovaries and testosterone produced in the testes and stimulated by the hypothalamus.

The attraction category focuses intense attention on the potential partner with intrusive thinking, focused attention and a sense of exhilaration. It is associated with the catecholamines adrenaline and noradrenaline. These neurotransmitters create the so-called adrenaline rush, that buzzy feeling of excitement, the sweaty palms and racing heart, the butterflies in your stomach, dizziness, increased alertness and arousal that come with a new attraction. This can also affect your appetite and your ability to sleep.

Dopamine and serotonin are also involved here. The brain's reward pathway activates and releases dopamine when we do something that feels good, creating the sense of euphoria. In attraction there is a reduced serotonin level. It has been suggested that this drop in serotonin is responsible for the features of preoccupation or infatuation, because it is a similar feature to the low serotonin levels seen in obsessive-compulsive disorder.

Attachment is characterised by the warm and comfortable feeling of a deep and hopefully reciprocated emotional bond with a partner. This sense of wellbeing and emotional security is associated with the hormones/neurotransmitters vasopressin

and oxytocin. Oxytocin is a hormone released during sex, childbirth and breastfeeding, so it has a strong association to bonding and attachment.

WHEN LOVE GOES WRONG

All is not always rosy in the garden of love. The same hormones that can feel so good when things are going right can also be in play when love goes wrong.

Strong sexual desire can turn off your critical thinking ability and cause you to act in reckless ways that you otherwise might not. Similarly, too much oxytocin in the wrong context can cause you to focus only on the positives in this new attraction to another person, leaving you unable to see the other person or the world around you in perspective.

Attraction also brings with it the features of emotional dependency, with feelings of vulnerability, insecurity, fear of loss or rejection, jealousy and mood swings that follow the ebbs and flows of the relationship. This is particularly the case when attraction is not reciprocated, or when one person is more enthusiastic about a relationship than the other.

If your brain is releasing a lot of dopamine in response to a strong attraction to another person and that attraction is not reciprocated, the sensations of not being able to see that person or have your feelings reciprocated is akin to withdrawing from an addiction.

Connection to other humans is a fundamental drive. Instinct tells us that healthy social connections can play a role in maintaining and enhancing brain health. So does science.

According to the Australian Institute of Health and Welfare, loneliness is a significant health issue. It has been linked to premature death, poor physical and mental health, and general dissatisfaction with life.

Social isolation has also been linked to mental illness, emotional distress, suicide, the development of dementia, premature death, poor health behaviours, smoking, physical inactivity, poor sleep, and biological effects, including high blood pressure and poorer immune function.

Just being in a relationship or part of a family group is no antidote to loneliness. Some of the loneliest people I have met are in unhealthy, unfulfilling or toxic personal or family relationships. Being in a toxic relationship is itself a risk to your brain health.

TOXIC RELATIONSHIPS

How do you recognise a toxic relationship?

A toxic relationship can be an intimate personal relationship, a family relationship, a friendship or a work relationship. Think about the people you have interacted with over time, and those who are currently a part of your orbit. Do you find yourself making excuses to avoid family functions or heading home for the holidays? Is there a person in your extended family or friendship group who creates conflict, criticises you unfairly or makes you feel bad about yourself?

What about your workplace? Is there someone who undermines you, or makes you feel dread when you know you are likely to interact with them?

Here are some of the ways you might recognise a toxic relationship. It is a relationship with another person that:

- makes you feel bad about yourself through criticisms or unwelcome suggestions about how you might ‘improve’ yourself
- makes you feel sad, anxious, upset or just resigned
- makes you feel physically or emotionally unsafe

- makes you think there is something very wrong with you
- feels hostile
- discourages your friendships, family relationships or other supportive social contacts
- makes you constantly feel insecure, or controlled
- causes you to feel mentally or physically drained.

Just as supportive relationships help you cope with stress, a toxic relationship creates chronic stress.

The science tells us that major life stressors, especially those involving interpersonal stress and social rejection, are among the strongest risk factors for depression. The theory is that the chronic stress of a toxic relationship activates a type of gene expression in the brain associated with inflammation and low immunity. This in turn initiates depressive symptoms such as sad mood, loss of enjoyment in life, fatigue, slowing of thought processes and social withdrawal.

The chronic inflammatory response related to chronic stress also causes an overlapping of depression with other health problems, including asthma, rheumatoid arthritis, chronic pain, metabolic syndrome, cardiovascular disease, obesity and neurodegenerative conditions.

It can be difficult to address a toxic relationship, however, because these relationships can make you feel powerless. The closer the level of intimacy and the longer the relationship, the more difficult it can be to recognise how unhealthy the relationship is for you, and to unravel the connections.

You can ‘name the beast’, telling the other person how they make you feel, and sort out any misunderstandings or differences, or at least agree to disagree. I don’t mean to make this sound easy, because it may not be. It may take a psychologist or a mediator with experience and wisdom to sort

out more serious interpersonal differences, and both people need to be willing to engage in the process.

Addressing toxic workplace relationships depends on the nature and structure of the workplace. Larger organisations have human resource departments tasked with sorting out issues like workplace bullying. In smaller workplaces, you would ideally approach a more senior person in the organisation, or the employer, to let them know what is happening and the effect it is having on you. It can be very difficult to change a workplace culture, and sometimes the best option is to leave and find a healthier workplace.

Some toxic relationships cannot be mended because of the people involved or the complexity of the system supporting the toxic behaviour. In this situation, you need to consider when and how to end it.

You can decide to make a strategic withdrawal from a toxic workplace culture or a toxic friendship or relationship. Again, this is not as easy as it sounds.

Professional counselling is usually necessary so that you can work out, in a safe space, how you feel about your relationship and what you need for your future. The result may be changing the way you behave within the relationship, or it may be making the decision to end the relationship.

However, if you change nothing, nothing will change. You will continue to feel miserable, and this will affect many aspects of your health, including your brain health.

Until you have taken the steps to deal with the problem of a toxic relationship, relaxation strategies such as mindfulness, meditation or yoga can help reduce the physical impact of stress.

The final word on toxic relationships? Mend them or end them!

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Sleep

Sleep is anything but a passive state. In fact, it is an extremely busy time for your brain. Quality sleep is essential to your brain's ability to function.

It's good to know that the time you are sleeping is not wasted, because it occupies up to a third of your life.

Some people can fall asleep as soon as their head hits the pillow, stay asleep undisturbed during the night and wake refreshed. But not everyone is so lucky.

Sleep problems are some of the most common problems we see in general practice. Sometimes it is the sleep problem itself that is distressing, but poor sleep can also cause significant health problems such as brain fog, depression, irritability, impaired immunity, high blood pressure, obesity, type 2 diabetes, hormonal disruption and clumsiness leading to a higher risk of accidents.

For our purposes, I will focus on the importance of sleep for brain health.

Sleep enables your brain to process the learning of the day and to consolidate the memory of new information and new skills. We also believe that sleep facilitates the efficient removal of waste products from your brain cells.

Sleep is so important that even if you go without sleep for a night, your brain will want a ‘recovery’ sleep the following night of several hours greater duration than normal, with more deep sleep included in the mix.

We know that if you are sleep deprived you have trouble thinking clearly and have difficulty remembering new information. You can become moody, anxious and depressed.

Sleep becomes a problem for many people with dementia. Between a quarter and half of people with dementia have sleep disturbances. This is probably at least partly due to the disruption in normal brain functions governing sleep cycles, but there will also be other factors to consider, such as medication effects, pain and other medical conditions. Sleep changes can also be one of the early signs of dementia.

SLEEP THROUGHOUT THE LIFE CYCLE

HOW MUCH SLEEP DO WE NEED?

Newborn babies: at least 18 hours a day

Adults aged 26–64 years: seven to nine hours

Adults aged 65 and older: seven to eight hours

Elderly people: might only sleep an average of six hours a night, but may need a nap during the day.

Your sleep today is also important to your brain health in the future.

During adolescence, sleep patterns change significantly. We know that the adolescent brain is undergoing significant structural and functional transformation, and that brain activity patterns during sleep become demonstrably different in adolescence.

Electroencephalogram (EEG) studies show that during adolescence ‘there is a 50% reduction of deep (stage 4) sleep and a 75% reduction in the peak amplitude of delta waves during nonrapid-eye movement sleep’.

During adolescence there are also behavioural changes that affect sleep, including a tendency to stay up later, meaning later sleep onset and less hours asleep, partly because they have to be up early for school on weekdays. This often results in inadequate sleep, averaging 6.5 to 7.5 hours a night.

Chronic lack of sleep in adolescence can contribute to behavioural and mental health problems such as depression, poor decision-making, and lack of energy or interest. It will also reduce academic performance at school by causing a reduced attention span, difficulty concentrating, impaired memory formation and more days off school.

Chronic sleep deprivation in young healthy people has been reported to:

- increase appetite
- increase levels of proinflammatory cytokines
- increase blood pressure
- increase evening cortisol levels
- elevate insulin and blood glucose.

All these physiological changes can have an impact on brain structure and function.

With the normal ageing process, sleep quality and quantity changes. As we age, sleep becomes more fragmented, and there is a decline in the quantity and quality of the ‘deep’ stages of sleep, such as slow-wave sleep and REM (rapid eye movement) sleep.

Interestingly, research suggests a number of interesting trends:

- Sleep deprivation causes greater cognitive impairments in young adults than in older adults.
- Sleep promotes memory consolidation in young adults more than in older adults.

- Napping and improved night-time sleep benefit cognitive functioning in young and middle-aged adults, but often not in older adults.

Research tells us that maintaining good sleep quality, at least in young adulthood and middle age, promotes better cognitive functioning and serves to protect against age-related cognitive decline.

In older age it becomes harder to get to sleep and to stay asleep. Some say you need less sleep as you get older. An alternative view suggests that you don't need less sleep, you just get less sleep than you need.

Older people do have a less intense rebound sleep following a period of sleep deprivation, and are less likely to feel sleepy under sleep restriction conditions. Older people also suffer less from lapses of attention after sleep deprivation than younger people.

However, there is still a minimum amount of good-quality sleep required. For some older people, it has been suggested that the brain's ability to generate that sleep or to catch up on a sleep deficit can become impaired.

Sleep reinforces new memories, so sleep disruption will have an effect on short-term memory recall. Deterioration of the prefrontal cortex diminishes the slow waves that occur during deep sleep. Slow brain waves are thought to enhance the transfer of information from the hippocampus to other parts of the brain for long-term storage.

That said, there is a recognised association between sleep disruption and cognitive decline and dementia. Between 60 and 70 per cent of people with cognitive impairment or dementia have sleep disturbances. It is reasonable to say that sleep disturbances impair your brain functions across the lifespan, and that impaired brain function can disrupt healthy sleep patterns.

PHASES OF SLEEP

It is important to understand the normal phases of sleep. There are two main types of sleep: REM (rapid eye movement) sleep and non-REM sleep.

REM sleep refers to a stage of sleep where the eyes move rapidly beneath your closed eyelids, your muscles go floppy and your heart rate and breathing become irregular. An electroencephalogram (EEG) brain activity pattern shows a rapid low-voltage pattern similar to the brain waves seen while you are awake. This is when dreaming occurs.

There are four or five episodes of REM sleep each night, with about 90 minutes between episodes. They last from a few minutes up to 30 or 40 minutes. If you are woken during REM sleep you may recall vivid dreams.

Non-REM sleep has three stages based on the type of brain activity that occurs during each stage. As you sleep, your brain cycles repeatedly between REM and non-REM sleep. Quiet or non-REM sleep accounts for most (80 per cent) of the sleep period.

Stage 1: You drift in and out of a light sleep state and can easily be roused. You might experience sudden muscle jerks, called ‘myoclonic jerks’, during this phase. Eyes move slowly and muscle movements slow right down. On the EEG recording, alpha waves disappear and theta waves appear.

Stage 2: Eye movements stop and brain activity slows. You can be easily woken during this stage, and dreaming rarely occurs. EEG shows some bursts of faster brain waves called ‘sleep spindles’.

Stage 3: On EEG, very slow brain waves called ‘delta waves’ appear, mixed with faster waves. This is deep sleep, and it is most difficult to rouse somebody during this stage. There is no eye movement or muscle activity. Dreaming does

occur in this stage, though not as much as during REM sleep, and these dreams tend to be less vivid and less memorable.

A feature of this typical sleep pattern cycling between REM and non-REM sleep is that there is spontaneous lightening of sleep following each deep-sleep phase. It is normal to awaken briefly out of the lighter non-REM sleep phase. In younger people, awakenings are usually brief and not likely to be remembered. As you get older, the normal ageing process means sleep becomes lighter, and it is more likely that you will recall the times when you wake. This can become a normal sleep pattern, and does not necessarily mean that you will be unable to function normally during the day.

YOUR BRAIN AND SLEEP

Different parts of your brain are involved in sleep in a variety of ways. It is important that all areas of your brain function well to give you a healthy night's sleep.

The actions and interactions are complex, but here is a brief summary of the main functions of different parts of the brain involved in the sleep cycle.

Hypothalamus: The hypothalamus acts as the control centre governing the rhythms of sleep and arousal. It contains the suprachiasmatic nucleus (SCN), a sort of internal biological clock that receives information about light exposure and the day–night cycle directly from the optic nerve. The SCN in turn regulates the circadian rhythms of many different body functions, including hormone release, body temperature regulation and the sleep cycle. When the sun goes down and it becomes dark, the SCN turns on the pineal gland to produce melatonin (see page 289).

Brain stem: The brain stem communicates with the hypothalamus to control the transition from sleep to wakefulness. In particular, GABA reduces the activity of

arousal centres in the hypothalamus and brain stem. Different neurotransmitters and different groups of neurons in the brain stem are involved in switching between REM and non-REM sleep.

Thalamus: the thalamus is active during REM sleep, sending audiovisual content to the cerebral cortex to populate your dreams.

Amygdala: The amygdala is responsible for impulses and emotions. It is active during REM sleep and dreaming.

Pineal gland: The hormone most involved in the rhythm of sleep is melatonin. Melatonin secretion is inhibited by light and triggered by darkness. A tiny gland just above the middle of the brain called the pineal gland responds to light and dark. It produces and secretes melatonin from about 9 pm until about 4 am. Melatonin levels stay elevated in the blood for about 12 hours. Maximum sleepiness occurs at around 4 or 5 am.

For most people, the optimum window for sleep is between 11 pm and 7 am. Going to bed too early or too late may disturb the rhythm.

The main signal for sleep rhythm is exposure of the brain to light via the retina and the optic nerve.

The brain also has a process for clearing away waste, including beta-amyloid. The glymphatic system is a waste clearance system involved in the transport of cerebrospinal fluid via channels around blood vessels to reach the lymphatic system in the neck. This waste removal system is mainly activated during sleep, and is largely disengaged while you are awake. It has also been recently discovered that this system delivers essential nutrients to the brain, including lipids and glucose.

SLEEP GOALS

Sleep is vital to our brain and body's ability to function. In order to achieve optimal sleep, you should aim to achieve the following goals:

- To fall asleep without difficulty.
- To sleep undisturbed or with just one or two waking times in the night, but getting back to sleep without difficulty.
- To wake refreshed, feeling as though you have had enough quality sleep.

Keeping a sleep diary will give you some guidance on where you are now with sleep, and how your sleep pattern changes over time.

How do you know if you have a sleep problem? Here are some signs:

- It takes longer than half an hour to fall asleep.
- You wake more than once or twice during the night.
- You wake after a few hours of sleep or in the early morning and you cannot get back to sleep.
- You are told that you snore loudly, stopping breathing for intervals.
- You wake feeling unrefreshed.

One caveat I need to note is that sleep quality is notoriously difficult to self-assess. Apart from not being able to recall brief waking during the sleep cycle, it is also common to overestimate the amount of time you are awake, and to underestimate your total sleep time, especially with age.

There are many different types of sleep problems, some more serious than others. A formal sleep study may be the only way to truly ascertain the nature and severity of some of the more serious individual sleep problems.

For our purposes, I will focus on the most common and treatable sleep problems, which can often be resolved by changing your sleep habits.

You may have a medical problem that makes sleep difficult, or your sleep problem may be causing a medical problem. This needs to be discussed with your doctor.

The causes of some sleep problems are obvious – a noisy room, drinking too much caffeine, smoking tobacco, drinking too much alcohol, not giving yourself enough time in bed to get enough sleep, you have a bladder or prostate problem, you have unmanaged pain that wakes you in the night, or indigestion or another medical problem, or you share a bed with a partner who snores.

Knowing the cause goes a long way towards fixing the problem.

If you believe you have a sleep problem, we can document your day-to-day sleep habits with a sleep diary, which looks like this:

Sleep diary

Day	Bedtime	Time you spent reading/ watching TV in bed before sleep	How long did it take to fall asleep?	How many times did you wake in the night? At what times? Why?	How many hours did you sleep?
MON					
TUES					
WED					
THURS					
FRI					
SAT					
SUN					

This is a simple way to diarise some of your sleep habits, and will quickly identify patterns that can be changed.

Once you have identified your individual sleep pattern you can start solving your sleep problems. This might involve some changes of sleep hygiene habits. Sleep disturbances that are more severe or are more difficult to resolve will need a sleep assessment and possibly referral to a sleep specialist.

RECOMMENDATIONS

Sleep hygiene

'Sleep hygiene' refers to the basic sleeping environment and habits that contribute to a good night's sleep. A lot of these recommendations will sound like common sense, but it is amazing how often one of these basic elements is overlooked. Going through this checklist may help you identify a way to ensure you get a restful night's sleep.

Your sleeping environment

I know this sounds obvious, but the comfort of your sleeping environment is really fundamental. Make sure your mattress is supportive and comfortable and you have bedding that is clean and suitable for the weather – not too hot or too cold. Make sure that your pillow supports your neck.

The physical aspects of your bedroom are also very important. If there is too much light in the room, say from a streetlight outside, can you install a blackout curtain? If not, consider an eye mask.

If you are bothered by external noise, and it is not feasible to sleep in a quieter part of your home, earplugs may be a possible solution.

Your sleeping partner

Very often, the reason it is difficult to sleep is that your partner is keeping you awake with their snoring. The resulting sleep deprivation can put pressure on relationships. There are short-term and long-term solutions to this problem. The short-term fix is to see if you can sleep elsewhere in the house, at least some nights, to catch up on sleep. The long-term solution is to cure the snoring. Encourage your partner to visit their GP to discuss what options there are for treatment. These may involve weight loss, reducing alcohol, stopping smoking, use of dental splints or surgery. The solution will be individualised depending on the underlying cause.

Pets

If you have a pet in the bed or the bedroom – and many people do – there are psychological benefits but sharing a bed or a bedroom with pets can cause sleep disruption. You may have some luck training them to sleep in their own bed in the bedroom. Even then, some animals are restless at night. They may need to be let out to go to the toilet, a dog may bark to

alert you to a noise outside, or they may be restless and just feel like a wander. Once a pet establishes their presence in your bed, you will have a very difficult time extracting them. You may need to talk to your vet or an animal behaviourist (or a relationship therapist) for a solution.

The bedtime ritual

The sleep–wake cycle responds to light and dark, and the initiation of sleep responds to bedtime habits. Set your alarm for the morning so that you get up at a regular time and get some exposure to natural morning light. This is particularly important for indoor workers. Dim the lights in your home for about an hour before bedtime and avoid digital screens and other bright light sources. A warm bath before bed will help you to relax. When you start to feel sleepy, make use of that window of opportunity and head to bed rather than nodding off in front of the television. Try to settle any arguments or disagreements or talk through any emotional stresses before you head to bed.

Therapy

If you have unresolved emotional distress due to issues from your past, conflict in your family or friendship group, financial stress, work stress or for any other reason, you may be able to talk to a trusted friend. Your GP can also help you with counselling and possibly a referral to a psychologist for professional help.

Fix medical problems affecting your sleep

There are many medical problems that disrupt sleep. The most common is pain, such as arthritis or back pain. Urinary problems or prostate enlargement can trigger frequent waking to go to the bathroom. Coughing from asthma or bronchitis, trouble breathing from heart failure or indigestion from gastro-

oesophageal reflux will also affect sleep. Raise your sleep problems with your doctor to see what can be done.

Medication review

Many medications can affect sleep quality. Steroids, some anti-depressant medications, some asthma medications and beta blockers are examples. Ask your GP or pharmacist to review your medications and discuss ways of reducing or changing medication so that your sleep quality improves.

I commonly see people who have been using sleeping pills 'just in case' for years, out of fear of insomnia. Some people use over-the-counter preparations such as antihistamines for their sedative effect, and find they have a medication hangover the next day. High-dose B vitamins can also cause sleep disturbance. All this can be discussed with your GP.

Physical activity

Physical activity helps you to manage stress, improves your sleep quality at night and enhances your alertness during the day. The first priority is to get some exercise each day. The right timing is a bonus. Aim to exercise in the morning, ideally. If you exercise in the afternoon, try to make it several hours before bedtime. This is so that you do not interfere with the release of melatonin, which is necessary for your sleep–wake cycle. Some forms of exercise, such as tai chi and yoga, incorporate stretching and relaxation, breathing exercises and a form of meditation, which helps sleep too.

What you eat

What you eat is important to sleep quality. People who are overweight or obese are more likely to suffer from obstructive sleep apnoea, which interrupts sleep many times a night. Gastro-oesophageal reflux can cause indigestion, which affects

sleep. To resolve this, limit fatty foods and spicy foods, and reduce the portion size of evening meals. The amino acid tryptophan in foods such as warm milk and seaweed products stimulates melatonin production.

Limit alcohol

Alcohol is a common go-to for self-medication in people with sleeping problems, but while it does help you to fall asleep and sleep more deeply initially, it reduces REM sleep, and therefore reduces the overall quality of your sleep pattern.

Limit caffeine

Caffeine is a brain stimulant that increases alertness. That is a problem if you are trying to get to sleep. If you drink a lot of coffee, tea or cola drinks, try cutting them out after 3 pm. Then gradually reduce the number of caffeinated drinks to two or less a day, and preferably consume them early in the day.

Avoid nicotine

Nicotine in all forms (smoked, chewed, vaped) is a stimulant that can impede your ability to go into a deep sleep. Smoking also causes respiratory inflammation, which can cause snoring.

Teens

- Follow sleep hygiene recommendations.
- Establish or re-establish a healthy body clock.
- Develop a relaxing bedtime routine and avoid late nights.
- Set a regular wake-up time.
- Ensure regular physical activity.
- Remove all screens from bedrooms.

- Arrange schedules so that overcommitment is avoided, and rest and sleep are considered.
- Avoid caffeine and other drugs (including alcohol, cannabis, cocaine and nicotine).

Can I take ‘something’?

Having trouble sleeping can be very distressing and frustrating. As a GP I am often asked for ‘something’ to help with sleep, even in the short term while lifestyle and other techniques are being trialled. The choice depends on how urgent or serious the sleep problem is, and whether there is a cause that can be treated, such as pain management.

Some herbal therapies are very effective for relaxation and sleep. These include Valerian (*Valeriana officinalis*), hops, lavender, skullcap, passionflower, lemon balm and chamomile. It is best to ask for professional advice on herbal therapies.

Tryptophan or 5-hydroxytryptophan are supplements commonly taken to relieve insomnia. They must be avoided if you are already taking an SSRI antidepressant medication because of an interaction called serotonin syndrome, where too much serotonin can cause shivering, diarrhoea, muscle rigidity, fever and seizures.

Melatonin is commonly prescribed as a sleep medication, particularly in older people. It is not a sedative like a benzodiazepine. As mentioned on page 289, it is a naturally occurring hormone produced by the pineal gland when it is dark, and it regulates your sleep–wake cycle. Your natural production of melatonin tends to decrease with age, and this can affect your sleep pattern.

Prescribed medication

Talk to your doctors about whether short-term medication might help in, say, a crisis situation. Longer term use of medications such as those in the benzodiazepine group can exaggerate cognitive decline and cause depression and mental dullness. In older people, these medications can also cause clumsiness, leading to falls, especially when getting up at night to go to the bathroom.

If you are assessed as having sleep problems due to an anxiety disorder or depression, lifestyle measures such as exercise, psychological therapies and sometimes specific medication might be prescribed.

OBSTRUCTIVE SLEEP APNOEA

Some people with sleep disorders will need to be referred to a specialist sleep clinic for more advanced investigation and treatment techniques. The most significant sleep disorder for brain health is obstructive sleep apnoea (OSA). This is a common condition with repetitive episodes of upper airway collapse and obstruction to airflow during sleep. These episodes can cause an intermittent drop in blood oxygen saturation (hypoxia), resulting in lower oxygen levels in the blood supplying brain tissue, and fragmentation of sleep.

Another possible mechanism is the disruption of the glymphatic system, the brain's waste-removal process, which occurs during sleep. It has been suggested that disruption to this system because of fragmented sleep could lead to accumulation of potentially toxic substances, such as beta-amyloid, which can eventually lead to the build up of the plaques we see in Alzheimer's disease.

How do you know if you have obstructive sleep apnoea? The most common symptoms are daytime sleepiness and fatigue even though you seem to have enough sleep time. You may find you have trouble concentrating. A sleeping partner

might notice that you snore, stop breathing at times for 10 to 30 seconds, and then gasp for breath or appear to be choking in your sleep. Each one of these episodes means that you are being roused from sleep multiple times a night.

If you suspect you have sleep apnoea, it must be reported to your GP for specialist investigation and treatment. Treatment includes lifestyle measures such as avoiding smoking, limiting alcohol and achieving a healthy weight, and either a dental device or CPAP (Continuous Positive Airway Pressure) device.

There is growing evidence that untreated obstructive sleep apnoea has significant effects on brain structure and function. OSA has been linked to decreased grey matter in the hippocampus, cingulate and cerebellum, as well as the temporal, frontal and parietal lobes. It has also been associated with decreased brain activation in several parts of the brain, particularly those involved in memory tasks.

One review reported that patients over 40 years old suffering from OSA were 26 per cent more likely to develop signs of cognitive decline or dementia. Another study found that people with sleep-disordered breathing developed mild cognitive impairment or Alzheimer's disease related dementia at a younger age.

The Australasian Sleep Association website has a lot of excellent further information, at www.sleep.org.au

If there is one compelling argument for diagnosing and treating obstructive sleep apnoea, it is the finding that long-term CPAP treatment of people with OSA can reverse any non-permanent brain structural damage, increase the overall volume of the cerebral cortex and delay the progression of cognitive decline.

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Mind–Body Therapies

We have established that the brain regulates your body processes. Psychological states such as chronic stress, depression, anxiety and fear produce profound and medically significant effects in the body.

If you have been through a major or prolonged period of stress in your life, you will be familiar with some of its effects. You can't think straight, you have trouble making decisions, you forget important dates or events, you toss and turn at night, thoughts go round in your head, you feel anxious much the time, you can be clumsy or accident-prone.

It is almost impossible to go through life without experiencing some episodes of stress. Think of the times in your life that have had the most emotional impact on you: the death of a loved one, loss of a job or a business, a legal battle, falling out with a close friend, moving to a new home or neighbourhood, financial hardship, preparing for important exams.

Even 'normal' daily life can be stressful if you do not have a reserve of emotional and physical energy to achieve all that you need to do.

Some stressors are inescapable, and it is through facing challenges that we learn how to adapt to change. Learning to conquer the effects of stress is an essential life skill.

In response to stressful situations, physical and psychological or emotional, the brain assesses and processes these inputs or perceived threats in the hippocampus, amygdala and prefrontal cortex (the so-called limbic system). The brain responds by stimulating the adrenal glands to release corticosteroid hormones, in turn increasing arousal, vigilance, alertness and cognitive processing to deal with the perceived threat. This is known colloquially as the 'fight or flight response', the body's preparedness to either run from a threat or to stay and fight. The body's physiological responses include a fast heart rate, elevated blood pressure, sweating, mobilisation of energy stores for fuel leading to increased blood glucose, increased breathing rate, mobilisation of white blood cells and activation of inflammatory mediators such as cytokines and interleukins, in case of tissue damage.

This fight or flight response prepares the body to deal with danger. It is a protective mechanism that is necessary to preserve life, provided that it is switched on appropriately and switched off when it is no longer needed, and the stress response is not prolonged.

It is when you lose the ability to stay on top of life's pressures in the long term, or when you operate at 'alert' level most of the time without long periods of respite, that you experience the emotional and physical consequences we call 'stress'. In other words, your body is treating everything as if it is an emergency.

What may seem stressful to one person might seem exciting and challenging to someone else. Stress is a very individual experience based on your perception of those stressful circumstances in your work or home life, and your strategies for managing them.

Stress can also trigger or exacerbate many medical conditions. If the stress response is unwarranted or out of proportion to the threat, or is prolonged, it can have detrimental effects on your body. These detrimental effects can include inflammation, impaired immunity, increased risk of abnormal glucose metabolism and type 2 diabetes, increased risk of atherosclerosis leading to ischaemic heart disease and premature ageing.

Short-term stress can temporarily improve the function of the brain, and therefore memory, under specific conditions that are, for example, life-threatening, unfamiliar or unpredictable. You will know what I mean if you have ever had to compete in an important sporting event or speak in public. Properly harnessed, the rush of stress hormones can help to focus your attention and draw the most out of your mind and body, maximising your performance.

Signs of stress

There are many signs that stress is getting beyond your control. They might include:

- fatigue
- headaches
- heart palpitations
- feeling depressed or anxious, irritable or aggressive
- feeling overwhelmed and unable to cope
- a drop in your work performance
- an increase in sick days
- trouble sleeping
- trouble concentrating or making decisions

- gastrointestinal upsets, such as nausea, diarrhoea or constipation
- anorexia
- an increase in the use of drugs, alcohol, medications, coffee, chocolate
- deterioration of your personal relationships
- increased susceptibility to accidents
- poor health, including an increased risk of infections, cardiovascular disease and inflammatory conditions.

In the long term, stress can cause functional changes in the brain, mood changes including anxiety and depression, and structural changes including atrophy or shrinkage of nerve cells in the hippocampus and prefrontal cortex of the brain, as well as decreased neurogenesis in the hippocampus. This can also affect memory and learning.

The impact of stress on the brain is determined by the type of stress, its intensity, its timing and its duration. The overall effect of stress on brain function results in reduced cognition such as attention, learning, decision-making, and judgement can be adversely affected by chronic stress.

In summary, stress and inappropriate or prolonged stress responses cause changes to the structure and function of the brain that lead to behavioural, mood and cognitive changes.

There are evidence-supported ways of preventing or reversing the effect of chronic stress on your brain.

MEDITATION

The practice of meditation has its origins in the Ayurvedic tradition in India. There are several types of meditation in common use. These include:

- mindfulness

- contemplation
- use of nature sounds such as the ocean, the forest or flowing water
- guided meditation
- meditative movement exercises such as yoga and tai chi or qigong
- breathing exercises.

MINDFULNESS

So much of our brain activity is devoted to thinking over what's happened in the past and working out what we have to do tomorrow, next week, even years ahead.

Mindfulness involves developing the skill of being in the moment. It focuses you on the present by paying close attention to every detail: your breathing, skin sensations, your thoughts and feelings.

The practice of mindfulness may be able to change the actual structure and function of your brain. Several studies have shown that regular meditation practice induces the brain changes involved in neuroplasticity, including the reduction of age-related brain degeneration and improved cognitive function. Mindfulness meditation can change the brain's grey matter and the brain regions linked with memory, sense of self and regulation of emotions.

There is a growing body of scientific research that demonstrates the effectiveness of mindfulness in managing stress and reducing anxiety, improving attention and memory, increasing empathy and self-regulation of emotions, and relieving depression.

An exercise in mindfulness

There are many different mindfulness routines. Here are some everyday examples:

Cooking porridge

Mindful cooking is a simple way to incorporate mindfulness practice into some of your everyday activities. Find a simple familiar recipe like oatmeal porridge. Gather the ingredients and place them in a saucepan on low heat on the stove.

As you start to stir, notice your breathing, breathing in and breathing out through your nose. You don't have to change the rhythm, just notice it. As the porridge heats up, you notice the bubbles starting to form, the sound they make as they break the surface. Notice your breathing again. If you start to think about something else, just put that thought aside and return to the moment.

Now notice the change in the aroma of the cooking oatmeal, the thickening texture. Continue stirring, noticing the oatmeal sticking to the spoon.

The food is ready. Five minutes have passed and you have completed a mindfulness exercise.

Sit quietly

Find a quiet space where you will not be interrupted. Sit up straight with your arms by your side and your hands in your lap. Close your eyes and take a deep breath in and out. Notice the rise and fall of your chest. Notice the subtle sensation of the air passing in and out of your nose. What can you hear? Your breath? Children playing in the distance? The wind in the trees outside? Notice them and return the focus to your breathing. Notice any sensations on your skin. Your feet in your shoes, a cool breeze on your face, even an unpleasant sensation. Notice these sensations and return to your

breathing. In and out. After 10 to 20 minutes you have completed an exercise in mindfulness.

There are other mindfulness meditation techniques and programs available online.

TAKING CONTROL OF STRESS

Many of the patients I see are suffering the emotional or physical consequences of unmanaged stress. Here is my advice on how to manage stress so that your whole body benefits, including your brain:

- Identify the causes of stress and change them or eliminate them. Some changes you can manage yourself, while others will need the cooperation of others. This might involve people at work or at home, and you may also benefit from professional help from a psychologist.
- List your tasks in order of priority. Organise your schedule so that the most difficult tasks of each day are planned for times when you are fresh, such as first thing in the morning.
- Optimise your nutrition. In particular, make sure you eat three meals a day, include the major food groups and essential nutrients, two serves of fruit and five serves of vegetables a day, grains, nuts, protein. If you're not sure what to do, see a dietician to organise a well-constructed eating plan focusing on healthy brain foods. (See chapter 24: Brain Food.)
- Do a form of aerobic exercise every day. Include weight training about three times a week.
- Try meditation, tai chi or yoga or some form of relaxation.
- Practise mindfulness for 10 to 20 minutes twice a day.

- Make sure you have enough free time to yourself every week to do the things you love to do, not just the things you have to do.
- Don’t take out your stress on loved ones. Instead, tell them about your problems and ask for their support and suggestions.
- Avoid smoking, illicit drugs and excessive drinking. They won’t alleviate stress and can cause additional health problems, including adverse effects on your brain.
- Seek professional counselling from a psychologist to help you with techniques for managing stressful situations or family disharmony.
- Have regular medical check-ups to identify and take action on any health risks.

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Brain and Pets

For many people, the decision to get a pet is a natural one, because they grew up with pets and a ‘home’ feels incomplete without one. Some people are looking for company as an antidote to sadness or loneliness, or because they seek unconditional loyalty or motivation to get up in the morning. Some parents want their children to learn the responsibility of caring for a pet.

When I was growing up we always had a dog in our home. Interestingly, I never felt like any of them was ‘my’ dog, and didn’t feel a particularly strong connection.

Then one day my wife, Jackie, started talking about getting a puppy. I resisted, knowing how much work and attention it would need. But anyone who knows Jackie will also know that she can be very persistent. Eventually I relented, and we welcomed a tiny black toy poodle into our family. We called her Paris. (*French* poodle, right?) Eight months later, Lulu arrived, another tiny poodle. They changed our lives in ways I could never have anticipated.

More of that later.

The profound psychological effects of having a family pet are well documented. Animal lovers know that having a pet

can make you feel calmer, less anxious and more loved.

There is a particular joy to being greeted by an excited dog when you get home from a long day at work, or even just when you come back in from putting the garbage out!

A friend of mine took that a bit further, joking (confessing?) that she secretly liked her dogs more than her children because the dogs gave her less trouble, made her feel better about herself and they loved her unconditionally.

Other friends have told me that they consider their family dog or cat as ‘one of their children’, or their ‘fur baby’. Interestingly, this has been tested in a scientific trial where similar brain responses were found in mothers when looking at their child and their dog. These responses were much greater than when looking at an unfamiliar child or dog.

> A study at Massachusetts General Hospital in the United States examined functional MRI brain activation patterns as mothers viewed images of their own child and dog and an unfamiliar child and dog.
>
> Researchers reported that there was a common network of brain regions involved in emotion, reward, affiliation, visual processing and social cognition when mothers viewed images of both their child and dog. However, there was a difference in the part of the brain activated by their dog compared with their child.

We also have evidence of the positive physical effects of having a dog, such as improved fitness (if you are the one who walks your dog), lower blood pressure, lower cholesterol and triglyceride levels and lower risk of heart attack. The lower blood pressure is not just a result of walking your dog for exercise. The blood-pressure drop is an immediate effect of patting a dog.

In 2013, a group of cardiologists reviewed the evidence on pet ownership and heart disease for the American Heart Association. They concluded that ‘Pet ownership, particularly

dog ownership, is probably associated with decreased cardiovascular disease risk.'

More recently, in 2017 a study found that dog ownership appears to be associated with lower risk of cardiovascular disease in single-person households and reduced risk of cardiovascular and all-cause death in the general population.

What about your brain health? As technology for examining brain function develops, we are increasingly gathering evidence that having a pet changes your brain chemistry and therefore your brain function in a positive way.

The effect starts in childhood. There is evidence for an association between pet ownership in childhood and a wide range of emotional health benefits. Overall, pet ownership shows benefits to child and adolescent emotional, cognitive, behavioural, educational and social development. These effects are particularly seen in the areas of self-esteem, loneliness and social competence.

In older people, we know that pet ownership can improve a person's mental health by providing companionship, meaning and purpose, relieving loneliness and encouraging social interaction.

That is the effect of having a pet, but what is the underlying mechanism? What actually happens in the brain to make these positive changes?

Pets lower the levels of cortisol, the 'stress hormone', and provide relief of depression, anxiety and social isolation. Some neurotransmitters, including oxytocin, serotonin and dopamine, have also been studied to identify how they are affected when we interact with our pets.

Let's have a look at these neurotransmitters more closely.

OXYTOCIN

Oxytocin is one of the body's 'feel good' chemicals. It is produced in the hypothalamus and then transported to and released by the posterior pituitary gland at the base of the brain. It is known as a neurotransmitter and a hormone, and has a number of specific functions in women, including reproduction and orgasm. It also has an integral role in childbirth and breastfeeding. Oxytocin is released when a mother bonds with her child.

Oxytocin has a number of psychological effects, too. It relieves feelings of stress, and enhances a sense of trust and connectedness with others.

When you stroke or pat your dog or cat, your oxytocin levels rise significantly, creating a sense of calm. This is the same reaction a mother has when she holds her child.

There is no doubt that the emotional attachment to a pet can be extremely strong, with many people saying that their pet is as much a member of their family as the human members.

DOPAMINE

As discussed earlier, dopamine is a type of neurotransmitter, a chemical produced in the body and used to convey messages between brain cells.

Dopamine is involved in positive feelings and bonding. Abnormal levels of dopamine in different parts of the brain are associated with several neurological disorders such as schizophrenia, bipolar disorder, Tourette syndrome, Parkinson's disease, Alzheimer's disease and ADHD.

Dopamine has been called the 'pleasure hormone' because it is associated with the human experience of pleasure. Being with your dog also releases dopamine. This boosts both your mood and long-term memory.

SEROTONIN

Serotonin is another type of neurotransmitter with a profound impact on mood. A commonly prescribed type of antidepressant medication, selective serotonin reuptake inhibitors (SSRIs), increases levels of serotonin in the brain by blocking the reuptake of serotonin into nerve cells in the brain.

Researchers have discovered that patting dogs causes a spike in serotonin levels. Elevated serotonin levels can give you a sense of calm, reduce anxiety and promote feelings of happiness.

That makes your pet a type of natural antidepressant.

A WORD ABOUT PRACTICALITIES

Of course, while all of this evidence is intriguing, the decision to get a dog cannot be made on an emotional basis. That decision needs to take into account many factors, including the time you have to train, exercise and care for a dog, particularly in the puppy stage, and the financial and practical commitments if it becomes sick or elderly. A dog is a considerable commitment, and it is not for everyone. Other practical considerations include upkeep and vet bills, which can cause a lot of financial stress if things go wrong.

You also have to try to look ahead up to 15 years or longer. What will that mean for your personal life plans and the wellbeing of the animal? Will you want to move house or relocate to another country? What will happen to the pet of an elderly person if they become unable to look after themselves or the animal, or have to move into a residential aged care facility that does not allow animals?

Another problem I see is when puppies are bought for someone as a surprise by a well-meaning friend or relative,

and that person is not prepared for the adjustments that will mean to their life.

Your heart or brain health is a positive benefit, but not a reason to make the significant commitment of getting a pet.

There are also some potential negative health effects of having pets, including allergies or a pet with a behavioural problem like excessive barking or destroying things around the home.

Before you decide to get a pet, make a careful and well-informed decision about whether you are physically, mentally and financially able to provide it with the care it needs for its whole life. Are you prepared to do the training, walking, feeding, caring, grooming, cleaning up and visits to the vet?

Once you have worked through the practicalities and confirmed that adopting a pet is the right thing for you and your family, you can expect some positive side benefits for your health, particularly for your brain.

PARIS

Before we had a dog of our own, I did not really understand the profound impact a pet can have on your life. This is an extract of a eulogy I wrote for our dog Paris after we lost her at age 11 from an aggressive melanoma in her throat.

> ‘How do we say goodbye? How can we measure this loss?
>
> Paris and I understood each other. We were soulmates in the truest sense of the word. Whenever I sat down, Paris would sit as close as she could beside me with one paw on my leg. Always on my left. For while we both loved an adventure, we were also creatures of ritual, perfectionism and strong preferences. The people she loved, she loved with a passion. They know who they are. To the rest she was indifferent.
>
> When Jackie and I decided to bring a poodle into our lives, I had one stipulation. She would not be sleeping on the bed. That lasted about, hmmm let me think … two weeks. I came to appreciate this over time.

If ever one of us was sick, there was no better nurse than Paris. She took her nursing duties very seriously and would not leave your side until you were up and about again.

When I looked into the eyes of this serious, intense and, as it turned out, remarkably intelligent puppy, I saw something rather unexpected. I saw myself reflected back at me. Just as my children did, she brought out every protective instinct in me. But I did not expect that this self-reflection would fundamentally change me. She made me become more patient. She helped me to understand for the first time how deeply special the bond between human and dog can be. She let me be my better self and if she saw any negatives in my personality, there was no judgement and no need for forgiveness. Neither did we have need for words. Her expressive brown eyes and her articulate body language told me anything she needed me to know …

One day we discovered she had an aggressive and untreatable malignant melanoma in her throat. No room for bargaining or denial. No room for negotiation.

So we say goodbye. It is unbearable but we are so very grateful to have had the privilege of loving Paris and protecting her and being loved back for that 11 years.

The angels must have needed her extraordinary and pure spirit to join them.

One thing I know, she will be happy that there are no leashes where she is going.'

Sometimes the value of a relationship is most recognised in its loss. This is true of pets.

At the time, a friend said to me, 'That's what you sign up for when you get a puppy. You just don't realise it at the time.'

It was worth it.

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Personal Stories

When I was first planning this book, I asked around my friends and family what they thought about brain health.

It turned out that there was a very common but largely unspoken fear that what had happened to a family member could happen to you. I asked people I knew to reflect on their thoughts about their own brain health, what motivated them to consider lifestyle measures directed at supporting their brain into old age, and whether they consciously took steps to protect their brains. Here are some of those reflections.

Jackie (age 68)

From a very young age I valued my brain above all else. Being smart got me into a selective high school where the headmistress told us regularly how valuable it was to be intelligent and we should use our brains well. From an early age I read voraciously, wrote poetry and short stories, engaged in as many conversations as possible and was very socially active. Every day I did crosswords with my mother. The first time I realised a brain could deteriorate was when my paternal grandmother started to show signs of dementia. She had been an intelligent woman who spoke five languages. She became incoherent over time and physically aggressive. She ended up

in a home being restrained. I became acutely aware of the importance of keeping my brain healthy. I learnt bridge, continue to do crosswords and word puzzles. I work with finances and running building projects as well as being an actively engaged parent, having adopted my daughter when I was 56 and she was nine. I remain politically engaged and run two houses. I make sure that I have multi-generational friendships so I remain connected to all age groups. I eat well and while I recognise with age could come some memory loss, I monitor my brain function closely and continue to look after it to the best of my ability.

Rebecca (age 60)

Brain health is increasingly important to me as I age.

My father had motor neurone disease (diagnosed at a late stage) and the doctors misdiagnosed, thinking he had Alzheimer's disease because of memory loss. I observed what happened to this brilliant man's mind and it was devastating to me. As I watched him lose capacity and confidence it reminded me of how important good brain health is and to always set new challenges for the neural pathways.

I started to go different ways in testing geography and instead of always turning right I turned left.

I am more interested in learning my piano (which I stopped playing at age 15) as I think it forces my brain to stay young.

Learning new things is something I am committed to as I know it assists good brain health.

I am also exercising regularly as I think that keeps the brain engaged and I also think about food that is anti-inflammatory, which I think is also helpful for the brain.

Char (age 64)

Witnessing first-hand experiences with a parent (my father) suffering dementia has influenced my perception of the disease.

Seeing a loved one disappear in front of one's eyes while still being physically present is devastating.

Additionally, having worked clinically in the dementia space for many years has shown me the deep effect that the illness has not only on the sufferer, but also has profound effects on the family and loved ones.

I am extremely mindful of the importance of brain health as the thought of being debilitated by any neurological illness is terrifying.

I am extremely mindful of maintaining good brain health by trying to keep my brain active – reading/healthy eating/exercise etc.

I think your book is so important and will no doubt help many people.

Wendy (age 80)

Brain health is extremely important to me.

I have no concerns for my own brain health now or into the future, as I think I am performing/living my age well.

No one in my family has had dementia, but my brother had a stroke at 49 and died shortly after.

It changed how I felt about my own brain health. I took it seriously and examined my lifestyle. I decided to switch jobs to one whose issues I cared more about. And I expanded my exercise program to include yoga.

I still exercise regularly, drink alcohol moderately, eat well, read a lot and have regular social contact.

Corrie (age 74)

Brain health is very important to me. I worry about it all the time.

Getting old is not easy. I can cope with the fact that I can't do stairs as easily as I used to and have problems with vertigo but can manage that, however the thought of getting dementia or Alzheimer's is totally different matter and worries me a lot.

My short-term memory is getting very bad as well, which I find really frustrating.

Someone on my mother's side of the family had dementia, which changed the way I thought about my brain health; also the fact that I have experienced visits to aged care homes the last couple of years and find it really stressful seeing people wandering about not knowing who or where they are. I never want to be in that situation and I am a supporter of euthanasia.

I try to walk at least 3–5 km five times a week. I play Scrabble and Backgammon apps as I believe games are good for brain function, and I have a fairly healthy diet.

Lucy (age 60)

When I think about it, brain health is extremely important to me as this organ can't be transplanted and it controls the ability to think, talk, feel, see, hear, have memories, move and so much more. Losing any of these functions would be devastating to me.

But because I don't see it in the mirror or feel it in my body, like when my knees or back hurt, it's easy to not pay much attention to it.

My father and his siblings all developed dementia in later life. I am concerned as I want to maintain my cognitive skills, quality of life and be able to live independently. Sometimes I

cannot recall a name or a memory and wonder if this is just ageing or am I developing early dementia.

I did not change the way I thought about my brain health until I reached my fifties and saw the decline in my father's mental state. In my younger years I felt invincible and of the opinion it wasn't going to happen to me, or if it did then it would be far off in the future.

I have taken the approach that a healthy body will lead to a healthy brain. I watch my diet, do Pilates, get enough sleep most nights, drink less alcohol (unless it's great champagne or a really good red) and the dog takes me for a walk every day. I occasionally check my blood pressure and have recently taken up yoga for relaxation and to improve my flexibility and strength.

Mandy (age 22)

My views on brain health have drastically changed from when I graduated high school to now being in my honours year of an advanced science degree majoring in neuroscience. I knew back then that alcohol, illicit drugs and cigarettes were bad for your health in general, but only now do I have much stronger appreciation for how drastically they can impact your cognitive function. If studying the brain has taught me anything, it is that the nervous system is a mysterious yet magical part of our body capable of so much, yet very susceptible to irreparable damage if we do not look after it. My number one priority as a young adult now is to look after my brain as best as I can, especially as it continues to develop into early adulthood. As we now know, the brain continues to develop up until your mid 20s so really I still have a few more years of crucial development, and many of the neuroprotective actions that I, and others my age, can take to look after our brains need to start as early as possible to achieve the most benefit.

PART 4

HOW TO KEEP YOUR BRAIN YOUNG

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The Plan

Your brain is an astonishingly complex organ. The more we find out about it, the more we realise we are yet to discover. Looking at all of the evidence, here is a plan for protecting and enhancing your brain throughout life.

GOOD HABITS START FROM THE BEGINNING

If you are planning a pregnancy, the choices you make, such as the things you eat and drink, any medications you take and the way you manage stresses in your life will all have an influence on the health of your baby. Of course, this includes the development of their brain and nervous system.

If possible, before you get pregnant, or at least as soon as you know you are pregnant, see your doctor and if necessary a dietician to optimise the environment for your unborn baby's development to give them the best possible 'head start'.

CHILDHOOD

Prevent brain injury by selecting sports for your child that have a low incidence of concussions.

Make sure your child is fully immunised to prevent some of the childhood illnesses that can cause brain damage.

Pay careful attention to nutrition for your growing child.

MOVE YOUR BODY

Moving your body helps to keep your brain young. In the chapter on exercise, we looked at how physical activity increases the flow of blood and oxygen to brain cells, facilitating the growth of new neurons and increasing the connection between them.

Regular exercise is one of the fundamental elements of reducing cardiovascular risk factors by helping to improve cholesterol levels, maintain healthy blood sugar levels and manage emotional stress.

OPTIMISE YOUR DIET

Like any organ, your brain can only be at its best if it is getting the best possible fuel in the form of brain-healthy nutrients. Chapter 24: Brain Food will help you understand which ingredients to include in your everyday diet to enhance brain function and mood. Optimising your diet reduces the risk of cognitive impairment and dementia in older age.

CONTROL YOUR BLOOD SUGAR

Insulin resistance and type 2 diabetes are risk factors for cognitive decline. You can maintain healthy blood sugar levels with regular exercise, an appropriate diet and maintaining a healthy body weight. Your doctor may recommend medication.

MANAGE YOUR CHOLESTEROL

High levels of LDL ('bad') cholesterol are associated with an increased risk of dementia, particularly vascular dementia. Take a comprehensive lifestyle approach to improving your cholesterol by eating a diet low in saturated fats, doing regular exercise and maintaining a healthy weight.

If you have known heart disease or you are assessed to be at higher risk of cardiovascular disease, your doctor will advise you on whether to take medication to lower your cholesterol.

IMPROVE YOUR GUT HEALTH

Your gut and brain function are closely interconnected. By paying attention to your gut health through diet, the right probiotics and other measures, you can improve your brain function and emotional health.

CONTROL YOUR BLOOD PRESSURE

Hypertension (high blood pressure) in midlife increases the risk of cognitive impairment, vascular dementia and Alzheimer's disease. The lifestyle changes that really work to reduce high blood pressure are:

- Determine your healthy weight range, and if you are overweight or obese, reduce your weight until you are in that range.
- Reduce salt in your diet. Don't add salt in your cooking, and check the sodium content in packaged or processed foods to avoid hidden salt.
- If you smoke, quit.
- Keep alcohol to healthy limits (see chapter 5: Alcohol and Your Brain).
- Exercise regularly.

- Check any medications you are taking to see if they might cause an increase in blood pressure.
- Manage stress.
- If you have been diagnosed with hypertension, get a home blood pressure monitor so you can measure your blood pressure regularly. Tell your doctor if it is out of the agreed optimal range for you, so that decisions such as changes of medication can be made.

Medication may be necessary to keep your blood pressure in a safe range, along with lifestyle measures.

BUILD AND MAINTAIN SOCIAL NETWORKS

Strong social connections are associated with lower risk of dementia and longer life expectancy. Research shows that older people who are more socially engaged and have supportive social networks tend to have a higher level of cognitive function.

SLEEP SOUNDLY

Sleep plays an essential role in brain health by helping to consolidate memory and regulating emotion. During sleep, your brain clears away any build-up of toxins that accumulate when you are awake.

Sleep deprivation increases amyloid deposition, a process implicated in the development of Alzheimer's disease.

Avoid any stimulants such as caffeine, chocolate or nicotine in the hours before going to bed.

Practise good sleep hygiene, including allowing time to relax before going to bed, turning off screens, and ensuring you have a quiet, dark and comfortable sleeping environment to give yourself the best opportunity for a good night's sleep.

STIMULATE YOUR MIND

Research tells us that a variety of stimulating brain activities encourage new connections between neurons and may even help the brain to generate new cells, harness neuroplasticity and build up a functional reserve against possible future neuron loss.

The choice of brain activity depends on your interests, but should involve things that interest and challenge you. Examples are card games, chess games, maths puzzles, brain training apps and music lessons.

It is also important to include activities that provide challenges for your manual dexterity, such as taking an art class or another practical or creative pursuit.

TAKE CARE OF YOUR EMOTIONS

Your brain will work most efficiently if you are not stressed, anxious, sleep-deprived or overwhelmed.

Practise meditation and mindfulness to help manage your stress.

If you have interpersonal or work stresses, make a plan to resolve them. Reach out to a trusted friend or seek professional help if you are not able to manage them yourself.

BE CAREFUL WITH PRESCRIBED AND OVER THE COUNTER PHARMACEUTICALS

Many medications can adversely affect your brain function. This can be due to a drug side effect having a direct effect on your brain, or because of an interaction, such as a depletion of nutrients caused by the medication.

If you are taking one or a combination of medications and you are experiencing any adverse brain effects or psychiatric

symptoms that appeared since you started the medication, this should trigger a medication review with your doctor to discuss a change of dose or a different medication, or a non-pharmaceutical approach to manage your medical condition.

PREVENT BRAIN INJURY

Brain injury can result in cognitive impairment. You won't be able to eliminate every possible risk of brain injury, but there are ways of reducing your risk with sensible protective measures:

- Always wear a seatbelt when you are driving or a passenger in a car.
- Make sure children are secured in a properly fitted safety seat or booster.
- Child-proof your house to prevent risk of falls. This includes safety guards on high windows and barriers on stairways.
- Wear a helmet when you are riding a bicycle.
- Wear a helmet when you are skiing or snowboarding, or in other sports where helmets are recommended.
- Consider carefully the most appropriate sport for your child's physical abilities, developmental stage, size and strength.
- Wear all safety equipment recommended for a sport.
- Never drive, cycle or engage in risky sports under the influence of alcohol or other drugs that can impair reaction times.

AVOID ILLICIT DRUGS

Illicit drugs are treacherous territory for brain health. While you and many people you know will think they are 'getting

away with it', maybe for years, there is the potential for unexpected ingredients, and unexpected adverse events, including brain damage and death.

In the long term, the use of illicit drugs can cause structural and physiological changes to your brain that can result in problems with mental health and thinking ability and changes in personality. There is no room for negotiation with an illicit substance. It will either cause you immediate or long-term harm or it won't.

The law is an attempt to discourage illicit drug use for the sake of public health and safety.

Your brain health now and into the future is a crucial part of the decision-making process for each individual. You are the only one who can decide if it is worth the risk.

DON'T OVERUSE ALCOHOL

Avoid alcohol when you are planning a pregnancy and during a pregnancy, and after a cancer diagnosis.

You can expect your tolerance level to alcohol to decrease as you get older.

If you choose to drink alcohol, go easy. Light drinking, between one and six drinks total in any week (but no more than four on any given day), seems to show similar outcomes for brain health when compared to abstinence.

Excessive chronic alcohol use increases the risk of alcohol-related brain damage and dementia.

SMOKING

Don't smoke tobacco. Ever. Smoking has no health benefits for any organ, including the brain.

CONSIDER SUPPLEMENTS AND HERBS

Correct your nutrition by introducing brain-healthy foods and eliminating brain-unhealthy foods. You can make up for some deficiencies with carefully selected supplements.

There are a number of supplements and herbs that have been shown to have a benefit or a potential benefit to brain health. It is important not to self-prescribe, but to seek expert advice from a health professional with experience in prescribing supplements. This is particularly important if you are taking any medications likely to interact with a supplement.

Acknowledgements

This year is the 40th anniversary of my graduation from medical school.

For the 40 years I have been in clinical practice, every day has been a learning experience. We learn from the results of medical research, from our medical colleagues and colleagues in other healthcare disciplines, and from our patients who challenge us to keep pushing the boundaries of treatments supported by evidence to find solutions to their health problems.

One of the extraordinary things about closely following advances in medical science is that each discovery simultaneously expands our knowledge, while highlighting how much there is still to discover. This is no more true than in the study of the brain.

In writing this book, I acknowledge the many researchers around the world who continue to explore the limits of our understanding of the human brain in all its complexity.

Thanks to Prof Teresa Mitchell-Paterson for reviewing the content on herbs and supplements, with her knowledge of evidence and clinical expertise in herbal medicine.

I want to express my appreciation to the team at Pan Macmillan: my publisher Ingrid Ohlsson, editor Alex Lloyd,

copy editor Vanessa Lanaway and creative editor Naomi van Groll. This is my fourth project with Pan Macmillan and they always make the process such a pleasure.

This book was started shortly before I made the decision to run for Federal Parliament. We put it on hold during two gruelling political campaigns and an eventful stint in Canberra, which may find its way into a future book! So credit to the Pan Macmillan team for their patience.

Finally, a thank you to my wife Jackie Stricker-Phelps for her encouragement, feedback and unerring confidence in me throughout the adventures of our life together.

Endnotes

6. A study at the University of Utah …: Nielsen JA, Zielinski BA, Ferguson MA & et. al. 'An Evaluation of the Left-Brain vs. Right-Brain Hypothesis with Resting State Functional Connectivity Magnetic Resonance Imaging'. *PLoS ONE*, vol. 8, no. 8, 2013.

10. The amygdalae receive information about the …: Janak PH & Tye KM. 'From circuits to behaviour in the amygdala'. *Nature*, vol. 517, no. 7534, 2015.

11. A study of healthy young adults …: Kanai R, Feilden T, Firth C & et. al. 'Political orientations are correlated with brain structure in young adults'. *Current Biology*, vol. 21, no. 8, 2011, p. 677–80.

12. In adult humans, it has been estimated …: Spalding KL, Bergmann O, Alkass K & et. al. 'Dynamics of hippocampal neurogenesis in adult humans'. *Cell*, vol. 154, no. 6, 2013, p. 1219–27.

16. **Microglial cells** throughout the brain …: Purves D, Augustine GJ, Fitzpatrick D & et. al. (eds). *Neuroscience*, 2nd edition. Sinauer Associates, Sunderland, 2001.

19. GABA also has effects on other organs …: Ngo DH & Vo TS. 'An updated review on pharmaceutical properties of gamma-aminobutyric acid'. *Molecules*, vol. 24, no. 15, 2019, p. 2678.

19. Dopamine acts as a neurotransmitter in …: Ko JH & Strafella AP. 'Dopaminergic neurotransmission in the human brain: new lessons from perturbation and imaging'. *Neuroscientist*, vol. 18, no. 2, 2012, p. 149–68.

20. Serotonin is not only found in …: Berger M, Gray JA & Roth BL. 'The expanded biology of serotonin'. *Annual Review of Medicine*, vol. 60, 2009, p. 355–66.

20. There is some recent evidence to suggest …: Passani MB, Panula P & Lin JS. 'Histamine in the brain'. *Frontiers in Systems Neuroscience*, vol. 8, no. 64, 2014.

21. Prolonged use is a risk factor …: Richardson K, Fox C, Maidment I & et. al. 'Anticholinergic drugs and risk of dementia: case-control study'. *BMJ*, vol. 361, 2018.

22. During adolescence there is a changing …: Giedd JN. ‘Linking adolescent sleep, brain maturation, and behavior’. *Journal of Adolescent Health*, vol. 45, no. 4, 2009, p. 319–20. ; Giedd JN. ‘The teen brain: insights from neuroimaging’. *Journal of Adolescent Health*, vol. 42, no. 4, 2008, p. 335–43.

23. The process of ageing in the …: Peters R. ‘Ageing and the brain’. *Postgraduate Medical Journal*, vol. 82, no. 964, 2006, p. 84–8.

24. However, testosterone supplementation in older men …: Resnick SM, Matsumoto AM, Stephens-Shields AJ & et al. ‘Testosterone Treatment and Cognitive Function in Older Men With Low Testosterone and Age-Associated Memory Impairment’. *JAMA*, vol. 317, no. 7, 2017, p. 717–27.

26. Neuroplasticity after an injury to the brain …: Puderbaugh M & Emmady PD. *Neuroplasticity*. StatPearls Publishing, 2021. Sophie Su YR, Veeravagu A & Grant G. ‘Neuroplasticity after traumatic brain injury’. In Laskowitz D & Grant G (eds). *Translational Research in Traumatic Brain Injury*. CRC Press/Taylor and Francis Group, Boca Raton (FL), 2016.

26–7. Researchers found what they described as …: Månsson KNT, Salami A, Frick A & et. al. ‘Neuroplasticity in response to cognitive behavior therapy for social anxiety disorder’. *Translational Psychiatry*, vol. 6, no. 727, 2016.

27. A group of elderly people were …: Seinfeld S, Figueroa H, Ortiz-Gil J & et. al. ‘Effects of music learning and piano practice on cognitive function, mood and quality of life in older adults’. *Frontiers in Psychology*, vol. 4, no. 810, 2013.

28. Exercise has been shown to improve …: Niemann C, Godde B & Voelcker-Rehage C. ‘Not only cardiovascular, but also coordinative exercise increases hippocampal volume in older adults’. *Frontiers in Aging Neuroscience*, vol. 6, no. 170, 2014.

30. This risk at least doubles with …: Goldman JS, Hahn SE, Catania JW & et. al. ‘Genetic counseling and testing for Alzheimer disease: Joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors’. *Genetics in Medicine*, vol. 13, no. 6, 2011, p. 597–605.

36. Influenza in pregnant women has been …: Cordeiro CN, Tsimis M & Burd I. ‘Infections and Brain Development’. *Obstetrical & gynecological survey*, vol. 70, no. 10, 2015, p. 644–55.

36. It is now recommended that COVID-19 …: Department of Health, ‘Joint statement between RANZCOG and ATAGI about COVID-19 vaccination for pregnant women’, *Department of Health*, 9 June 2021.

38. The consequences of maternal stress on …: Buss C, Entringer S, Swanson JM & et. al. ‘The role of stress in brain development: the gestational environment’s long-term effects on the brain. *Cerebrum*, vol. 2012, no. 4, 2012.

41. It is also advisable to eat foods …: The Royal Women’s Hospital Victoria Australia, ‘Food & nutrition in pregnancy’, *The Women’s*, www.thewomens.org.au.

42. One study published in *Pediatrics* found …: Hart PH, Lucas RM, Walsh JP & et. al. 'Vitamin D in Fetal Development: Findings From a Birth Cohort Study'. *Pediatrics*, vol. 135, no. 1, 2015.

42. Researchers from the University of Surrey …: Darling A, Rayman MP, Steer CD & et. al. 'Association between maternal vitamin D status in pregnancy and neurodevelopmental outcomes in childhood: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)'. *British Journal of Nutrition*, vol, 1, 2017.

43. The impact on the brain development …: University of Sydney, 'Low level alcohol use during pregnancy can impact child's brain development', *University of Sydney*, 25 Sep 2020, www.sydney.edu.au. ; Smith AM, Dwoskin LP & Pauly JR. 'Early exposure to nicotine during critical periods of brain development: Mechanisms and consequences'. *Journal of Pediatric Biochemistry*, vol. 1, no. 2, 2010, p. 125–41.

49. 'After adjustment for numerous potential confounders …': University of Sydney, 'Low level alcohol use during pregnancy can impact child's brain development'. *University of Sydney*, 25 September 2020, www.sydney.edu.au.

51. The Australian guidelines developed by the …: NHMRC, 'Australian guidelines to reduce health risks from drinking alcohol'. *NHMRC*, 2020, www.nhmrc.gov.au.

51. Foetal brain development is extremely sensitive …: Charness ME, Riley EP & Sowell ER. 'Drinking During Pregnancy and the Developing Brain: Is Any Amount Safe?'. *Trends in Cognitive Sciences*, vol. 20, no. 2, 2016, p. 80–2.

52. For example, repeated binge drinking increases …: Kyzar EJ, Floreani C, Teppen TL & et. al. 'Adolescent Alcohol Exposure: Burden of Epigenetic Reprogramming, Synaptic Remodeling, and Adult Psychopathology'. *Frontiers in Neuroscience*, vol. 10, no. 222, 2016.

52. While many Australians do start drinking …: Australian Institute of Health and Welfare, 'Alcohol, tobacco & other drugs in Australia'. *Australian Institute of Health and Welfare*, 16 April 2021, www.aihw.gov.au.

56. Generally, older age is associated with …: Le Couteur DG, McLachlan AJ & de Cabo R. 'Aging, Drugs, and Drug Metabolism'. *The Journals of Gerontology: Series A*, vol. 67A, no. 2, 2012, p. 137–9.

58. 'Information about the potential for generally …': US Food & Drug Administration. 'FDA drug safety communication: important safety label changes to cholesterol-lowering statin drugs'. *US Food & Drug Administration*, 2016, www.fda.gov.

61. A 2012 French study published in …: de Gage SB, Bégaud B, Bazin F & et. al. 'Benzodiazepine use and risk of dementia: prospective population based study'. *BMJ*, vol. 345, 2012.

61. More recent studies suggest that any …: Salzman C. 'Do Benzodiazepines Cause Alzheimer's Disease?'. *American Journal of Psychiatry*, vol. 177, no. 6, 2020, p. 476–8.

63. It has been estimated that in Australia …: Ball PA, Morrissey H & Pilotto LSJ. 'Anticholinergic burden assessed using general practice electronic records'. *Journal of Pharmacy Practice and Research*, vol. 43, no. 3, 2013, p. 202–5.

64. In 2016, a review was published …: Marvanova M. 'Drug-induced cognitive impairment: Effect of cardiovascular agents'. *Mental Health Clinician*, vol. 6, no. 4, 2016, p. 201–6.

65. The cognitive impairment that occurs with …: Lam RW, Kennedy SH, Mclntyre RS & et. al. 'Cognitive dysfunction in major depressive disorder: effects on psychosocial functioning and implications for treatment'. *Canadian Journal of Psychiatry*, vol. 59, no. 12, 2014, p. 649–54.

65. Some studies have found that the …: Sayyah M, Eslami K, AlaiShehni S & et. al. 'Cognitive function before and during treatment with selective serotonin reuptake inhibitors in patients with depression or obsessive-compulsive disorder'. *Psychiatry Journal*, vol. 2016, no. 5480391, 2016.

66. However, they do also have some …: Ciriaco M, Ventrice P, Russo G & et. al. 'Corticosteroid-related central nervous system side effects'. *Journal of Pharmacology & Pharmacotherapeutics*, vol. 4, suppl. 1, 2013.

66. About 20 per cent of patients …: The Boston Collaborative Drug Surveillance Program. 'Acute adverse reactions to prednisone in relation to dosage'. *Clinical Pharmacology & Therapeutics*, vol. 13, 1972, p. 694–8.

66. Most psychiatric symptoms are reversible when …: Wolkowitz OM. 'Prospective controlled studies of the behavioral and biological effects of exogenous corticosteroids'. *Psychoneuroendocrinology*, vol. 19, 1994, p. 233–55.

70. There are many types of cancer …: Wefel JS, Vardy J, Ahles T & et. al. 'International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer'. *The Lancet Oncology*, vol. 12, no. 7, 2011, p. 703–8.

70. 'these problems can be detected in …': Janelsins MC, Kesler SR, Ahles TA & et. al. 'Prevalence, mechanisms, and management of cancer-related cognitive impairment'. *International Review of Psychiatry*, vol. 26, no. 1, 2014, p. 102–13.

71. An interesting study at Sydney Medical School …: Vardy JL, Dhillon HM, Pond GR & et. al. 'Cognitive function in patients with colorectal cancer who do and do not receive chemotherapy: a prospective, longitudinal, controlled study'. *Journal of Clinical Oncology*, vol. 33, no. 34, 2015, p. 4085–95.

72. These brain scans have shown reductions in grey …: Deprez S, Kesler SR, Saykin AJ & et. al. 'International cognition and cancer task force recommendations for neuroimaging methods in the study of cognitive impairment in non-CNS cancer patients'. *Journal of the National Cancer Institute*, vol. 110, no. 3, 2018, p. 223–31.

76. Commonly used anaesthetic agents target neuronal …: Brown EN & Flores FJ. 'General anesthesia causes telltatel brain activity patterns'. *The Scientist*, March 2019, www.the-scientist.com.

76. In recent years there has been …: Wu L, Zhao H, Weng H & et. al. 'Lasting effects of general anesthetics on the brain in the young and elderly: "mixed picture" of neurotoxicity, neuroprotection and cognitive impairment'. *Journal of Anesthesia*, vol. 33, no. 2, 2019, p. 321–35.

77. In 2016 in the United States …: US Food & Drug Administration. 'FDA drug safety communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women', *US Food & Drug Administration*, August 2018, www.fda.gov.

77. This is more commonly seen in …: Ballard C, Jones E, Gauge N & et. al. 'Optimised anaesthesia to reduce post operative cognitive decline (POCD) in older patients undergoing elective surgery, a randomised controlled trial'. *PLoS ONE*, vol. 7, no. 6, 2012.

83. That is one of the reasons …: Shields B. 'Doctor-turned MP Kerryn Phelps floats pill-testing trial', *Sydney Morning Herald*, January 2019, www.smh.com.au.

83. A UK pilot trial was undertaken …: Measham C. 'Drug safety testing, disposals and dealing in an English field: Exploring the operational and behavioural outcomes of the UK's first onsite "drug checking" service'. *International Journal of Drug Policy*, vol. 67, 2019, p. 102–7.

83. One of the first Australian trials …: Lowrey T. 'Second pill-testing trial at Groovin the Moo hailed a success as partygoers dump dangerous drugs', *ABC News*, April 2019, www.abc.net.au.

85. According to the Australian Institute of Health and Welfare …: Australian Institute of Health and Welfare. 'Alcohol, tobacco & other drugs in Australia', *Australian Institute of Health and Welfare*. December 2020, www.aihw.gov.au.

87. Cannabis alters normal brain communication by …: NIDA. 'How does marijuana produce its effects?'. *National Institute on Drug Abuse*, April 2021, www.drugabuse.gov.

89. One study found that heavy, chronic …: Filbey FM, Aslan S, Calhoun VD & et. al. 'Long-term effects of marijuana use on the brain'. *Proceedings of the National Academy of Sciences of the United States of America*, vol. 111, no. 47, 2014, p 16913–8.

89. A study of adolescent cannabis users …: Hanson KL, Winward JL, Schweinsburg AD & et. al. 'Longitudinal study of cognition among adolescent marijuana users over three weeks of abstinence'. *Addictive Behaviors*, vol. 35, no. 11, 2010, p. 970–6.

90. AIHW data shows that cocaine use …: Australian Institute of Health and Welfare. 'Alcohol, tobacco & other drugs in Australia'. *Australian Institute of Health and Welfare*, December 2020, www.aihw.gov.au.

91. Regular cocaine use has been shown …: Department of Health. 'Pharmacology of cocaine'. *Department of Health*, April 2004, www1.health.gov.au.

92. It is one of the most commonly…: Australian Institute of Health and Welfare. 'Illicit drug use'. *Australian Institute of Health and Welfare*, July 2020,

www.aihw.gov.au.

92. The feelings of emotional warmth, disproportionate …: Rothman RB, Baumann MH, Dersch CM & et. al. 'Amphetamine-type central nervous system stimulants release norepinephrine more potently than they release dopamine and serotonin'. *Synapse*, vol. 39, no. 1, 2001, p. 32–41.

92. Fatalities related to ecstasy are not …: DrugWise. 'Why do people die after taking ecstasy?'. *DrugWise*, January 2017, www.drugwise.org.uk.

93. A study from the European Monitoring …: European Monitoring Centre for Drugs and Drug Addiction. 'Recent changes in Europe's MDMA/ecstasy market'. *European Monitoring Centre for Drugs and Drug Addiction*, April 2016, www.emcdda.europa.eu.

93. Research tells us that continued use …: National Institute on Drug Abuse. 'What are MDMA's effects on the brain?'. *National Institute on Drug Abuse*, September 2017, www.drugabuse.gov.

93. PET scanning shows lasting effects in …: Obrocki J, Buchert R, Väterlein O & et. al. 'Ecstasy – long-term effects on the human central nervous system revealed by positron emission tomography'. *British Journal of Psychiatry*, vol. 175, no. 2, 1999, p. 186–8. ; Bosch OG, Wagner M, Jessen F & et. al. 'Verbal memory deficits are correlated with prefrontal hypometabolism in (18)FDG PET of recreational MDMA users'. *PLoS ONE*, vol. 8, no. 4, 2013.

94. Methamphetamine is considered to be the …: Australian Institute of Health and Welfare. 'Illicit use of drugs'. *Australian Institute of Health and Welfare*, January 2018, www.aihw.gov.au.

95. There has been a rapid increase …: Australian Institute of Health and Welfare, 'Alcohol, tobacco & other drugs in Australia', *Australian Institute of Health and Welfare*, April 2021, www.aihw.gov.au.

97. In people who are diagnosed with …: Yelland GW. 'Gluten-induced cognitive impairment ('brain fog') in coeliac disease'. *European Journal of Gastroenterology & Hepatology*, vol. 32, suppl. 1, 2017, p. 90–3.

98. Gluten ataxia is an immune-mediated disorder …: Khwaja GA, Bohra V, Duggal A & et. al. 'Gluten sensitivity – a potentially reversible cause of progressive cerebellar ataxia and myoclonus – a case report'. *Journal of Clinical and Diagnostic Research*, vol. 9, no. 11, 2015.

98. This experience reflects the findings of …: Hadjivassiliou M, Davies-Jones GA, Sanders DS & et. al. 'Dietary treatment of gluten ataxia'. *Journal of Neurology, Neurosurgery, and Psychiatry*, vol. 74, no. 9, 2003, p. 1221–4.

98. These include chronic headache, developmental delay …: Niederhofer H & Pittschieler K. 'A preliminary investigation of ADHD symptoms in persons with celiac disease'. *Journal of Attention Disorders*, vol. 10, no. 2, 2006, p. 200–4.

99. 'serotonergic dysfunction due to impaired availability …': Pynnonen PA. 'Gluten-free diet may alleviate depressive and behavioural symptoms in adolescents with coeliac disease: a prospective follow-up case-series study'. *BMC Psychiatry*, vol. 17, no. 5, 2005, p. 14.

100. Schizophrenia in children with coeliac disease …: Dohan FC & Grasberger JC. 'Relapsed schizophrenics: earlier discharge from the hospital after cereal-free, milk-free diet'. *Am J* Psychiatry, vol. 130, no. 6, 1973, p. 685–8.

100. There was a case report of …: Lionetti E, Leonardi S, Franzonello C & et. al. 'Gluten psychosis: confirmation of a new clinical entity'. *Nutrients*, vol. 7, 2015, p. 5532–9.

100. Medical research offers a number of suggested …: Makhlouf S, Messelmani M, Zaouali J & et. al. 'Cognitive impairment in celiac disease and non-celiac gluten sensitivity: review of literature on the main cognitive impairments, the imaging and the effect of gluten free diet'. *Acta Neurologica Belgica*, vol. 118, no. 1, 2018, p. 21–7.

100. In a 2004 study, regional cerebral …: Addolorato G, DiGiuda D, DeRossi G & et. al. 'Regional cerebral hypoperfusion in patients with celiac disease'. *The American Journal of Medicine*, vol. 116, 2004, p. 312–7.

101. These blood flow changes seem to …: Usai P, Serra A, Marini B & et. al. 'Frontal cortical perfusion abnormalities related to gluten intake and associated autoimmune disease in adult coeliac disease: 99mTc-ECD brain SPECT study'. *Digestive and Liver Disease*, vol. 36, no. 8, 2004, p. 513–8.

102. High blood glucose and insulin …: Ott A, Stolk RP, Hofman A & et. al. 'Association of diabetes mellitus and dementia: the Rotterdam Study'. *Diabetologia*, vol. 39, no. 11, 1996, p. 1392–7.

104. We know that higher fasting blood …: Karlamangla AS, Miller-Martinez D, Lachman ME & et. al. 'Biological correlates of adult cognition: midlife in the United States (MIDUS)'. *Neurobiology of Aging*, vol. 35, no. 2, 2014, p. 387–94.

104. A 2012 study found that even …: Cherbuin N, Sachdev P & Anstey KJ. 'Higher normal fasting plasma glucose is associated with hippocampal atrophy: The PATH Study'. *Neurology*, vol. 79, no. 10, 2012, p. 1019–26.

104. A large community-based prospective cohort …: Rawlings AM, Sharrett AR, Schneider AL & et. al. 'Diabetes in midlife and cognitive change over 20 years: a cohort study'. *Annals of Internal Medicine*, vol. 161, no. 11, 2014, p. 785–93.

104. In women with obstructive sleep apnoea …: Lal C, Hardiman G, Kumbhare S & et. al. 'Proteomic biomarkers of cognitive impairment in obstructive sleep apnea syndrome'. *Sleep Breath*, vol. 23, 2019, p. 251–7.

105. It is also believed that insulin …: Li L & Hölscher C. 'Common pathological processes in Alzheimer disease and type 2 diabetes: a review'. *Brain Research Reviews*, vol. 56, 2007, p. 384–402.

105. So what is the role of …: Cholerton B, Baker LD & Craft S. 'Insulin, cognition, and dementia'. *European Journal of Pharmacology*, vol. 719, no. 1–3, 2013, p. 170–9.

107. A new research study, conducted over …: Samaras K. 'Treatment linked to slowed cognitive decline', *Garvan Institute of Medical Research*, September 2020, www.garvan.org.au.

109. According to the US Surgeon-General …: U.S. Department of Health and Human Services, 'Know the Risks e-cigarettes & young people', *Know the Risks e-cigarettes & young people*, 2021, e-cigarettes.surgeongeneral.gov/knowtherisks.html.

110. A study of children aged between …: Yolton K, Dietrich K, Auinger P & et. al. 'Exposure to environmental tobacco smoke and cognitive abilities among U.S. children and adolescents'. *Environmental Health Perspectives, vol. 113, no. 1, 2005, p. 98–103*.

110. Adolescent smokers also suffer from attention …: Goriounova NA & Mansfelder HD. 'Short- and long-term consequences of nicotine exposure during adolescence for prefrontal cortex. neuronal network function'. *Cold Spring Harbor Perspectives in Medicine*, vol. 2, no. 12, 2012.

110. Smokers experience more rapid cognitive decline …: Zhong G, Wang Y, Zhang Y & et. al. 'Smoking is associated with an increased risk of dementia: a meta-analysis of prospective cohort studies with investigation of potential effect modifiers'. *PLoS One*, vol. 10, no. 3, 2015.

110. There are many possible ways that …: Swan GE & Lessov-Schlaggar CN. 'The effects of tobacco smoke and nicotine on cognition and the brain'. *Neuropsychology Review*, vol. 17, no. 3, 2007, p. 259–73.

111. A study found that, compared with …: Alberg A. 'The influence of cigarette smoking on circulating concentrations of antioxidant micronutrients'. *Toxicology, vol. 180, no. 2, 2002, p. 121–37*.

111. Swedish research showed for the first …: European Lung Foundation, 'E-cigarettes linked to increased arterial stiffness, blood pressure and heart rate in humans, *Science Daily*, September 2017, www.sciencedaily.com.

115. This means that microbleeds are likely …: Akoudad S, Wolters FJ, Viswanathan A & et. al. 'Association of cerebral microbleeds with cognitive decline and dementia'. *JAMA Neurology*, vol. 73, no. 8, 2016, p. 934–43.

116. With the increasing availability of imaging …: Elmståhl S, Ellström K, Siennicki-Lantz A & et. al. 'Association between cerebral microbleeds and hypertension in the Swedish general population "Good Aging in Skåne" study'. *Journal of Clinical Hypertension (Greenwich)*, vol. 21, no. 8, 2019, p. 1099–107.

121. However, even if there are no …: Maki PM. 'Verbal memory and menopause'. *Maturitas*, vol. 82, no. 3, 2015, p. 288–90.

121. One study at the University of Rochester …: Weber MT, Rubin LH & Maki PM. 'Cognition in perimenopause: The effect of transition stage. *Menopause, vol. 20, no. 5, 2013, p. 511–7*.

122. It has been shown that women …: Bove R, Secor E, Chibnik LB & et al. 'Age at surgical menopause influences cognitive decline and Alzheimer pathology in older women'. *Neurology*, vol. 82, no. 3, 2014, p. 222–9.

124. A study presented to the Endocrine Society …: Morselli L. 'Weight loss improved memory performance in obese women', *Healio*, June 2013, www.healio.com.

129. Disturbances of the Brain-Gut Microbiome Axis …: Valles-Colomer M, Falony G, Darzi Y & et. al. 'The neuroactive potential of the human gut microbiota in quality of life and depression'. *Nature Microbiology*, vol. 4, 2019, p. 623–32. ; Foster JA & Neufeld K-AM. 'Gut–brain axis: how the microbiome influences anxiety and depression'. *Trends in Neurosciences*, vol. 36, no. 5, 2013, p. 305–12. ; Mulak A & Bonaz B. 'Brain-gut-microbiota axis in Parkinson's disease'. *World Journal of Gastroenterology*, vol. 21, no. 37, 2015, 10609. ; Galland L. 'The gut microbiome and the brain'. *Journal of Medicinal Food*, vol. 17, no. 12, 2014, p. 1261–72.

130. The microbiome and the brain communicate …: Cryan JF, O'Riordan KJ, Cowan CSM & et. al. 'The Microbiota-Gut-Brain Axis'. *Physiological Reviews*, vol. 99, no. 4, 2019, p. 1877–2013.

131. Animal-derived foods that are high …: Uribarri J, Woodruff S, Goodman S & et. al. 'Advanced glycation end products in foods and a practical guide to their reduction in the diet', *Journal of the American Dietetic Association*, vol. 110, no. 6, 2010, p. 911–6.

131. They include red meat, butter …: Akhter F, Chen D, Akhter A & et al. 'High Dietary Advanced Glycation End Products Impair Mitochondrial and Cognitive Function'. *J Alzheimers Dis*, vol. 76, no. 1, 2020, p. 165–78.

134. Recent evidence also suggests that aerobic …: Dalton A, Mermier C & Zuhl M. 'Exercise influence on the microbiome-gut-brain axis'. *Gut Microbes*, vol. 10, no. 5, 2019, p. 555–68.

134. Research has found that total microbiome …: Smith RP, Easson C, Lyle SM & et. al. 'Gut microbiome diversity is associated with sleep physiology in humans'. *PLoS One*, vol. 14, no. 10, 2019.

134. This is an exciting time as knowledge …: Tan AH, Hor JW, Chong CW & et. al, 'Probiotics for Parkinson's disease: Current evidence and future directions', *JGH Open*, 2021, vol. 5, p. 414–9.

138. Infants with iron deficiency test lower …: Lozoff B & Georgieff MK. 'Iron deficiency and brain development'. *Seminars in Pediatric Neurology*, vol. 13, no. 3, 2006, p. 158–65.

138. One study of women aged between …: Murray-Kolb LE & Beard JL. 'Iron treatment normalizes cognitive functioning in young women'. *The American Journal of Clinical Nutrition*, vol. 85, no. 3, 2007, p. 778–87.

139. Iron deficiency (with or without anaemia) understandably …: Yavuz BB, Cankurtaran M, Haznedaroglu IC & et. al. 'Iron deficiency can cause cognitive impairment in geriatric patients'. *The Journal of Nutrition, Health & Aging*, vol. 16, 2012, p. 220–4.

144. It is surprisingly common for an older …: Loughrey DG, Kelly ME, Kelley GA & et. al. 'Association of age-related hearing loss with cognitive function, cognitive impairment, and dementia: a systematic review and meta-analysis'. *JAMA Otolaryngology – Head and Neck Surgery*, vol. 144, no. 2, 2018, p. 115–26.

146. It shrinks the brain's frontal cortex …: Rosenbloom MJ & Pfefferbaum A. 'Magnetic resonance imaging of the living brain: Evidence for brain degeneration among alcoholics and recovery with abstinence'. *Alcohol Research & Health*, vol. 31, no. 4, 2008, p. 362–76.

146. Research has shown that abstinence from …: Durazzo TC, Mon A, Gazdzinski S & et. al. 'Serial longitudinal magnetic resonance imaging data indicate non-linear regional gray matter volume recovery in abstinent alcohol-dependent individuals'. *Addiction Biology*, vol. 20, no. 5, 2015, p. 956–67.

147. In my career as a health communicator …: AMA Media Centre. 'Dr Kerryn Phelps, AMA President, with Grant Goldman, Radio 2SM', *Australian Medical Association*, July 2002, https://ama.com.au.

148. More severe traumatic brain injury (TBI) …: Gardner RC & Yaffe K. 'Epidemiology of mild traumatic brain injury and neurodegenerative disease'. *Molecular and Cellular Neuroscience*, vol. 66, pt. B, 2015, p. 75–80.

151. Researchers at University College London found …: Ling H, Morris HR, Neal JW & et. al. 'Mixed pathologies including chronic traumatic encephalopathy account for dementia in retired association football (soccer) players'. *Acta Neuropathologica*, vol. 133, no. 3, 2017, p. 337–52.

152. According to research published in the …: Kirkwood G, Parekh N, Ofori-Asenso R & et. al. 'Concussion in youth rugby union and rugby league: a systematic review'. *British Journal of Sports Medicine*, vol. 49, 2015, p. 506–10.

153. Research tells us that about 10 million …: Haider AH, Saleem T, Bilaniuk JW & et. al. 'An evidence based review: efficacy of safety helmets in reduction of head injuries in recreational skiers and snowboarders'. *The Journal of Trauma and Acute Care Surgery*, vol. 73, no. 5, 2012, p. 1340–7.

158. Symptoms may appear as intellectual decline …: Noble JM, Canoll P & Honig LS. 'Brain tumor-associated dementia'. *Science of Aging Knowledge Environment, vol. 2005, no. 34, 2005*.

160. Exposure to medical radiation is the …: Cancer Research UK. 'Risks and causes of brain tumours', *Cancer Research UK*, October 2019, www.cancerresearchuk.org.

161. Because of conflicting information regarding risk …: World Health Organization. 'Electromagnetic fields and public health: mobile phones', *World Health Organization*, October 2014, www.who.int.

161. The American Cancer Society also recommends …: American Cancer Society. 'Cellular (Cell) Phones', *American Cancer Society*, June 2020, www.cancer.org.

166. Through advances in neuroimaging techniques such …: Bremner JD. 'Structural changes in the brain in depression and relationship to symptom recurrence'. *CNS Spectrums, vol. 7, no. 2, 2002, p. 129–30, 135–9*.

166. Reduced hippocampal volume is associated with …: Sheline YI, Sanghavi M, Mintun MA & et. al. 'Depression duration but not age predicts hippocampal

volume loss in medically healthy women with recurrent major depression'. *The Journal of Neuroscience*, vol. 19, no. 12, 1999, p. 5034–43.

167. Interestingly, clinical improvement is believed …: Frodl T, Meisenzahl EM, Zetzsche T & et. al. 'Hippocampal and amygdale changes in patients with major depressive disorder and healthy controls during a 1-year follow-up'. *The Journal of Clinical Psychiatry*, vol. 65, 2004, p. 492–9.

167. Evidence suggests that stress hormones play …: Muller N & Ackenheil M. 'Psychoneuroimmunology and the cytokine action in the CNS: implications for psychiatric disorders'. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, vol. 22, no. 1, 1998, p. 1–33. ; Porter RJ, Gallagher P, Watson S & et. al. 'Corticosteroid-serotonin interactions in depression: a review of the human evidence'. *Psychopharmacology (Berl)*, vol. 173, no. 1/2, 2004, p. 1–17.

168. Evidence is emerging that the gut …: Limbana T, Khan F & Eskander N. 'Gut Microbiome and Depression: How Microbes Affect the Way We Think'. *Cureus*, vol. 12, no. 8, 2020.

170. A study known as the PREVENT trial …: Kuyken W, Hayes R, Barrett B & et. al., 'Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial', *The Lancet*, vol. 386, no. 9988, 2015, p. 63–73.

170. Yoga practice has been shown to help …: Bridges L & Sharma M. 'The efficacy of yoga as a form of treatment for depression'. *Journal of Evidence-Based Complementary and Alternative Medicine*, vol. 22, no. 4, 2017, p. 1017–28.

170. Having an active search for meaning …: McCullough M & Larson D. 'Religion and depression: a review of the literature'. *Twin Research*, vol. 2, no. 2, 1999, p. 126–36.

170. It can also help you to …: Koenig H, George L & Perterson B. 'Religiosity and remission of depression in medically ill older patients'. *Am J Psychiatry*, vol. 155, 1998, p. 536–42.

171. Evidence about the effectiveness of antidepressant …: The Department of Health, 'What are the treatments for depression?'. *The Department of Health*, June 2005, www1.health.gov.au.

172. It has been estimated that 15 to 38 …: Alpert JF & Fava M. 'Nutrition and depression. The role of folate'. *Nutr Rev*, vol. 55, no. 5, 1997, p. 145–9.

172. Low dietary folate, low folate levels …: Tolmunen T, Hintikka J, Ruusunen A & et al. 'Dietary folate and the risk of depression in Finnish middle-aged men: a prospective follow-up study'. *Psychother Psychosom*, vol. 73, no. 6, 2004, p. 334–9. ; Kelly C, McDonnell AP, Johnston TG & et al. 'The MTHFR C677T polymorphism is associated with depressive episodes in patients from Northern Ireland'. *J Psychopharmacol*, vol. 18, no. 4, 2004, p. 567–71.

172. There is evidence of a reduced …: Papakostas G, Petersen T, Lebowitz BD & et al. 'The relationship between serum folate, vitamin B12 and homocysteine

levels in major depressive disorder and the timing of improvement with fluoxetine'. *Int J Neuropsychopharmacol*, vol. 8, no. 4, 2005, p. 523–8.

172. Preliminary studies have also shown folate …: Taylor MJ, Carney SM, Goodwin GM & et al. 'Folate for depressive disorders: systematic review and meta-analysis of randomized controlled trials'. *J Psychopharmacol*, vol. 18, 2004, p. 251–6.

172. SAMe is superior to placebo …: Fetrow CW & Avila JR. 'Efficacy of the dietary supplement S-adenosyl-L-methionine'. *Ann Pharmacother*, vol. 35, no. 11, 2001, p. 1414–25.

173. **5-HTP (5-hydroxytryptophan)**: This is an amino acid …: Birdsall T. '5-hydroxytryptophan: a clinically effective serotonin precursor'. *Alt Med Rev*, vol. 3, no. 4, 1998, p. 271–80.

173. A Cochrane Review found that …: Linde K, Berner MM & Kriston L. 'St John's wort for major depression'. *Cochrane Database of Systematic Reviews*, vol. 2008, issue 4, 2008.

173. One review reported that the commonly …: Saeed SA, Bloch RM & Antonacci DJ. 'Herbal and dietary supplements for treatment of anxiety disorders'. *Am Fam Physician*, vol. 76, no. 4, 2007, p. 549–56. ; Bilia AR, Gallon S & Vincieri FF. 'Kava-kava and anxiety: growing knowledge about the efficacy and safety'. *Life Sci*, vol. 70, no. 22, 2002, p. 2581–97. Akhondzadeh S, Naghavi HR, Vazirian M & et al. 'Passionflower in the treatment of generalised anxiety: a pilot double-blind randomized controlled trial with oxazepam'. *J Clin Pharm Ther*, vol. 26, 2001, p. 362–7.

179. After the age of 70, numerous …: Morley JE, Morris JC, Berg-Weger M & et. al. 'Brain health: the importance of recognizing cognitive impairment: an IAGG consensus conference'. *Journal of the American Medical Directors Association*, vol. 16, no. 9, 2015, p. 731–9.

179. The main aspect that will determine …: Knopman DS & Petersen RC. 'Mild cognitive impairment and mild dementia: a clinical perspective'. *Mayo Clin Proceedings*, vol. 89, no. 10, 2014, p. 1452–9.

179. 'In 2019, there [are] an estimated …': Dementia Australia, 'Dementia Prevalence Data 2018–2058', *Dementia Australia*, 2021, www.dementia.org.au.

183. Neurologist Dr Dale Bredesen and his …: Bredesen DE, Amos EC, Canick J & et. al. 'Reversal of cognitive decline in Alzheimer's disease'. *Aging (Albany NY)*, vol. 8, no. 6, 2016, p. 1250–8.

185. One study found that, compared with …: Wang HX, Wahlin A, Fastbom J & et. al. 'Vitamin B12 and folate in relation to the development of Alzheimer's Disease'. *Neurology*, vol. 56, no. 9, 2001, p. 1188–94.

185. Multivitamins reliably lower homocysteine in most …: Seshadri S, Beiser A, Selhub J & et. al. 'Plasma homocysteine as a risk factor for dementia and Alzheimer's disease'. *The New England Journal of Medicine*, vol. 346, no. 7, 2002, p. 476–83. ; Chinthapalli K. 'Alzheimer's disease: still a perplexing problem'. *BMJ*, vol. 349, 2014.

187. They are associated with cognitive impairment …: Wardlaw JM, Valdés Hernández MC & Muñoz-Maniega S. 'What are white matter hyperintensities made of? Relevance to vascular cognitive impairment'. *Journal of the American Heart Association*, vol. 4, no. 6, 2015.

190. In most cases of Lewy body …: Haider A, Spurling BC & Sánchez-Manso JC. 'Lewy Body Dementia'. In: *StatPearls*, StatPearls Publishing, Treasure Island (FL), January 2021.

192. Where thiamine deficiency due to chronic …: Arts NJ, Walvoort SJ & Kessels RP. 'Korsakoff's syndrome: a critical review'. *Neuropsychiatric Disease and Treatment*, vol. 13, 2017, p. 2875–90.

195. Across populations, it has been shown …: Verghese J, Lipton RB, Katz MJ & et. al. 'Leisure activities and the risk of dementia in the elderly'. *The New England Journal of Medicine*, vol. 348, no. 25, 2003, p. 2508–16.

195. Consider micronutrients essential to brain function …: Cardoso BR, Cominetti C & Cozzolino SM. 'Importance and management of micronutrient deficiencies in patients with Alzheimer's disease'. *Clinical Interventions in Aging*, vol. 8, 2013, p. 531–42.

198. Indeed, the condition is rare in …: Ball N, Teo WP, Chandra S & et. al. 'Parkinson's disease and the environment'. *Frontiers in Neurology*, vol. 10, 2019, p. 218.

200. The majority of people with Parkinson's …: Yang Y, Tang BS & Guo JF. 'Parkinson's disease and cognitive impairment'. *Parkinsons Disease*, vol. 2016, 2016.

201. illicit drug taking with amphetamine-like …: Ferreira C, Almeida C, Tenreiro S & et al. 'Neuroprotection or Neurotoxicity of Illicit Drugs on Parkinson's Disease'. *Life (Basel)*, vol. 10, no. 6, 2020, p. 86.

201. There has been some fascinating new …: Smith LM & Parr-Brownlie LC. 'A neuroscience perspective of the gut theory of Parkinson's disease'. *European Journal of Neuroscience*, vol. 49, no. 6, 2019, p. 817–23.

202. Levodopa is the most common medication …: The Michael J. Fox Foundation, 'About Parkinson's Medications & Treatments', *The Michael J. Fox Foundation*, www.michaeljfox.org.

203. Deep brain stimulation …: Groiss SJ, Wojtecki L, Südmeyer M & et. al. 'Deep brain stimulation in Parkinson's disease'. *Therapeutic Advances in Neurological Disorders*, vol. 2, no. 6, 2009, p. 20–8.

203. A meta-analysis has shown that …: Lee SH & Lim S. 'Clinical effectiveness of acupuncture on Parkinson disease: A PRISMA-compliant systematic review and meta-analysis'. *Medicine (Baltimore)*, vol. 96, no. 3, 2017.

204. The Ayurvedic herb *Mucuna pruriens* or …: Katzenschlager R, Evans A, Manson A & et. al. '*Mucuna pruriens* in Parkinson's disease: a double blind clinical and pharmacological study'. *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 75, 2004, p. 1672–7.

204. The pharmaceutical preparation HP-200, which …: Manyam BV, Dhanasekaran M & Hare TA. 'Effect of antiparkinson drug HP-200 (Mucuna pruriens) on the central monoaminergic neurotransmitters'. *Phytotherapy Research*, vol. 18, no. 2, 2004, p. 97–101.

204. A meta-analysis of these antioxidants …: Etminan M, Gill SS & Samii A. 'Intake of vitamin E, vitamin C, and carotenoids and the risk of Parkinson's disease: a meta-analysis'. *The Lancet Neurology*, vol. 4, no. 6, 2005, p. 362–5.

204. A more recent study in 2017 …: Yang F, Wolk A, Håkansson N & et. al. 'Dietary antioxidants and risk of Parkinson's disease in two population-based cohorts'. *Movement Disorders*, vol. 32, no. 11, 2017, p. 1631–6.

205. The association between vitamin D and …: Fullard ME & Duda JE. 'A review of the relationship between vitamin d and parkinson disease symptoms'. *Frontiers in Neurology*, vol. 11, 2020, p. 454.

205. People with Parkinson's treated with levodopa …: Triantafyllou NI, Nikolau C, Boufidou F & et. al. 's.l.: Folate and Vit B12 levels in L-dopa treated Parkinson's disease patients: their relationship to clinical maifestations, mood and cognition'. *Parkinsonism & Related Disorders*, vol. 14, no. 4, 2008, p. 321–5.

205. Interestingly, those patients with Parkinson's and …: Lamberti P, Zoccolella S, Armenise E & et. al. 's.l.: Hyperhomocysteinaemia in L-dopa treated Parkinson's disease patients: effect of cobalamin and folate administration'. *European Journal of Neurology*, vol. 12, no. 5, 2005, p. 365–8.

205. Adequate dietary intake of vitamin B6 …: de Lau LM, Koudstaal PJ, Witteman JC & et. al. 's.l.: Dietary folate, Vitamin B12 and Vitamin B6 and the risk of Parkinson's disease'. *Neurology*, vol. 67, no. 2, 2006, p. 315–8.

206. Animal studies have shown that magnesium …: Hashimoto T, Nishi K, Nagasao J & et. al. 's.l.: Mg exerts both preventative and ameliorating effects in an in vivo rat Parkinson's disease model involving MPP+ toxicity in dopaminergic neurons'. *Brain Research*, vol. 1197, 2008, p. 143–51.

206. People with Parkinson's disease show significantly …: Forsleff L, Schauss AG, Bier ID & et. al. 's.l.: Evidence of functional zinc deficiency in Parkinson's disease'. *Journal of Alternative and Complementary Medicine*, vol. 5, no. 1, 1999, p. 57–64. ; Du K, Liu MY, Zhong X & et al. 'Decreased circulating Zinc levels in Parkinson's disease: a meta-analysis study'. *Scientific Reports*, vol. 7, no. 1, 2017, p. 3902.

206. Higher intake of polyunsaturated fatty acids …: Qu Y, Chen X, Xu MM & et. al. 'Relationship between high dietary fat intake and Parkinson's disease risk: a meta-analysis', *Neural Regeneration Research*, 2019, vol. 14, no. 12, p. 2156–63.

206. In contrast, a typical Western diet …: Gao X, Chen H, Fung TT & et. al. 's.l.: Prospective study of dietary pattern and risk of Parkinson's disease'. *The American Journal of Clinical Nutrition*, vol. 86, no. 5, 2007, p. 1486–94; de Luis Roman D, Aller R & Castano O. 's.l.: Vegetarian diets: effects on health'. *Revista Clinical Española*, vol. 207, no. 3, 2007, p. 141–3.

209. ‘The top participants of the annual …’: Dresler M, Shirer WR, Konrad BN & et. al. ‘Mnemonic Training Reshapes Brain Networks to Support Superior Memory’. *Neuron*, vol. 93, no. 5, 2017, p. 1227–35.

211. It is a complex and multisensory …: Paraskevopoulos E, Kuchenbuch A, Herholz SC & et. al. ‘Multisensory integration during short-term music reading training enhances both uni- and multisensory cortical processing’. *Journal of Cognitive Neuroscience*, vol. 26, no. 10, 2014, p. 2224–38.

212. A number of studies have shown …: Toril P, Reales JM & Ballesteros S. ‘Video game training enhances cognition of older adults: a meta-analytic study’. *Psychology and Aging*, vol. 29, no. 3, 2014, p. 706–16.

212. There are now a number of …: Klimova B. ‘Computer-Based Cognitive Training in Aging’. *Front Aging Neurosci*, vol. 8, 2016, p. 313.

214. delay age-related mental decline, dementia …: Cotman C, Berchtold N & Christie LA. ‘Exercise builds brain health: key roles of growth factor cascades and inflammation’. *Trends in Neuroscience*, vol. 30, 2007, p. 464–72.

214. A recent analysis of the scientific …: Sibley BA & Etnier JL. ‘The relationship between physical activity and cognition in children: a meta-analysis’. *Pediatric Exercise Science*, vol. 15, 2003, p. 243–56.

216. Research has shown us that the …: So JH, Huang C, Ge M & et. al. ‘Intense exercise promotes adult hippocampal neurogenesis but not spatial discrimination’. *Frontiers in Cellular Neuroscience*, vol. 11, 2017, p. 13.

217. Evidence indicates that chronic inflammation …: Rosano C, Marsland AL & Gianaros PJ. ‘Maintaining brain health by monitoring inflammatory processes: a mechanism to promote successful aging’. *Aging and Disease*, vol. 3, no. 1, 2012, p. 16–33.

218. One recent study reported that significant …: van de Sande-Lee S, Pereira FR, Cintra DE & et. al. ‘Partial reversibility of hypothalamic dysfunction and changes in brain activity after body mass reduction in obese subjects’. *Diabetes*, vol. 60, no. 6, 2011, p. 199–704.

219. The Australian National Health Survey 2017–18 …: Australian Institute of Health and Welfare, ‘Insufficient physical activity, *Australian Institute of Health and Welfare*, Oct 2020, www.aihw.gov.au.

220. Tai chi has been shown to …: Wayne PM, Walsh JN, Taylor-Piliae RE, et. al. ‘Effect of tai chi on cognitive performance in older adults: systematic review and meta-analysis’. *J Am Geriatr Soc*, vol. 62, no. 1, 2014, p. 25–39.

224. The critical period for PUFAs in …: Bentsen H. ‘Dietary polyunsaturated fatty acids, brain function and mental health’. *Microbial Ecology in Health and Disease*, vol. 28, suppl. 1, 2017.

225. Mild to moderate iodine deficiency in …: Vermiglio F, Lo Presti VP, Moleti M & et. al. ‘Attention deficit and hyperactivity disorders in the offspring of mothers exposed to mild-moderate iodine deficiency: a possible novel iodine deficiency disorder in developed countries’. *The Journal of Clinical Endocrinology and Metabolism*, vol. 89, no. 12, 2004, p. 6054–60.

226. Where there is iron deficiency, iron …: Jáuregui-Lobera I. ‘Iron deficiency and cognitive functions’. *Neuropsychiatr Dis Treat*, vol. 10, 2014, p. 2087–95.

227. Protein is necessary for growth and …: Winick M. ‘Prenatal protein-calorie malnutrition and brain development’. *Progress in Clinical and Biological Research*, vol. 63, 1985, p. 397–402.

227. Research has found that a child’s …: Pongcharoen T, Ramakrishnan U, DiGirolamo AM & et. al. ‘Influence of prenatal and postnatal growth on intellectual functioning in school-aged children’, *Archives of Pediatrics & Adolescent Medicine*, vol. 166, no. 5, 2012, p. 411–6.

227. Vitamin A and its derivatives are …: Olson CR & Mello CV. ‘Significance of vitamin A to brain function, behavior and learning’. *Molecular Nutrition & Food Research*, vol. 54, no. 4, 2010, p. 489–95.

229. One study found a doubled risk …: Wang HX, Wahlin A, Basun H & et. al. ‘Vitamin B12 and folate in relation to the development of Alzheimer’s Disease’. *Neurology*, vol. 56, no. 9, 2001, p. 1188–94.

230. Folate supplements, particularly those that contain …: National Institute of Health. ‘Folate’, *National Institute of Health*, March 2021, https://ods.od.nih.gov.

232. They have the potential to protect …: Spencer JP. ‘Flavonoids and brain health: multiple effects underpinned by common mechanisms’. *Genes Nutrition*, vol. 4, no. 4, 2009, p. 243–50.

232. There is also evidence to suggest …: Commenges D, Scotet V, Renaud S & et. al. ‘Intake of flavonoids and risk of dementia’. *European Journal of Epidemiology*, vol. 16, 2001, p. 357–63.

232. Further, evidence shows that higher long-term …: Shishtar E, Rogers GT, Blumberg JB & et. al. ‘Long-term dietary flavonoid intake and risk of Alzheimer disease and related dementias in the Framingham Offspring Cohort’. *The American Journal of Clinical Nutrition*, vol. 112, no. 2, 2020, p. 343–53.

234. The Mediterranean diet has been associated …: Féart C, Samieri C, Barberger-Gateau P. ‘Mediterranean diet and cognitive function in older adults’. *Current Opinion in Clinical Nutrition & Metabolic Care*, vol. 13, no. 1, 2010, p. 14–8.

238. During the period when you are …: de Cabo R & Mattson MP. ‘Effects of intermittent fasting on health, aging, and disease’. *New England Journal of Medicine*, vol. 381, 2019, p. 2541–51.

238. Fasting has the potential to improve …: Shojaie M, Ghanbari F & Shojaie N. ‘Intermittent fasting could ameliorate cognitive function against distress by regulation of inflammatory response pathway’. *Journal of Advanced Research*, vol. 8, no. 6, 2017, p. 697–701.

238. In a clinical trial, older adults …: Witte AV, Fobker M, Gellner R & et. al. ‘Caloric restriction improves memory in elderly humans’. *Proceedings of the National Academy of Sciences of the United States of America*, vol. 106, 2009, p. 1255–60.

238. In a study involving overweight adults …: Horie NC, Serrao VT, Simon SS & et. al. 'Cognitive effects of intentional weight loss in elderly obese individuals with mild cognitive impairment'. *The Journal of Clinical Endocrinology and Metabolism*, vol. 101, 2016, p. 1104–12.

239. A large multicentre clinical trial showed …: Leclerc E, Trevizol AP, Grigolon RB & et. al. 'The effect of caloric restriction on working memory in healthy non-obese adults'. *CNS Spectrums*, vol. 25, no. 1, 2020, p. 2–8.

245. The properties of acetyl-L-carnitine …: Hudson S & Tabet N. 'Acetyl-L-carnitine for dementia'. *Cochrane Database of Systematic Reviews*, vol. 2003, no. 2, 2003.

245. Studies suggests that supplements of acetyl-L-carnitine …: Montgomery SA, Thal LJ & Amrein R. 'Meta-analysis of double blind randomized controlled clinical trials of acetyl-L-carnitine versus placebo in the treatment of mild cognitive impairment and mild Alzheimer's disease'. *International Clinical Psychopharmacology*, vol. 18, 2003, p. 61–71.

246. A 2017 pilot study of 50 adults …: Choudhary D & Bhattacharyya S. 'Efficacy and safety of Ashwagandha (*Withania somnifera* (L.) *Dunal*) root extract in improving memory and cognitive functions'. *Journal of Dietary Supplements*, vol. 14, no. 6, 2017, p. 1–14.

246. It has been extensively studied, and …: Stough C, Singh H & Zangara A. 'Mechanisms, efficacy, and safety of bacopa monnieri (brahmi) for cognitive and brain enhancement'. *Evidence-Based Complementary and Alternative Medicine*, vol. 2015, 2015.

246. Two Australian studies, one in generally …: Manap ASA, Vijayabalan S, Madhayan P & et. al. '*Bacopa monnieri*, a neuroprotective lead in alzheimer disease: a review on its properties, mechanisms of action, and preclinical and clinical studies'. *SAGE journals*, vol. 13, 2019.

247. Excessive and long-term alcohol consumption …: de Souza RSM, Rosa M Jr, Rodrigues TM & et. al. 'Lower choline rate in the left prefrontal cortex is associated with higher amount of alcohol use in alcohol use disorder'. *Frontiers in Psychiatry*, vol. 9, 2018, p. 563.

248. Cholesterol lowering medications (statins) interfere with …: Deichmann R. 'Coenzyme Q10 and statin-induced mitochondrial dysfunction.' *The Ochsner Journal*, vol. 10, no. 1, 2010, p. 16–21.

249. A 2002 study of CoQ10 and …: Shults CW. 'Effects of coenzyme Q10 in early Parkinson disease evidence of slowing of the functional decline'. *Archives of Neurology*, vol. 59, no. 10, 2002, p. 1541–50

249. An Australian trial investigating the effects …: Stough C, Nankivell M, Camfield DA & et. al. 'CoQ10 and cognition a review and study protocol for a 90-day randomized controlled trial investigating the cognitive effects of ubiquinol in the healthy elderly'. *Frontiers in Aging Neuroscience*, vol. 11, 2019, p. 103.

251. However, an eight-year trial called …: Snitz BE, O'Meara ES, Carlson MC & et. al. '*Ginkgo biloba* for preventing cognitive decline in older adults: a

randomized trial'. *Journal of the American Medical Association*, vol. 302, no. 24, 2009, p. 2663–70.

252. Various randomised trials and meta-analyses …: Hankey GJ. 'B vitamins for stroke prevention'. *Stroke and Vascular Neurology*, vol. 3, no. 2, 2018, p. 51–8.

252. Supplementing vitamin B12 (methylcobalamin), vitamin B9 …: Román GC, Mancera-Páez O & Bernal C. 'Epigenetic factors in late-onset Alzheimer's disease'. *International Journal of Molecular Sciences*, vol. 20, 2019, p. 319.

252. One study revealed that the cognitive …: Osimani A, Berger A, Friedman J & et. al. 'Neuropsychology of vitamin B12 deficiency in elderly dementia patients and control subjects'. *Journal of Geriatric Psychiatry and Neurology*, vol. 18, no. 1, 2005, p. 33–8.

254. In the context of MTHFR mutations …: Cajavilca CE, Gadhia RR & Román GC. ' *MTHFR* gene mutations correlate with white matter disease burden and predict cerebrovascular disease and dementia'. *Behavioral and Brain Sciences*, vol. 9, no. 9, 2019, p. 211.

255. It has antioxidant, neuroprotective and neuroregenerative …: Lokanathan Y, Omar N, Ahmad Puzi NN & et. al. 'Recent updates in neuroprotective and neuroregenerative potential of centella asiatica'. *Malaysian Journal of Medical Sciences*, vol. 23, no. 1, 2016, p. 4–14.

255. A systematic review found that centella …: Pttarak P, Dilokthornsakul P, Saokaew S & et. al. 'Effects of Centella asiatica (L.) Urb. on cognitive function and mood related outcomes: a systematic review and meta-analysis'. *Scientific reports*, vol. 7, no. 1, 2017.

255. In fact, recent data from the …: Australian Bureau of Statistics. 'Australian health survey: usual nutrient intakes', *Australian Bureau of Statistics*, March 2015, www.abs.gov.au.

255. More severe levels of magnesium deficiency …: National Institutes of Health. 'Magnesium', *National Institutes of Health*, September 2020, https://ods.od.nih.gov.

256. The neuroprotective effects of resveratrol in …: Andrade S, Ramalho MJ, Pereira MDC & et. al. 'Resveratrol brain delivery for neurological disorders prevention and treatment'. *Frontiers in Pharmacology*, vol. 9, 2018, p. 1261.

257. There is some initial evidence that …: Witte AV, Kerti L, Margulies DS & et. al. 'Effects of resveratrol on memory performance, hippocampal functional connectivity, and glucose metabolism in healthy older adults'. *The Journal of Neuroscience*, vol. 34, no. 23, 2014, p. 7862–70.

257. Borderline low or deficient selenium concentrations …: Akbaraly TN, Hininger-Favier I, Carriere I & et. al. 'Plasma selenium over time and cognitive decline in the elderly'. *Epidemiology*, vol. 18, 2007, p. 52–8.

258. A 2004 study described a direct …: Smorgon C, Mari E, Atti AR & et. al. 'Trace elements and cognitive impairment: an elderly cohort study'. *Archives of Gerontology and Geriatrics Supplement*, vol. 9, 2004, p. 393–402.

259. A small study at UCLA showed …: Small GW, Siddarth P, Li Z & et. al. ‘Memory and brain amyloid and tau effects of a bioavailable form of curcumin in non-demented adults: a double-blind, placebo-controlled 18-month trial’. *The American Journal of Geriatric Psychiatry*, vol. 26, no. 3, 2018, p. 266–77.

261. Low circulating levels of vitamin D …: Munger KL, Levin LI, Hollis BW & et. al. ‘Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis’. *Journal of the American Medical Association*, vol. 296, no. 23, 2006, p. 2832–8.

261. A study at the University of Cambridge …: Llewellyn DJ. ‘Serum 25-Hydroxyvitamin D concentration and cognitive impairment’. *Journal of Geriatric Psychiatry and Neurology*, vol. 22, no. 3, 2009, p. 188–95.

263. A 2017 study published in *The Lancet* ...: Soininen H, Solomon A, Visser PJ & et. al. ‘24-month intervention with a specific multinutrient in people with prodromal Alzheimer’s disease (LipiDiDiet): a randomised, double-blind, controlled trial’. *The Lancet Neurology*, vol. 16, no. 12, 2017, p. 965–75.

269. Social isolation is a known risk …: Yogman M, Garner A, Hutchinson J & et. al. ‘The power of play: a pediatric role in enhancing development in young children’. *Pediatrics*, vol. 142, no. 3, 2018.

270. A study of Romanian children investigated …: Sheridan M, Fox. N, Zeanah CH & et. al. ‘Variation in neural development as a result of institutionalization early in childhood’. *Proceedings of the National Academy of Sciences*, vol. 109, no. 32, 2012.

274. One study found that men who …: Berkman L, Leo-Summers L & Horwitz R. ‘Emotional support and survival after AMI: a prospective population-based study of the elderly’. *Annals of Internal Medicine*, vol. 117, 1992, p. 1003–9.

274. We also know that social and …: Glass TA, de Leon CM, Marottoli RA & et. al. ‘Population based study of social and productive activities as predictors of survival among elderly Americans’. *BMJ*, vol. 319, 1999, p. 478–83.

278. Dr Helen Fisher and a team …: Fisher H. ‘Lust, attraction, and attachment in mammalian reproduction’. *Human Nature*, vol. 9, no. 1, 1998.

279. According to the Australian Institute of …: Australian Institute of Health and Welfare. ‘Social isolation and loneliness’, *Australian Institute of Health and Welfare*, September 2019, www.aihw.gov.au.

281. The theory is that the chronic …: Slavich GM & Irwin MR. ‘From stress to inflammation and major depressive disorder: a social signal transduction theory of depression’. *Psychological Bulletin*, vol. 140, no. 3, 2014, p. 774–815.

284. Sleep becomes a problem for many …: Rose KM & Lorenz R. ‘Sleep disturbances in dementia’. *Journal of Gerontological Nursing*, vol. 36, no. 5, 2010, p. 9–14.

285. Electroencephalogram (EEG) studies show that during …: Dustman RE, Shearer DE & Emmerson RY. ‘Life-span changes in EEG spectral amplitude, amplitude variability and mean frequency’. *Clinical Neurophysiology*, vol. 110, no. 8, 1999, p. 1399–409.

285. Chronic sleep deprivation in young healthy …: McEwen BS. ‘Sleep deprivation as a neurobiologic and physiologic stressor: Allostasis and allostatic load’. *Metabolism*, vol. 55, no. 10, suppl. 2, 2006.

286. Research tells us that maintaining good …: Scullin MK & Bliwise DL. ‘Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research’. *Perspectives on Psychological Science*, vol. 10, no. 1, 2015, p. 97–137.

286. Between 60 and 70 per cent …: Wennberg AMV, Wu MN, Rosenberg PB & Spira AP. ‘Sleep disturbance, cognitive decline, and dementia: a review’. *Seminars in Neurology*, vol. 37, no. 4, 2017, p. 395–406.

289. This waste removal system is mainly …: Jessen NA, Munk AS, Lundgaard I & et. al. ‘The glymphatic system: a beginner’s guide’. *Neurochemical Research*, vol. 40, no. 12, 2015, p. 2583–99.

298. There is growing evidence that untreated …: Lajoie AC, Lafontaine AL, Kimoff RJ & et. al. ‘Obstructive sleep apnea in neurodegenerative disorders: current evidence in support of benefit from sleep apnea treatment’. *Journal of Clinical Medicine*, vol. 9, no. 2, 2020, p. 297.

298. One review reported that patients over …: Leng Y, McEvoy CT, Allen IE & et. al. ‘Association of sleep-disordered breathing with cognitive function and risk of cognitive impairment: a systematic review and meta-analysis’. *JAMA Neurology*, vol. 74, no. 10, 2017, p. 1237–45.

298. Another study found that people with …: Osorio RS, Gumb T, Pirraglia E & et. al. ‘Sleep-disordered breathing advances cognitive decline in the elderly’. *Neurology*, vol 84, 2015, p. 1964–71.

298. If there is one compelling argument …: Kim H, Joo E, Suh S & et. al. ‘Effects of long-term treatment on brain volume in patients with obstructive sleep apnea syndrome’. *Human Brain Mapping*, vol. 37, no. 1, 2016, p. 395–409.

300. If the stress response is unwarranted …: Yaribeygi H, Panahi Y, Sahraei H & et. al. ‘The impact of stress on body function: A review’. *EXCLI Journal*, vol. 16, 2017, p. 1057–72.

307. A study at Massachusetts General Hospital …: Stoeckel LE, Palley LS, Gollub RL & et. al. ‘Patterns of brain activation when mothers view their own child and dog: an fMRI study’. *PLoS ONE*, vol. 9, no. 10, 2014.

308. They concluded that ‘Pet ownership, particularly …: Levine GN, Allen K, Braun LT & et. al. ‘Pet ownership and cardiovascular risk. A scientific statement from the American Heart Association’. *Curculation*, vol. 127, no. 23, 2013.

308. More recently, in 2017 a study …: Mubanga M, Byberg L, Nowak C & et. al. ‘Dog ownership and the risk of cardiovascular disease and death – a nationwide cohort study’. *Scientific Reports*, vol. 7, no. 1, 2017.

308. These effects are particularly seen in …: Purewal R, Christley R, Kordas K & et. al. ‘Companion animals and child/adolescent development: a systematic review of the evidence’. *International Journal of Environmental Research and Public Health*, vol. 14, no. 3, 2017.

308. In older people, we know that …: Hui Gan GZ, Hill AM, Yeung P & et. al. ‘Pet ownership and its influence on mental health in older adults’. *Aging and Mental Health*, vol. 27, 2019, p. 1–8.

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About the Author

Professor Kerryn Phelps AM has been a general practitioner for over 40 years, and is a pioneer in the fields of health communication and integrative medicine in Australia.

Professor Phelps is a Conjoint Professor in the NICM Health Research Institute at Western Sydney University.

She is past president of the Australian Medical Association, and past president of the Australasian Integrative Medicine Association.

In 2001 she was awarded the Centenary of Federation Medal for services to Medicine and Australian society and in 2011 received an Order of Australia. In 2014 she was awarded an Honorary Doctorate of Letters by Western Sydney University.

She was elected to City of Sydney Council in 2016 and served as Deputy Lord Mayor of Sydney from 2016 to 2017, and as a Councillor until 2021.

Professor Phelps became a Member of the Australian Parliament when she won the 2018 Wentworth by-election, occasioned by the resignation from Parliament of Malcolm Turnbull following his removal as prime minister. She won the previously safe Liberal seat in a 19-point swing and was the first independent candidate to win the federal seat of Wentworth.

She is currently a general practitioner in Double Bay, is married to Jackie and has three children and two grandchildren.

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First published 2021 in Macmillan by Pan Macmillan Australia Pty Limited 1 Market Street, Sydney, New South Wales, Australia, 2000

Cataloguing-in-Publication entry is available from the National Library of Australia

http://catalogue.nla.gov.au

EPUB format: 9781760988616

Typeset by Midland Typesetters, Australia

Cover design by Debra Billson

Cover images: AAGGraphics/iStock

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