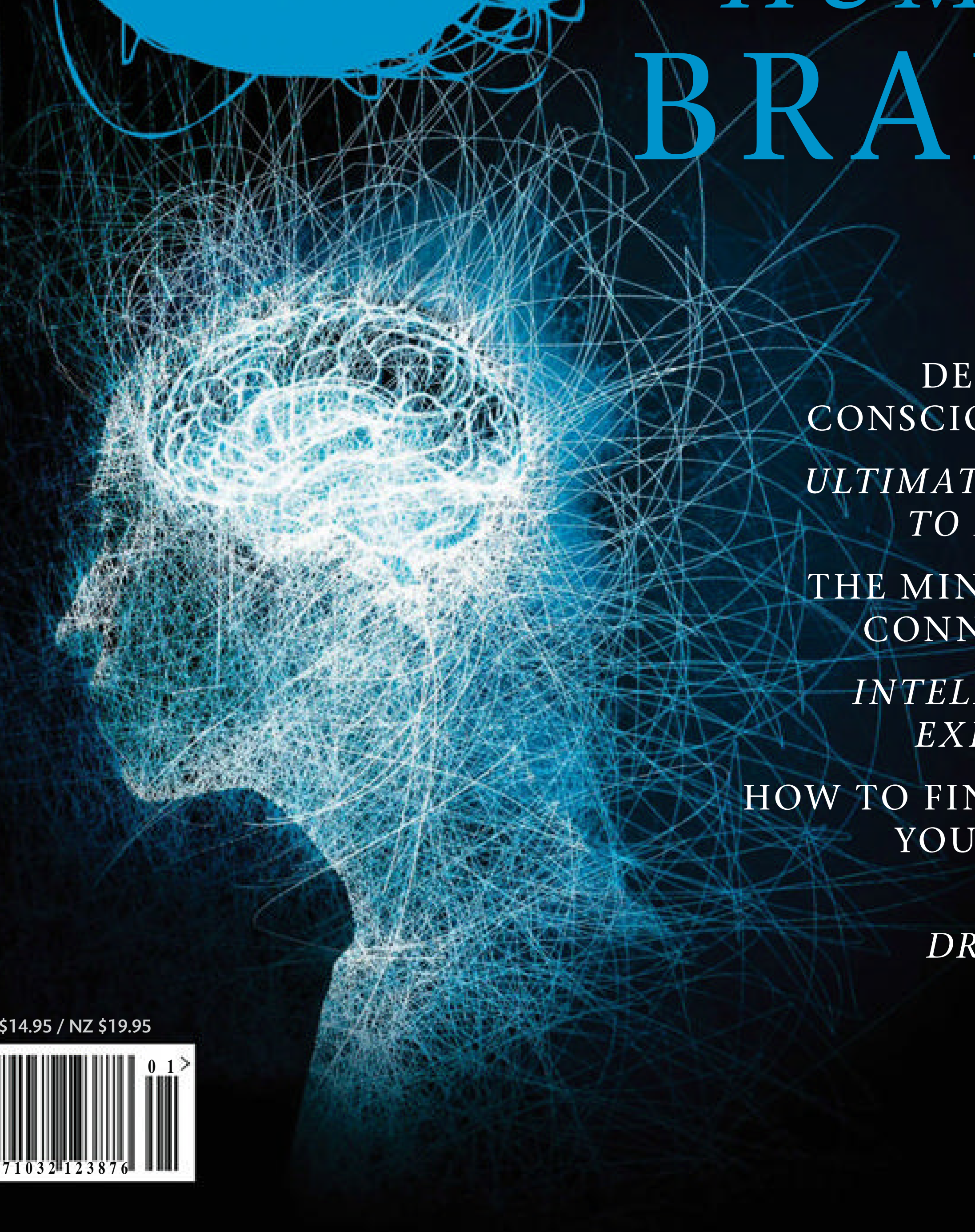
VOL TWO / ISSUE ONE

NewScientist
THE COLLECTION

THE HUMAN BRAIN



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Get inside your own head

The answers to the biggest questions of our existence – what is consciousness, what makes people behave the way they do, what is intelligence, and why do you sleep and dream – are all rooted in the 1.4 kilograms of soft stuff between your ears. These are questions about what it means to be human, about what makes you "you".

For millennia, questions like these have driven the pursuit to understand the human brain. It has been 2500 years since Hippocrates suggested that the mind resides not in the heart, but in our heads. And yet until relatively recently, the brain remained a black box, inaccessible without cracking open the skull or studying people with brain damage.

Modern technology is changing that. If the 19th century was dominated by chemistry and the 20th saw the birth of modern physics, we might rightly consider the 21st century to be that of neuroscience. Imaging techniques are allowing us to see the brain in action. We now know it is the place where our thoughts, desires, habits and personalities originate, not to mention the conscious state of being.

There are many questions still to answer about just how this tangle of 100 billion neurons pulls off such a feat, but science is now shining a light into this black box, and the findings are remarkable.

This fifth issue of *New Scientist: The Collection* is dedicated to the most complex object in the known universe – the human brain. A compilation of classic articles from *New Scientist*, it will show you what's going on inside your head, and what happens when the workings of the mind go awry.

Chapter 1 lays the foundations of our knowledge – from our early understanding of the brain's structure to the technical challenges of building a more detailed picture.

Chapter 2 dives inside your mind to tackle the slippery subject of thought, and the inner speech that often accompanies thinking.

If thinking about thinking is a challenge, Chapter 3 might be helpful. It deals with intelligence. What makes someone smart? And are we all getting more stupid?

Chapter 4 looks at what happens when the mind goes wrong, and how our knowledge of the brain might help treat conditions like schizophrenia, depression and dementia.

Chapter 5 charts how your brain changes during your life. Why can't you remember much from your early years, what do babies think about, and how do male and female brains differ?

Chapter 6 tackles one of the trickiest questions in science – how the physical processes of the brain generate the feeling of being conscious.

Chapter 7 reveals how the mind extends beyond the body to the world around us, and shows how you can use your body to fine-tune your mind.

Chapter 8 examines one of the most crucial functions of the brain – memory, which dictates how we think, act and make decisions, and even defines our identity.

Chapter 9 gives you the tools to get the best out of your brain, from how to stay attentive, to boosting your creativity and learning.

And finally, Chapter 10 switches off the lights to look at one of the most mysterious and intimate brain states – sleep. What is it for, why do we dream and can we glean meaning from the unconscious meanderings of our minds? It's time to get to know yourself better.

Catherine de Lange, Editor

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THE HUMAN BRAIN

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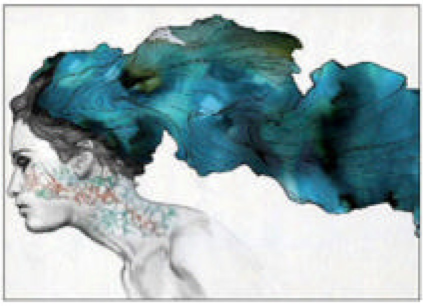

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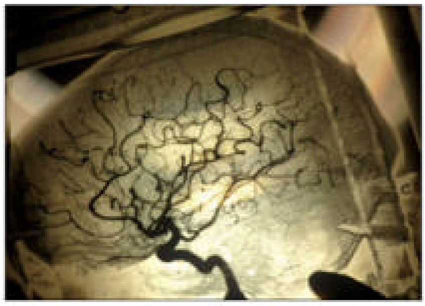

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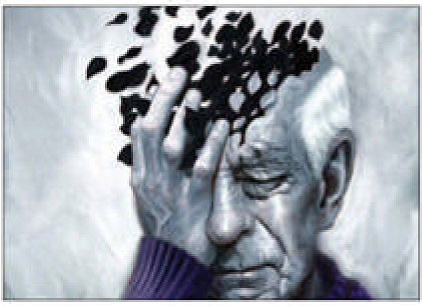

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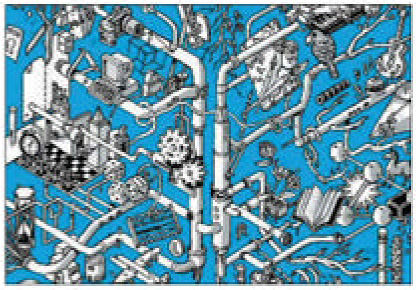

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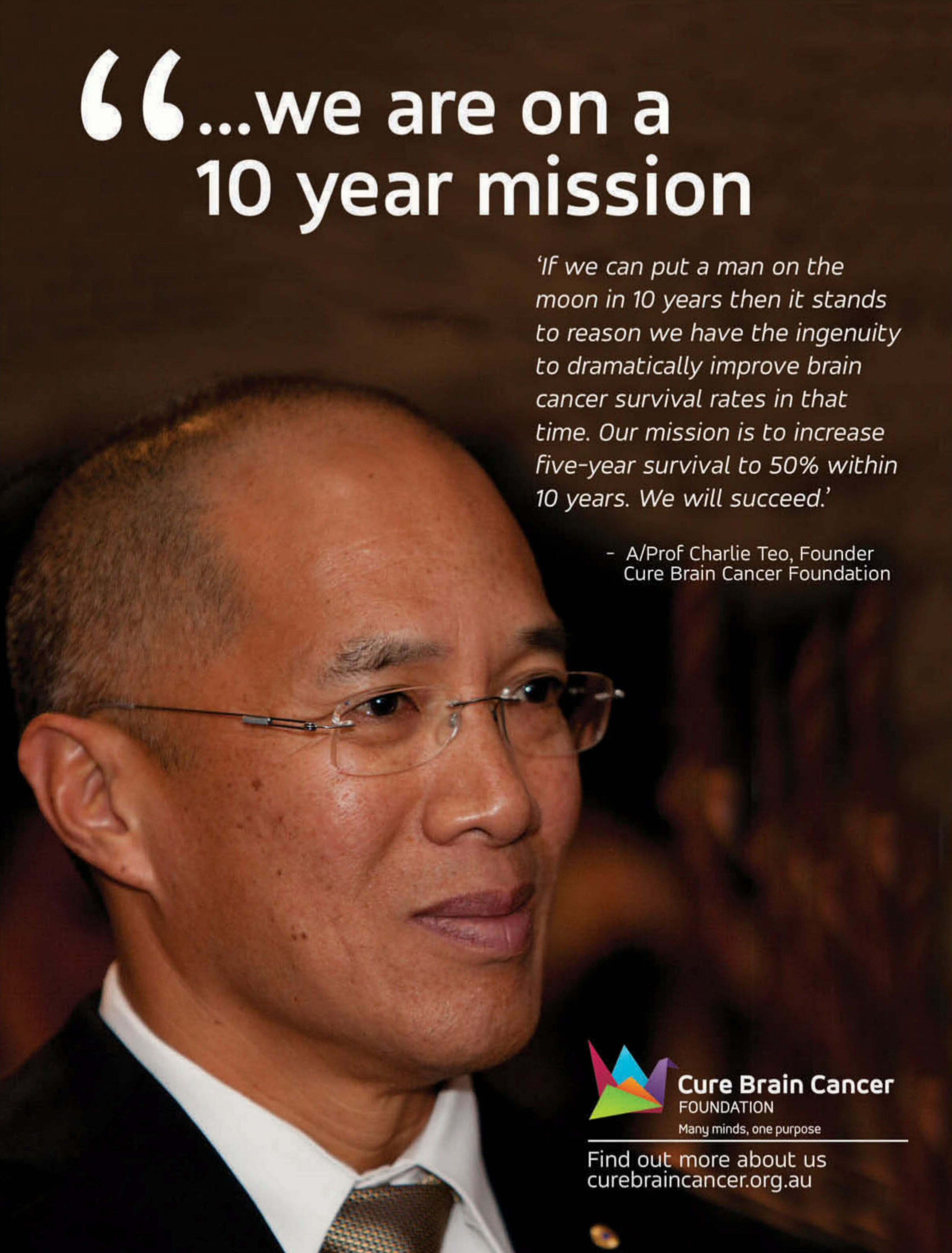
“...we are on a 10 year mission
‘If we can put a man on the moon in 10 years then it stands to reason we have the ingenuity to dramatically improve brain cancer survival rates in that time. Our mission is to increase five-year survival to 50% within 10 years. We will succeed.’
- A/Prof Charlie Teo, Founder Cure Brain Cancer Foundation
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BRAIN CANCER

KILLS MORE CHILDREN THAN ANY OTHER DISEASE

Yet 90% of Australians are unaware of this fact

*SOURCE CURE BRAIN CANCER RESEARCH OF 1,010 NATIONALLY REPRESENTATIVE AUSTRALIAN ADULTS AGED 18+ JULY 2014

150	117	55	51	49
Brain Cancer	Leukaemia	Heart Disease	Heart Defect	Thyroid Cancer

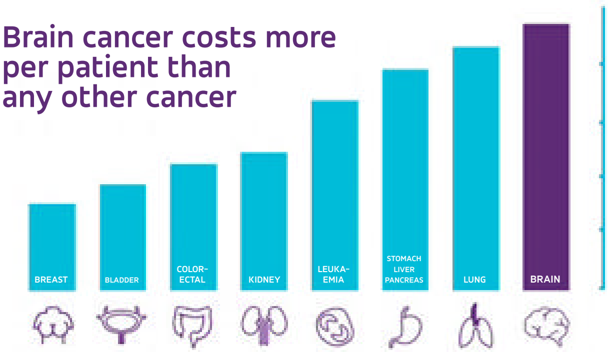
Number of deaths between 2008-2012

*SOURCE AUSTRALIAN BUREAU OF STATISTICS (2010 – 2014), 3303.0 CAUSES OF DEATH, AUSTRALIA (2008 – 2012) TABLE 1.3: UNDERLYING CAUSE OF DEATH, SELECTED CAUSES BY AGE AT DEATH, NUMBERS AND RATES, AUSTRALIA (2008 – 2012)

Brain cancer kills more Australians under 40 than any other cancer.

*SOURCE AIHW NATIONAL CANCER STATISTICS

Brain cancer costs more per patient than any other cancer



Index of lifetime cost per patient

*SOURCE THE COST OF CANCER NSW – REPORT BY ACCESS ECONOMICS, AUSTRALIA WIDE, APRIL 2007

Brain cancer is deadly, survival rates are low

90% OF CHILDREN SURVIVE LEUKAEMIA

90% OF PEOPLE SURVIVE BREAST CANCER

20% OF PEOPLE SURVIVE BRAIN CANCER

*SOURCE AIHW NATIONAL CANCER STATISTICS

It gets worse. For some forms, such as Glioblastoma or DIPG, survival is much lower.

5% OF PEOPLE SURVIVE GLIOBLASTOMA

*SOURCE (OSTROM, Q, GITTLEMAN, H, FARAH, P, ONDRACEK, A, CHEN, Y, WOLINSKY, Y, STROUP, N.E, KRUCHKO, C & BARNHOLTZ-SLOAN, J.S, (2013). CBTRUS STATISTICAL REPORT: PRIMARY BRAIN AND CENTRAL NERVOUS SYSTEM TUMOURS DIAGNOSIS IN THE UNITED STATES IN 2006-2010. NEURO-ONCOLOGY, P50-51.

Yet it recieves just 3% of NHMRC/ Government Cancer Research Funding

*SOURCE NHMRC GRANT APPLICATION ROUND 2009-2013

34%	19%	18%	17%	2%
Prostate	Cancer	Bowel	Breast	Brain

* SOURCE: INCREASE IN SURVIVAL RATES 1982 - 2010. AIHW NATIONAL CANCER STATISTICS

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CHAPTER ONE

HOW IT WORKS

Milestones of neuroscience

We now have a good understanding of the brain's building block – the neuron. But it's taken us 2500 years, says Michael O'Shea

About 250,000 years ago, something quite extraordinary happened. Animals with an unprecedented capacity for thought appeared on the savannahs of Africa. Eventually, they were smart enough to start questioning the origins of their own intelligence. We are finally close to getting some answers, but it has not been a smooth journey.

THE BEGINNINGS

The birth of neuroscience began with Hippocrates some 2500 years ago. While his contemporaries, including Aristotle, believed that the mind resided in the heart, Hippocrates argued that the brain is the seat of thought, sensation, emotion and cognition.

It was a monumental step, but a deeper understanding of the brain took a long time to follow, with many early theories ignoring the solid brain tissue in favour of fluid filled cavities, or ventricles. The 2nd-century physician Galen – perhaps the most notable proponent of this idea – believed the human brain to have three ventricles, with each one responsible for a different mental faculty: imagination, reason and memory. According to his theory, the brain controlled our body's activities by pumping fluid from the ventricles through nerves to other organs (for more on this, see "Like clockwork", page 14).

Such was Galen's authority that the idea cast a long shadow over our understanding of the brain, and fluid theories of the brain dominated until well into the 17th century. Even such luminaries as French philosopher René Descartes compared the brain to a hydraulic-powered machine. Yet the idea had a major flaw: a fluid could not move quickly enough to explain the speed of our reactions.

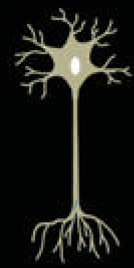
A more enlightened approach came when a new generation of anatomists began depicting the structure of the brain with increasing accuracy. Prominent among them was the 17th-century English doctor Thomas Willis, who argued that the key to how the brain worked lay in the solid cerebral tissues, not the ventricles. Then, 100 years later, Luigi Galvani and Alessandro Volta showed that an external source of electricity could activate nerves and muscle. This was a crucial development, since it finally suggested why we respond so rapidly to events. But it was not until the 19th century that German physiologist Emil Du Bois-Reymond confirmed that nerves and muscles themselves generate electrical impulses.

All of which paved the way for the modern era of neuroscience, beginning with the work of the Spanish anatomist Santiago Ramón y Cajal (pictured) at the dawn of the 20th century. His spectacular observations identified neurons as the building blocks of the brain. He found them to have a diversity of forms that is not found in the cells of other organs. Most surprisingly, he noted that insect neurons matched and sometimes exceeded the complexity of human brain cells. This suggested that our abilities depend on the way neurons are connected, not on any special features of the cells themselves.

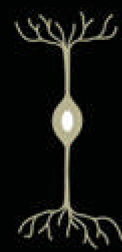
Cajal's "connectionist" view opened the door to a new way of thinking about information processing in the brain, and it still dominates today. ›

Santiago Ramón y Cajal is considered by many to be the father of modern neuroscience

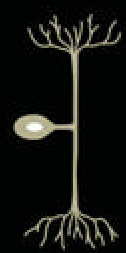
Neurons are some of the most diverse cells in the human body, though they all share the same basic features



MOTOR
Send signals to parts of the body, such as muscle, to direct movement



INTER
Provide a connective bridge between other neurons



SENSORY
Transmit signals to the brain from the rest of the body

PYRAMIDAL
Involved in many areas of cognition, such as object recognition within the visual cortex

SPL; LEFT: CAJAL LEGACY, INSTITUTO CAJAL (CSIC), MADRID, SPAIN

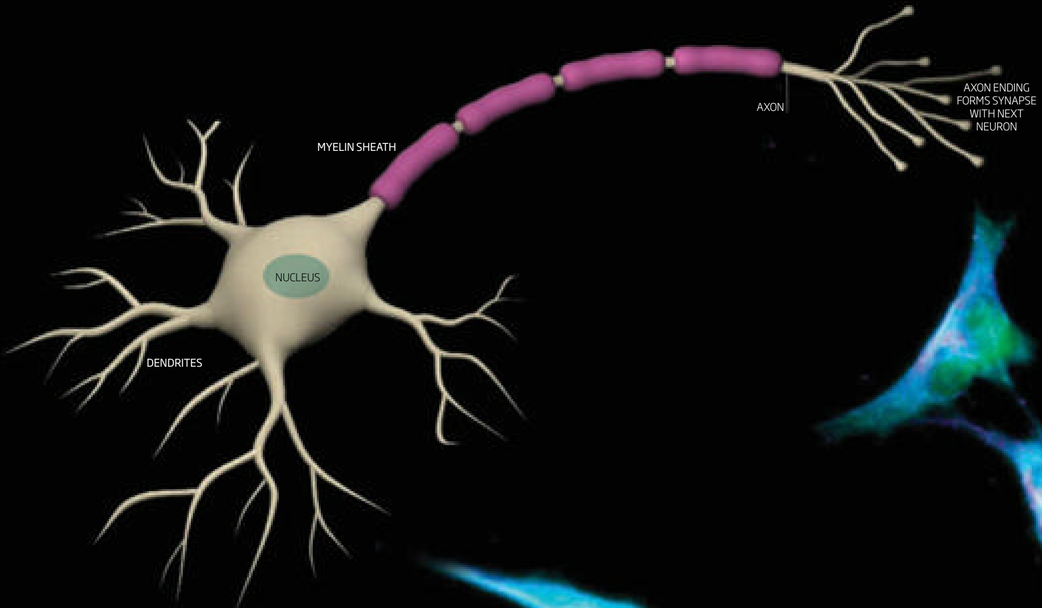
WIRED TO THINK

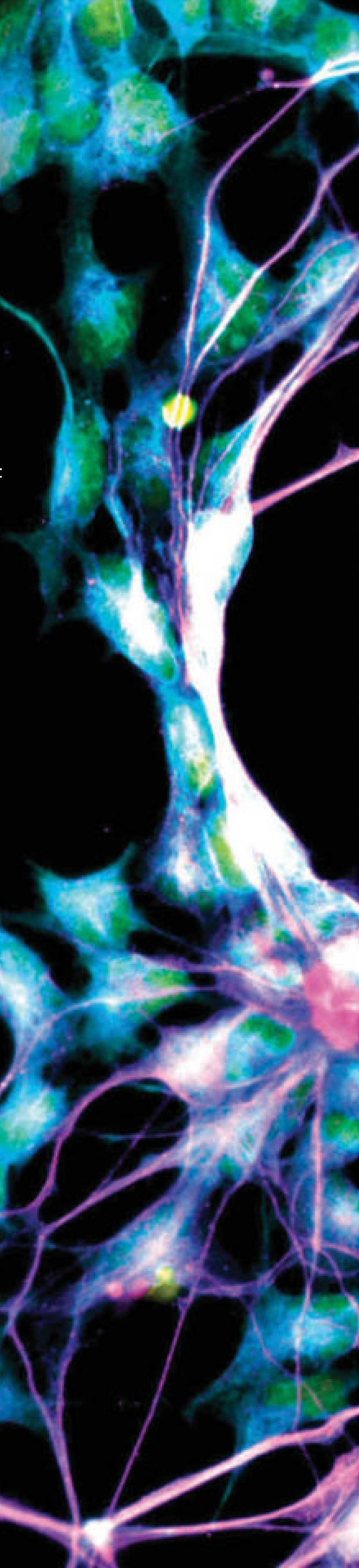
While investigating the anatomy of neurons in the 19th century, Santiago Ramón y Cajal proposed that signals flow through neurons in one direction. The cell body and its branched projections, known as dendrites, gather incoming information from other cells. Processed information is then transmitted along the neuron's long nerve fibre, called the axon, to the synapse, where the message is passed to the next neuron (see diagram, below).

It took until the 1940s and 50s for neuroscientists to get to grips with the finer details of this electrical signalling. We now know that the messages are transmitted as brief pulses called action potentials. They carry a small voltage – just 0.1 volts – and last only a few thousandths of a second, but they can travel great distances during that time, reaching speeds of 120 metres per second.

The nerve impulse's journey comes to an end when it hits a synapse, triggering the release of molecules called neurotransmitters, which carry the signal across the gap between neurons. Once they reach the other side, these molecules briefly flip electrical switches on the surface of the receiving neuron. This can either excite the neuron into sending its own signal, or it can temporarily inhibit its activity, making it less likely to fire in response to other incoming signals. Each is important for directing the flow of information that ultimately makes up our thoughts and feelings.

The complexity of the resulting network is staggering. We have around 100 billion neurons in our brains, each with 1000 synapses. The result is 100 trillion interconnections. If you started to count them at one per second you would still be counting 30 million years from now.





THE PLASTIC BRAIN

Unlike the electronic components of a computer, our networks of neurons are flexible thanks to a special class of neurotransmitter. These "neuromodulators" act a bit like a volume control, altering the amount of other neurotransmitters released at the synapse and the degree to which neurons respond to incoming signals. Some of these changes help to fine-tune brain activity in response to immediate events, while others rewire the brain in the long term, which is thought to explain how memories are stored.

Many neuromodulators act on just a few neurons, but some can penetrate through large swathes of brain tissue creating sweeping changes. Nitric oxide, for example, is so small (the 10th smallest molecule in the known universe, in fact) that it can easily spread away from the neuron at its source. It alters receptive neurons by changing the amount of neurotransmitter released with each nerve impulse, kicking off the changes that are necessary for memory formation in the hippocampus.

Through the actions of a multitude of chemical transmitters and modulators, the brain is constantly changing, allowing us to adapt to the world around us.

MAPPING THE MIND

Advanced imaging techniques have given us a detailed map of where different skills arise in the brain

Our billions of neurons, joined by trillions of neural connections, build the most intricate organ of the human body. Attempts to understand its architecture began with reports of people with brain damage. Localised damage results in highly specific impairments of particular skills – such as language or numeracy – suggesting that our brain is modular, with different locations responsible for different mental functions.

Advanced imaging techniques developed in the late 20th century gave a more nuanced approach by allowing researchers to peer into healthy brains as volunteers carried out different cognitive tasks. The result is a detailed map of where different skills arise in the brain – an important step on the road to understanding our complex mental lives.

FOREBRAIN

Many of our uniquely human capabilities arise in the forebrain, which expanded rapidly during the evolution of our mammalian ancestors. It includes the thalamus, a relay station that directs sensory information to the cerebral cortex for higher processing; the hypothalamus, which releases hormones into the bloodstream for distribution to the rest of the body; the amygdala, which deals with emotion; and the hippocampus, which plays a major role in the formation of spatial memories.

Among the most recently evolved parts are the basal ganglia, which regulate the speed and smoothness of intentional movements initiated by the cerebral cortex. Connections in this region are modulated by the neurotransmitter dopamine, provided by the midbrain's substantia nigra. A deficiency in this source is associated with many of the symptoms of Parkinson's disease, such as slowness of movement, tremor and impaired balance. Although drugs that boost levels of the neurotransmitter in the basal ganglia can help, a cure for Parkinson's is still out of reach.

Finally, there is the cerebral cortex – the enveloping hemispheres thought to make us human. Here plans are made, words are formed and ideas generated. Home of our creative intelligence, imagination and consciousness, this is where the mind is formed.

Structurally, the cortex is a single sheet of tissue made up of six crinkled layers folded inside the skull; if it were spread flat it would stretch over 1.6 square metres. Information enters and leaves the cortex through about a million neurons, but it has more than 10 billion internal connections, meaning the cortex spends most of its time talking to itself.

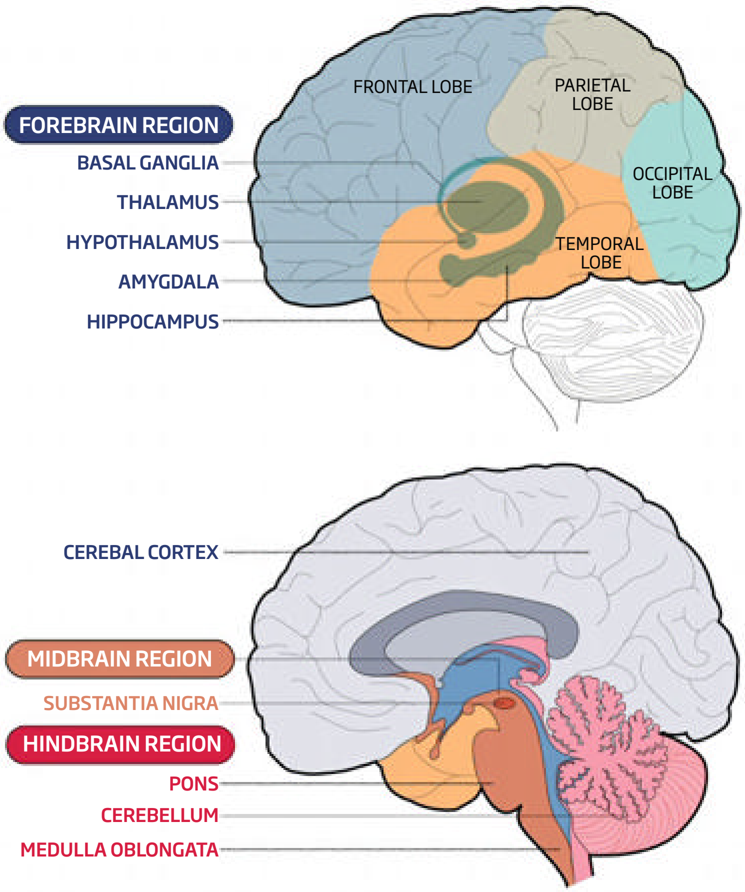
Each of the cortical hemispheres have four principal lobes (see upper diagram, right). The frontal lobes house the neural circuits for thinking and planning, and are also thought to be responsible for our individual personalities. The occipital and temporal lobes are mainly concerned with the processing of visual and auditory information, respectively. Finally, the parietal lobes are involved in attention and the integration of sensory information.

The body is "mapped" onto the cortex many times, including one map representing the senses and another controlling our movements. These maps tend to preserve the basic structure of the body, so that neurons processing feelings from your feet will be closer to those dealing with sensations from your legs than those crunching data from your nose, for example. But the proportions are distorted, with more brain tissue devoted to the hands and lips than the torso or legs. Redrawing the body to represent these maps results in grotesque figures like Penfield's homunculus (left).

The communications bridge between the two cerebral hemispheres is a tract of about a million axons, called the corpus callosum. Cutting this bridge, a procedure sometimes

performed to alleviate epileptic seizures, can split the unitary manifestation of "self". It is as if the body is controlled by two independently thinking brains. One smoker who had the surgery reported that when he reached for a cigarette with his right hand, his left hand would snatch it and throw it away!

As we have seen, different tasks are carried out by different cortical regions. Yet all you have to do is open your eyes to see that these tasks are combined smoothly: depth, shape, colour and motion all merge into a 3D image of the scene. Objects are recognised with no awareness of the fragmented nature of the brain's efforts. Precisely how this is achieved remains a puzzle. It's called the "problem of binding" and is one of the many questions left to be answered by tomorrow's neuroscientists.



MIDBRAIN

The midbrain plays a role in many of our physical actions. One of its central structures is the substantia nigra, so-called because it is a rich source of the neurotransmitter dopamine, which turns black in post-mortem tissue. Because dopamine is essential for the control of movement, the substantia nigra is said to "oil the wheels of motion". Dopamine is also the "reward" neurotransmitter and is necessary for many forms of learning, compulsive behaviour and addiction.

Other regions of the midbrain are concerned with hearing, visual information processing, the control of eye movements and the regulation of mood.

HINDBRAIN

As its name suggests, the hindbrain is located at the base of the skull, just above the neck. Comparisons of different organisms suggest it was the first brain structure to have evolved, with its precursor emerging in the earliest vertebrates. In humans it is made up of three structures: the medulla oblongata, pons and cerebellum.

The medulla oblongata is responsible for many of the automatic behaviours that keep us alive, such as breathing, regulating our heartbeat and swallowing. Significantly, its axons cross from one side of the brain to the other as they descend to the spinal cord, which explains why each side of the brain controls the opposite side of the body.

A little further up is the pons, which also controls vital functions such as breathing, heart rate, blood pressure and sleep. It also plays an important role in the control of facial expressions and in receiving information about the movements and orientation of the body in space.

The most prominent part of the hindbrain is the cerebellum, which has a very distinctive rippled surface with deep fissures. It is richly supplied with sensory information about the position and movements of the body and can encode and memorise the information needed to carry out complex fine-motor skills and movements. ■

The greatest map of all

Charting the connections between nerve cells could one day give us a read-out of our brains, says Douglas Fox

A STRANGE contraption, a cross between a deli meat slicer and a reel-to-reel film projector, sits in a windowless room in Cambridge, Massachusetts. It whirs along unsupervised for days at a time, only visited occasionally by Narayanan Kasthuri, a mop-haired postdoc at Harvard University, who examines the strip of film spewing out.

It may seem unlikely, but what's going on here signifies a revolution in neuroscience. Spaced every centimetre along the film are tiny dots, each of which is a slice of mouse brain, one-thousandth the thickness of a sheet of aluminium foil. This particular roll of film contains 6000 slices, representing a speck of brain the size of a grain of salt.

The slices of brain will be turned into digital images by an automated electron microscope. A computer will read those images, trace the outlines of nerve cells and stack the pictures into a 3D reconstruction.

In the jargon, they are building the mouse "connectome", named in line with the term "genome" for the sequence of all of an organism's genes, and "proteome" for all its proteins, and so on.

It's an epic undertaking. Using this technique, the full mouse connectome would produce hundreds of times more data than can be found on all of Google's computers, says Jeffrey Lichtman, the neuroanatomist leading the Harvard team. And yet it's just the beginning. Their efforts could be seen as a dry run for a project that is at least four orders of magnitude greater: mapping the human connectome.

With about 100 billion neurons, each with up to 10,000 connections, or synapses, the human brain is the most complex object in the known universe. To map the entire thing would arguably be the most ambitious project we have attempted and, for now, lies out of reach. Yet thanks to the constant acceleration of our computing and biotechnological capabilities, the first steps towards the roughest of drafts are already being taken.

In line with the scale of the challenges, the pay-offs could be huge. Even the most rudimentary blueprint of the brain could reveal how genes and experience shape our wiring, which in turn determines our individual differences. It would advance our understanding of conditions such as autism, schizophrenia and addiction – all of which are increasingly viewed as "connectopathies". It could even shed light on such mysteries as intelligence and consciousness. "Now is the time we're going to answer stuff that we've been waiting half a century to deal with," says Robert Marc, a vision scientist at the University of Utah in Salt Lake City.

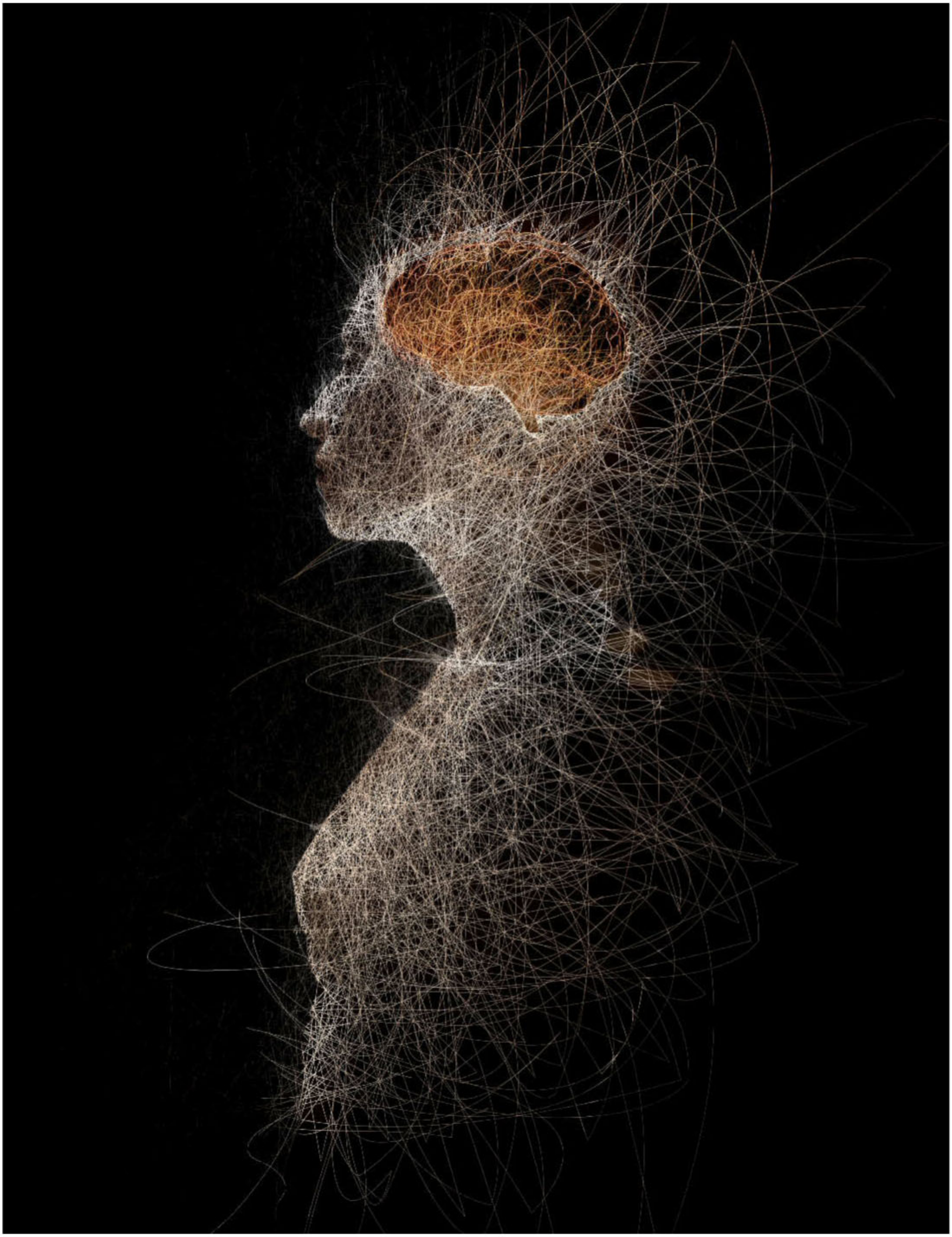
It is only in the past few decades that scanning techniques have allowed scientists to peer inside living brains. Magnetic resonance imaging (MRI) provides detailed anatomical images, and an enhanced version called functional MRI measures fluctuations in blood supply to different parts of the brain as people carry out specific mental tasks. On the assumption that blood supply reflects how hard neurons are working, this effectively lets neuroscientists watch the brain in action.

These techniques have led to a wealth of new insights, but they reveal nothing about neural connections. Brain tissue in these images looks more like the filling of a cream cake than the trillions of criss-crossing neural wires that are really there.

The first animal to have those wires mapped was a millimetre-long, dirt-dwelling roundworm called *Caenorhabditis elegans*, which turned out to have 302 neurons and 9000 synapses. Incredibly, this work started in the 1970s, with little of today's equipment. The worm was cut into several thousand slices before being imaged under an electron microscope.

In those days, the delicate slices were floated on a bead of water and manipulated using a toothpick with a human eyelash glued to the end. Touching the slices with the eyelash destroyed them, so the team had to gingerly brush the surrounding water to ›

"Our memories, and many other things that make us individuals, may be encoded in our connectomes"



BRUNO VERGAUWEN

nudge them into place – and for good measure, the slices were almost invisible on the water. Understandably, it took 14 years to assemble the wiring diagram, published in a landmark 446-page paper dubbed "The mind of a worm".

Technology has moved on since the days when an eyelash was part of the laboratory toolkit, and the Harvard team is not alone in coming up with a film-projector-like brain imager. The equipment is improving all the time. Even so, mapping an entire mammal brain in intricate detail is still a painstaking task, so a more pragmatic approach has been to focus on questions that can be answered by mapping discrete areas of the brain.

Kasthuri, for example, has been working on a connectome for the mouse cerebellum, a cauliflower-shaped structure at the base of the brain that has fine control over movements. Marc is concentrating on the retina, the patch of nerve-rich tissue at the back of each eyeball that is seen as an extension of the brain, in a bid to understand common causes of blindness such as glaucoma and retinitis pigmentosa. "Our connectomes are pouring out data faster than we imagined possible," he says.

Sebastian Seung, a computational neuroscientist now at Princeton University has been charting part of a zebra finch's brain to try to read the bird's song from its connectome. It may sound like an eccentric goal, but it would be an important proof of concept: that we could one day read a brain's memories.

Projects such as these have attracted the attention of "transhumanists", people who want to harness technology to live forever. They see connectomics as the first step to downloading their brains into computers. The Brain Preservation Foundation has offered a scaled-down version of the XPrize: up to $106,000 for the first lab to develop a way to preserve a whole mammal brain at the moment of death, so that its connectome could be read.

Whether because of the modest nature of the reward – the original XPrize for private space flight was $10 million – or the transhumanists' oddball reputation, most neuroscientists seem indifferent to the prize. "It doesn't motivate me at all," says Kasthuri. "I'm much more interested in using connectomics to understand biology."

"Miswired brains could be identified and treated years before symptoms begin to emerge"

The cell-by-cell approach has its critics, though. Charles Gilbert, a neurobiologist at Rockefeller University in New York, points out that synapses constantly change. He has found that in a mouse cortex, they turn over at the rate of 7 per cent per week. "You may take a snapshot of the connections," he says. "That doesn't necessarily mean that those are the connections that exist all the time."

Mouse brain

10^7

neurons

10^{10}

synapses

Human brain

10^{11}

neurons

10^{14}

synapses

Another drawback is that a typical speck of brain being mapped will have thousands of neurons coming in from distant areas, which are lopped off at the edge of the sample with no clue to their origin.

That's why other groups have taken a step back to look at the bigger picture. Instead of trying to map every single nerve cell, they are mapping just the long-distance connections.

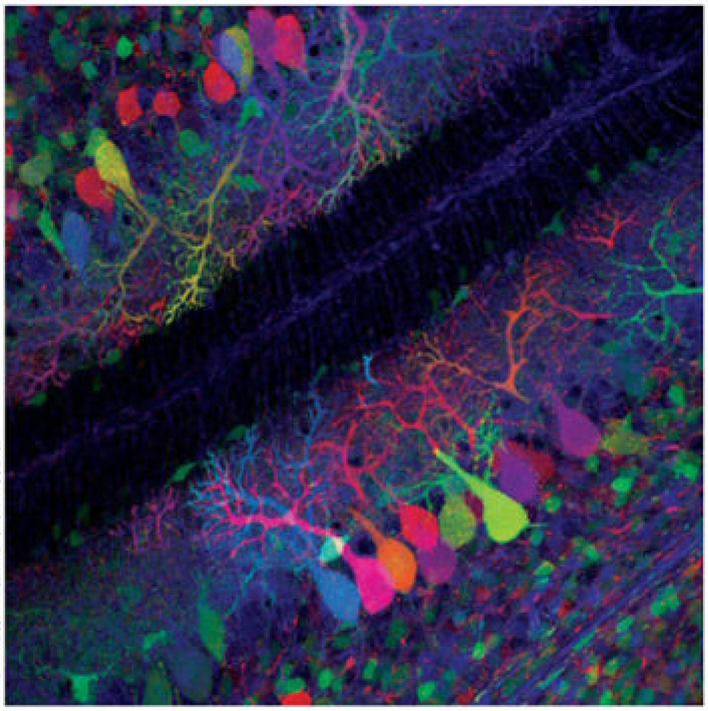
The brain is organised so that the outermost cortex contains the main bodies of the nerve cells and the short branches that connect to nearby cells. Underneath the cortex lie the cells' long projections, or axons, which connect distant areas. Axons are swaddled in a fatty coating called myelin, which improves electrical conduction. As the myelin is pale, the underlying part of the brain is known as the "white matter", in contrast with the "grey matter" of the cortex.

One technique for mapping axons is more than 100 years old: injecting dye into cells in one spot in the brain, and watching as it spreads to distant areas. Partha Mitra of Cold Spring Harbor Laboratory in New York is using an automated version of this technique to inject dye at 500 locations in a mouse brain and trace its course. He says he is well on his way to producing a draft of the mouse brain and hopes to map the brains of human cadavers in the same way. "We are trying to do the pragmatically defined project that will take us to the whole brain," he says.

Such a feat was announced by the Allen Institute for Brain Science in Seattle in 2014. Using a similar approach, a group there became the first to publish a full mouse connectome, but the picture is far from complete, says Marc. He calls the Allen map "a tour-de-force", but likens it to a national map of highways between cities. "Our approach involves mapping on a much higher resolution scale, analogous to tracking every street, house and house number, sidewalk, water line and power cable in a city," he says. "Both are critical for a richer understanding of neural information processing. You can't really dispense with either."

There are also newer ways to trace long-distance connections that do not entail injecting harmful dyes or slicing brains into prosciutto. These mean that, finally, we can start to look at living brains.

One method takes advantage of the fact that water molecules can diffuse more freely along axons lengthwise than they can pass through the fatty myelin coating. In 2007, it was reported that a technique called diffusion MRI could show how the trillions



TAMILY A. WEISSMAN/CENTRE FOR BRAIN SCIENCE

Will we one day read memories from the brain's connections?

of water molecules in the brain are jostling against one another (see "Mind readers", below right). Their direction of movement indicates the paths of hundreds of axon bundles in a living brain.

While still in its infancy, diffusion MRI is leading to important advances. For example, Heidi Johansen-Berg and Timothy Behrens of the University of Oxford are using it to study the effects of stroke, in which bleeding or a blood clot in the brain causes local nerve tissue to die from lack of oxygen. They have found that the death of the area affected by the stroke can have knock-on effects on other areas connected by axon bundles. Seeing those changes is important, because techniques are being developed to strengthen brain connections by applying electric currents or magnetic fields to the skull.

At Harvard, Van Wedeen, one of the original developers of diffusion MRI, has used it to reconstruct how the human brain rewires itself over time. His team's results show that between toddlerhood and adolescence, the brain becomes more centrally organised around a few major hubs, which might allow signals to traverse the brain more rapidly.

Rewiring problems may well underlie the tendency of mental illness to arise during adolescence and early adulthood. Diffusion MRI studies have already identified specific axon bundles that are altered in schizophrenia, alcoholism and other conditions. The hope is that miswired brains could be identified and treated years before symptoms emerge.

The insights are extending beyond medicine. Several studies show that the strength of specific axon bundles seems to correlate with skills such as arithmetic and rapid word recall. It may also shed light on how experiences shape minds, and how memories form. "My memories, many things that make me an individual, may be encoded in my connectome," says Seung. "The hypothesis is that I am my connectome."

In 2009, Johansen-Berg and Behrens showed that diffusion MRI could detect the effects of just six weeks of juggling practice, for example. Learning the new skill thickened the connections in several axon bundles involved in hand-eye coordination.

Another new scanning technique has developed from functional MRI, which was originally designed to see which parts of the brain crank up their workload when people carry out specific mental tasks. It was later found that even when people lie resting in the scanner, the activity of individual brain areas seems to gently fluctuate over a 10 to 30-second cycle. Crucially, many areas known to have strong connections have cycles that are in sync with each other, either in or out of phase. Discovering which areas match up in this way, using a technique known as functional connectivity MRI, is another source of information about the brain's long-distance connections.

It is thanks to developments such as these that the US National Institutes of Health (NIH) was able to launch its "human connectome project". In September 2010, it announced grants to two consortia of labs, worth $40 million over five years, to roughly map the brains of 1200 people using diffusion MRI, functional connectivity MRI and other techniques. Some will also undergo genetic and psychological tests to measure working memory, arithmetic skills and other mental abilities.

So far, the teams involved in the project have made some key findings, not least that the brain is not a spaghetti-like tangle of connecting nerve fibres, but is organised in a grid like format, more reminiscent of a 3D representation of New York City. This could help explain how brains develop – following simple grid-based rules that help the nervous system to develop in the early embryo.

The launch of the project hinted back to the scale and importance of the human genome project. An NIH press release called it "a grand and critical challenge: to map the wiring diagram of the entire, living human brain."

Some researchers remain sceptical about whether the project will prove its worth within the five-year deadline. But perhaps the most relevant lesson from the human genome project is how fast technology can advance.

It took 10 years and $3 billion to complete the first draft of the human genome. Now some 15 years later, there are firms claiming they will soon be able to read someone's genome in less than a day for $100.

Connectome researchers are convinced this field will generate as yet unimagined rewards. "You will see new hypotheses about how the nervous system works," says Kasthuri. "No one has ever seen data like this before." ■

MIND READERS

MAGNETIC RESONANCE IMAGING (MRI) Showing detailed anatomical images, it is like an X-ray for soft tissues

FUNCTIONAL MRI (fMRI) Displays changes in blood supply – assumed to correlate with local nerve activity – to different brain areas during mental tasks such as arithmetic or reading

DIFFUSION MRI (also called diffusion imaging, tractography) Reveals the brain's long-distance connections; works by tracking water molecules, which can diffuse along the length of axons more freely than escaping out through their fatty coating

FUNCTIONAL CONNECTIVITY MRI (resting-state MRI) Also shedding light on long-distance connections, it measures spontaneous fluctuations in activity in different brain areas, which reveals the degree to which they communicate


MARIA RENDON

Like clockwork

Our brains may run mechanically, like the springs and cogs in a finely tuned watch, says Anil Ananthaswamy

ONE of the first things William "Jamie" Tyler does when I meet him is show me a video of "one of the most devastating knockouts ever in boxing". In a 1990 clash, American pugilist Julian Jackson knocked his English counterpart Herol Graham unconscious with a right hook. Graham's lights went out before he hit the floor.

Tyler is a boxing fan who once worked out at the Harvard Boxing Club. But that's not why he's showing me the video. Instead, as a neuroscientist at Virginia Tech, Tyler uses it to highlight a problem: such knockouts are a bit of a mystery in our accepted understanding of the brain. We think of the brain as a biochemical and electrical organ, so how can a mechanical event, such as a punch to the face, cause unconsciousness? "We know without a doubt that there is no electrical transfer from that boxer's leather glove to that man's face. It's a mechanical impulse wave and [yet] he's unconscious," says Tyler. "Granted it's extreme, but it demonstrates how mechanically sensitive the brain is."

While no one is questioning whether brain cells use electrical and biochemical signals to talk to each other, Tyler and others think that's only part of the story. It seems neurons are also hooked together in a mechanical network, like the cogs in a finely tuned clock. The forces that pass between them might be an unknown way for our brains to store memory and adapt quickly to new circumstances – ensuring that they always run like well-oiled machines.

Not only could this help us probe age-old questions about what makes our thoughts go round, it also offers immediate practical benefits. For one thing, understanding disruptions to these mechanical processes might help us address certain types of brain injury. It could even be possible to tinker with the brain's mechanics using sound waves, which promises to lead to non-invasive therapies for disorders such as epilepsy.

The notion of a mechanical brain has its origins in the mistaken ideas of the 2nd century Greek physician Galen, who proposed that ventricles in the brain pumped fluids through nerves to control the body's functions (see "Milestones of neuroscience", page 6). Even as recently as the 17th century, René Descartes propounded a similar theory for how the brain functions. It wasn't until the 18th and 19th centuries that it became clear that nerves carried electrical signals. This culminated in the 1950s when Alan Hodgkin and Andrew Huxley showed how these electrical signals, called action potentials, are transmitted along nerve fibres.

"Tyler used to play loud music in the lab. To his surprise, he saw a spike in neural activity when the bass boomed, as if vibrations were causing brain changes"

But around the time that Hodgkin and Huxley were doing their Nobel prizewinning work, hints began to emerge that mechanical processes may be involved after all. The first clue came from observations of cuttlefish nerves, which seemed to shrink and swell when stimulated by a small electric current. The finding went largely unnoticed for decades until, in 1980, Ichiji Tasaki of the National Institute of Mental Health in Bethesda, Maryland, and colleagues saw something similar in nerves taken from the claws of blue crabs: as the action potential travelled along the nerve, so did a mechanical wave.

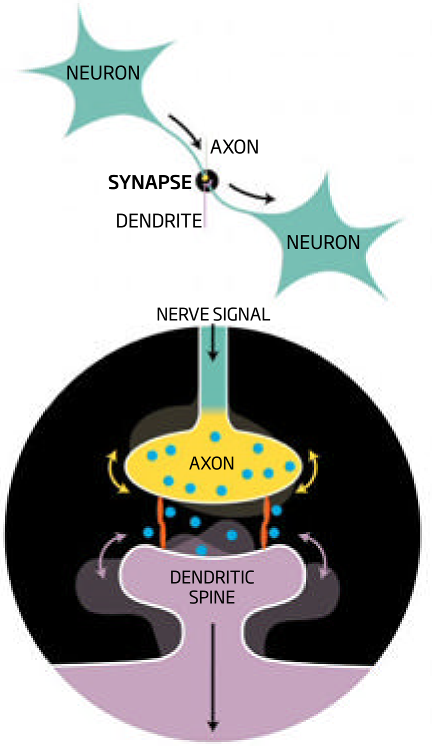
The finding helped to explain the energy exchange as a neuron fires. Hodgkin and Huxley had modelled the action potential as an electrical circuit. Such a circuit dissipates heat, but this is not what was experimentally observed: there is no overall heat loss during the propagation of a nerve impulse. However, if the nerve impulse could be treated as a mechanical wave in which heat is both released and absorbed (with no net loss), the energy accounting squared up nicely.

Perhaps more importantly, it showed that our nervous system is buzzing with movement – albeit at the nanometre scale – setting the scene for a mechanical understanding of the brain.

As well as mechanical waves moving along nerves, researchers have looked at the forces passing between neurons in the synapses. Here signals travel from one neuron to another through the release of charged ions and neurotransmitters. These molecules cross the gap to reach a small mushroom-shaped spine on the "dendrite" of the next neuron (see diagram, overleaf). ›

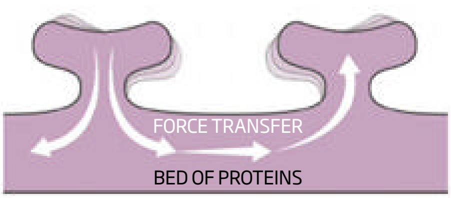
The buzz of thought

Brain cells were once thought to communicate using only electricity, but we now know that tiny mechanical forces can also play a part



When they receive a nerve impulse via chemical neurotransmitters, dendritic spines bend and sway, pulling on coupling molecules. These move the axon, altering the release of neurotransmitters

Dendritic spines may also communicate with their neighbours by transferring forces through a bed of proteins



This then relays the message onwards, starting a new chain of activity.

Importantly, dendritic spines are flexible – a fact that piqued the interest of Francis Crick, the co-discoverer of the structure of DNA. In the early 1980s, he hypothesised that the spines might twitch as neurons exchanged information, and that the changes in their shapes might somehow alter the strength of the signal passed between two neurons. These movements, he speculated, could even play a role in storing memories. No one had the technology to watch the synapse in action at the time but, by 1998, films made by powerful microscopes showed that dendritic spines do indeed move and change shape within seconds, just as Crick had predicted.

The cogs and wheels driving these movements were elusive, but a decade of research has suggested several possibilities, which Tyler recently outlined in a paper. We now know, for instance, that dendrites are full of a protein called actin, which can either assemble into large polymers or fall apart into smaller units, depending on the circumstances. This process generates forces that may be strong enough not just to bend the dendritic spine, but also to make it contract or expand.

Crucially, the dendritic spine on one side of a synapse is linked to the axon terminal on the other side by a chain of adhesive proteins. This means that when a dendritic spine moves, so does the axon terminal – with potentially important consequences. Taher Saif of the University of Illinois at Urbana-Champaign and colleagues have shown that the greater the force applied to an axon terminal, the greater the number of neurotransmitter molecules that are available for release across the synapse. In this way, the movements could alter the strength of the signal and consequently the plasticity of the synapse – key changes that might be a means of storing information during learning and memory.

> "After 15 seconds of brain stimulation, it felt like the buzz of a martini, and he continued to feel really good for about 2 hours"

That's not all. There could even be communication between neighbouring synapses. Tyler points out that neighbouring dendritic spines lie upon the same bed of actin and small rods called microtubules, which can store elastic energy like a spring. As one spine is stimulated, it seems to release chemicals that trigger changes to this structure, which pushes or pulls its neighbouring spines, shifting the balance of forces in their synapses.

No one has yet measured this transfer of movement in action, but there is indirect evidence that actin and microtubules do move in response to a spine's activity – and the scale and speed of these movements would be more than enough to tug or prod the neighbours, says Tyler. If so, the mechanism would add another route for signalling, perhaps helping synapses to coordinate their activity as we adapt to the situation at hand.

By controlling the flow of information in this way, such mechanisms could be crucial to tuning the neural networks that make our brain hum. But finding out for sure will be fiddly work – typically the forces extend over just 10 micrometres. So neuroscientists are turning to cutting-edge techniques such as magnetic particles, or laser beams that exert minuscule forces to tinker with these structures.

Tyler's interests, however, lie in a technique that may allow him to tweak the mechanics in the living brain. It started with a serendipitous observation while he was a graduate student. To liven up the long hours, Tyler played loud music, with a subwoofer placed next to the equipment recording electrical activity in neurons. To his surprise, he noticed spikes in neural activity each time the subwoofer boomed. "You'd see these synaptic events that seemed to correlate with the bass," says Tyler. "It was saying, 'Look! Mechanical vibrations in brain tissue can cause changes in neural activity'." But it didn't seem to be work worth publishing, so Tyler let it be.

Once in charge of his own lab at the Arizona State University in Tempe, Tyler revisited the issue. In 2008, his team took slices of mouse hippocampus and subjected them to low intensity, low frequency ultrasound waves – pressure waves that should jiggle the brain's mechanical structures. As suspected, it stimulated the neurons to fire, and increased the amount of neurotransmitter released at synapses.

Ultrasound therapy

The team next turned to live mice. By stimulating the motor cortices of the mice with pulses of ultrasound, they caused the mice to twitch their tails, forepaws and whiskers. They even implanted electrodes in the brains of the mice to confirm that spikes in neural activity accompanied the ultrasound stimulation.

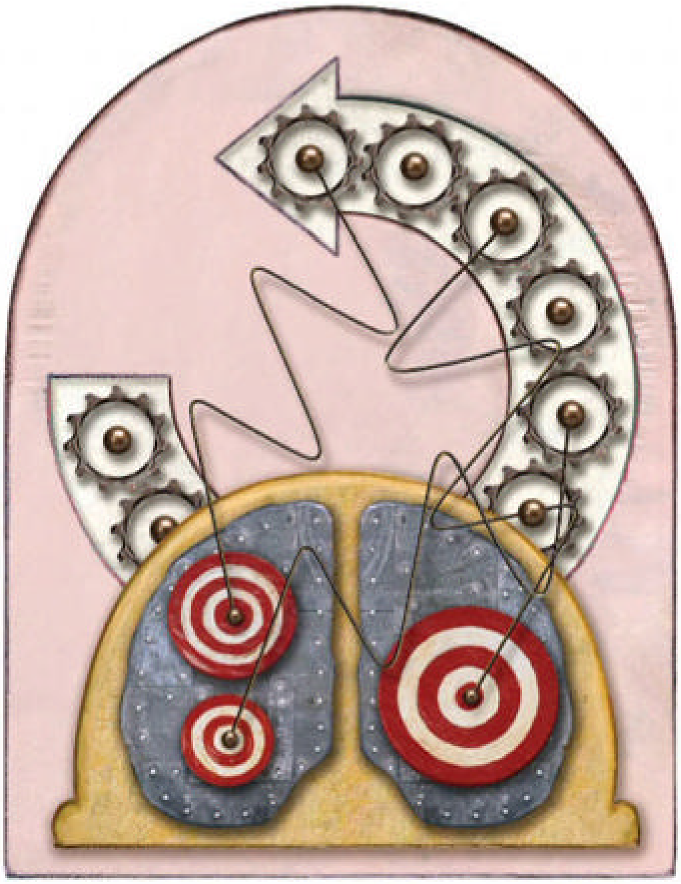
The results seem to confirm the suspicions that external mechanical forces can interfere with processes in the brain, potentially answering that mystery of the boxing knockouts. If our synapses and neurons are tuned to fine mechanical forces, then a blow to the head might disrupt their signalling, forcing them to open up ion channels and activate receptors. "One theory is that it instantaneously opens all the potassium channels or all the sodium channels," says Tyler. "That would render you unconscious."

The idea of the mechanical brain is beginning to draw interest from other researchers. Randy King, now at the US Food and Drug Administration recently replicated Tyler's experiment to stimulate mice with ultrasound when he was at Stanford University in California. He believes that the low intensity of the waves rules out the possibility that the ultrasound is influencing brain activity via other mechanisms, such as heating. Instead, a real mechanical interaction must be taking place. "It's showing that we can activate the brain non-invasively. And that would be just huge for the entire field of neuroscience," says King.

One reason for excitement is the possibility of using ultrasound to treat brain disorders. Unlike deep brain stimulation, which uses implanted electrodes to treat Parkinson's disease and depression, it wouldn't require surgery. It can also stimulate deeper areas of the brain than other non-invasive methods, such as transcranial magnetic stimulation or transcranial direct current stimulation. That's because they use electrodes on the scalp to pass electric or magnetic fields through the skull, both of which have a fairly shallow reach.

Tyler has so far investigated whether ultrasound stimulation could stop epileptic seizures, in which lots of brain regions start firing in synchrony. In one of their first experiments along these lines, Tyler's team induced seizures in mice before applying ultrasound pulses to their skulls. The sound waves broke up the synchronous firing, ending the seizure. He has high hopes that the technique could be used to treat people with head injuries, who often have seizures. "What if you could develop a device that was an automatic external defibrillator, except for the brain, to treat brain injury?" says Tyler. "That's my vision."

The work has inspired Stuart Hameroff to test the technique on himself. An anaesthesiologist and consciousness researcher at the University of Arizona Health Sciences Center in Tucson, Hameroff first suggested to a colleague that they try the therapy to treat chronic pain. The colleague agreed, on one condition. "He looked at me and said, 'you have a nice shaped head, why don't we try it on you'," says Hameroff.



Mood lifter

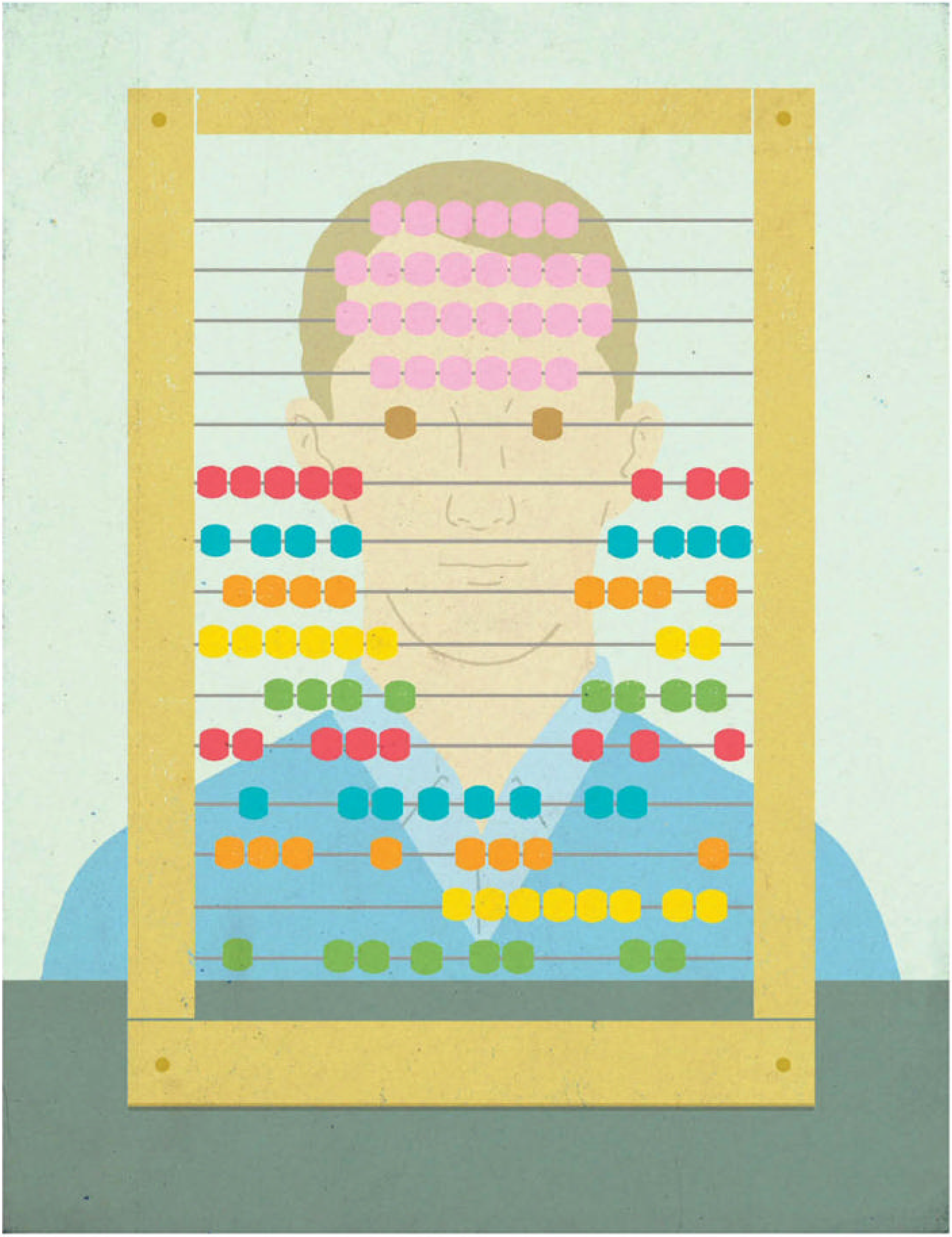
So they did. They applied ultrasound to Hameroff's temple for 15 seconds. Nothing happened immediately. "But about a minute later, I started to get a buzz, like I had a martini, and felt really good for about 2 hours."

This led to a pilot study in which 31 people who had chronic pain received 15 seconds of ultrasound over their posterior frontal cortex. Neither the doctor administering the treatment nor the volunteer knew whether they were using ultrasound or a placebo. Those who received ultrasound reported a slight improvement in their pain, and their mood was enhanced for 40 minutes after the treatment.

Even so, Tyler and King agree there are safety issues to be worked out before ultrasound can be used as a treatment. King thinks we should be particularly careful. "If you damage the brain, it can be permanent. It's not like muscle, which if you damage might heal," says King. "It has huge implications if something goes wrong, and that would be bad for the whole field."

Tyler is impatient to resolve those safety issues quickly, because he believes the benefits of fiddling with the mechanical brain could stretch beyond the therapeutic applications. For example, ultrasound can be so finely focused that it should be possible to study tiny regions individually. So you could put a subject in an fMRI scanner and stimulate an area to see how it talks to other parts of the brain. That could help us to build maps of the brain's connectivity, and the functionality of different regions, with unprecedented resolution.

So far, however, progress has been slow, and Tyler is frustrated with the difficulties of finding funding for big projects. "If you want to change something, you can do it in 200 years making very small steps, or you can do it in 10 to 15 years, making very large leaps," he says. And large leaps are what he is after. "We could be on the cusp of having a technique that will redefine the way we go about conducting human neuroscience." ■



DAN PAGE

Mind maths

Can mathematics help us find elegant order behind the apparent pandemonium of our minds, asks Colin Barras

How could an equation or formula ever hope to capture something as complex and beautiful as the human mind? In a sense we've long been describing the brain with numbers – 86 billion neurons, 1200 cubic centimetres, 1400 grams. But you might expect that more ambitious attempts to explain the brain with mathematics would be doomed to failure.

Yet over the last few years, neuroscientists have built a mathematical framework for understanding many aspects of the brain. In the same way that Newton's laws of motion describe the dance of the stars and planets in the night sky, mathematical principles are now revealing telling patterns in the melee of our minds. What's surprising is just how often the brain's dynamics mimic other natural phenomena, from earthquakes and avalanches to the energy flow in a steam engine.

The equations we end up with describe everything from the brain's structure to the generation of our thoughts and feelings. They may even help us begin to understand the nature of consciousness itself. Join us as we explore the five laws that rule the mind.

SMALL WORLD, BIG CONNECTIONS

If you stretched out all the nerve fibres in the brain, they would wrap four times round the globe. Crammed into the skull, you might think this wiring is a tangled mess, but in fact mathematicians know its structure well – it is a form of the "small-world network".

The hallmark of a small-world network is the relatively short path between any two nodes. You've probably already heard of the famous "six degrees of separation" between you and anyone else in the world, which reflects the small-world structure of human societies. The average number of steps between any two brain regions is similarly small, and slight variations in this interconnectivity have been linked to measures of intelligence.

That may be because a small-world structure makes communication between different areas of a network rapid and efficient. Relatively few long-range connections are involved – just 1 in 25 nerve fibres connect distant brain regions, while the rest join neurons in their immediate vicinity. Long nerve fibres are costly to build and maintain, says Martijn van den Heuvel at the University Medical Center in Utrecht, the Netherlands, so a small-world-network architecture may be the best compromise between the cost of these fibres and the efficiency of messaging.

The brain's long-range connections aren't distributed evenly over the brain, though. Van den Heuvel and Olaf Sporns of Indiana University Bloomington recently discovered that clusters of these connections form a strong "backbone" that shuttles traffic between a dozen principal brain regions (see diagram, page 21). The backbone and these brain regions are together called a "rich club", reflecting the abundance of its interconnections.

No one knows why the brain is home to a rich club, says van den Heuvel, but it is clearly important because it carries so much traffic. That makes any problems here potentially very serious. "There's an emerging idea that perhaps schizophrenia is really a problem with integrating information within these rich-club hubs," he says. Improving rich-club traffic flow might be the best form of treatment, though it is not easy to say how that might be achieved.

What is clear for now is that this highly interconnected network is the perfect platform for our mental gymnastics, and it forms a backdrop for many of the other mathematical principles behind our thoughts and behaviour.

TEETERING ON THE EDGE OF CHAOS

The familiar chords of our favourite song reach the ear, and moments later a neuron fires. Because that neuron is linked into a highly connected small-world network, the signal can quickly spread far and wide, triggering a cascade of other cells to fire. Theoretically it could even snowball chaotically, potentially taking the brain offline in a seizure.

Thankfully, the chances of this happening are slight. "Perhaps 1 per cent of the population will experience a seizure at one time in their lives," says John Beggs at Indiana University Bloomington. This suggests there is a healthy balance in the brain – it must inhibit neural signals enough to prevent a chaotic flood without stopping the traffic altogether.

The sweet spot

An understanding of how the brain hits that sweet spot emerged in the 1970s, when Jack Cowan, now at the University of Chicago, realised that this balance represents a state known as the critical point or "the edge of chaos" that is well known to theoretical physicists. Cascades of firing neurons – or "neural avalanches" – are the moments when brain cells temporarily pass this critical point, before returning to the safe side, he said.

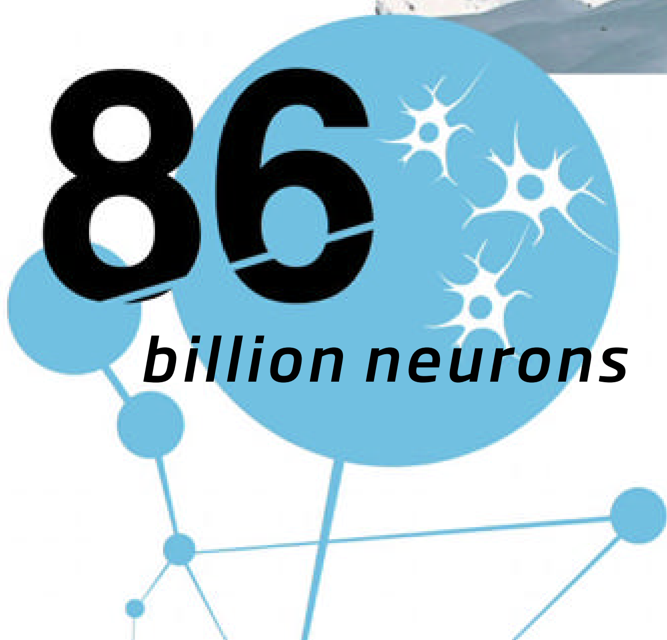
Avalanches, forest fires and earthquakes also result from systems lying at the critical point, and they all share certain mathematical characteristics. Chief among them is the so-called "power law" distribution, which means that bigger earthquakes or forest fires happen less often than smaller ones according to a strict mathematical ratio; an earthquake that is 10 times as strong as another quake is also just one-tenth as likely to happen, for instance.

How does the brain compare? In 2003, Beggs and Dietmar Plenz, both then at the National Institute of Mental Health in Bethesda, Maryland, checked whether neural activity matches Cowan's theory by using a grid-like array of electrodes hooked to a chunk of rat cortex. Sure enough, they found that an excited neuron passed its signal to just one neighbour on average, which is exactly what you would expect of a system on the edge of chaos: any more and the system would lie in permanent, full-blown disorder. Importantly, larger neural avalanches do occur, but they are much rarer. Like earthquakes and forest fires, their frequency drops with size according to the precise ratio predicted by a power law.

Since Beggs's initial work, further functional MRI scans have suggested that the same kind of edge-of-chaos activity can be found at much larger scales, across the whole human brain; indeed, computer models suggest it might be a result of the small-world structure of the brain.

Balancing on the edge of chaos may seem risky, but the critical state is thought to give the brain maximum flexibility – speeding up the transmission of signals and allowing it to quickly coordinate its activity in the face of a changing situation. Some of the researchers are beginning to wonder whether certain disorders might arise when the brain veers away from this delicate balance. "There's now some evidence that people with epilepsy are not at this critical point," says Beggs. "Just as there's a healthy heart rate and a healthy blood pressure, this may be what you need for a healthy brain."

"Avalanches, forest fires and cascades of firing neurons all share certain mathematical characteristics"

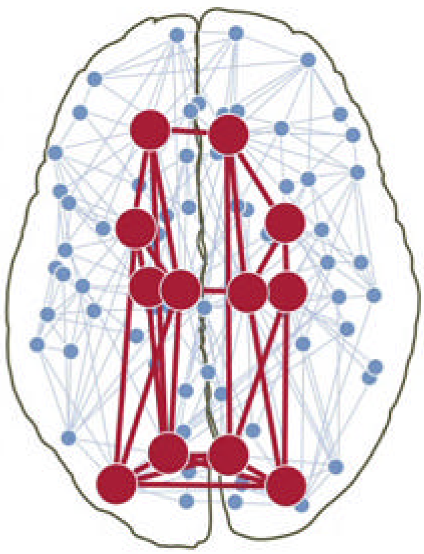


12 hyper-connected hubs that help direct traffic flow

COLIN MONTEATH/HEDGEHOG HOUSE/MINDEN/GETTY

The rule of the rich

The brain's wiring allows for the rapid transmission of information, with a set of particularly well-connected hubs, known as the **rich club**, directing much of the traffic between different parts of the brain



This group may be crucial for integrating all the thoughts and feelings that make up our conscious experience

KNACK FOR THE FUTURE

From its crackling electrical storm of activity, the brain needs to predict the surrounding world in a trustworthy way, whether that be working out which words are likely to crop up next in a conversation, or calculating if a gap in the traffic is big enough to cross the road. What lies behind its crystal-ball gazing?

One answer comes from an area of mathematics known as Bayesian statistics. Named after an 18th-century mathematician, Thomas Bayes, the theory offers a way of calculating the probability of a future event based on what has gone before, while constantly updating the picture with new data. For decades neuroscientists had speculated that the brain uses this principle to guide its predictions of the future, but Karl Friston at University College London took the idea one step further.

Friston looked specifically at the way the brain minimises the errors that can arise from these Bayesian predictions; in other words, how it avoids surprises. Realising that he could borrow the mathematics of thermodynamic systems like a steam engine to describe the way the brain achieves this, Friston called his theory "the free energy principle". Since prediction is so central to almost everything the brain does, he believes the principle could offer a general law for much, if not all, of our neural activity – the brain's equivalent of $E=mc^2$ in terms of its descriptive power and elegance.

So far, Friston has successfully used his free energy principle to describe the way neurons send signals backwards and forwards in the visual cortex in response to incoming sights. He believes the theory could also explain some of our physical actions. For instance, he has simulated our eye movements as we take in familiar or novel images, suggesting the way the brain builds up a picture with each sweep of our gaze to minimise any errors in its initial perception. In another paper he turned his attention to the delicate control of our arm as we reach for an object, using the free energy principle to describe how we update the muscle movements by combining internal signals from the turning joints with visual information.

Others are using the concept to explain some of the brain's more baffling behaviours. Dirk De Ridder at the University of Otago's Dunedin School of Medicine in New Zealand, for instance, has used the principle to explain the phantom pains and sounds people experience during sensory deprivation. He suggests they come from the neural processes at work as the brain casts about wildly to predict future events when there is little information to help guide its forecasts.

Friston points out that the brain's ability to update its thoughts and make predictions about the world depends on a finely tuned system. "Signals in the brain decay," he says, and if the decay is too fast, an important hypothesis may disappear by the time the brain makes its next observation and generates a new prediction." For this reason, the free energy principle relies on the brain's ability to hang in that "critical state" on the edge of chaos. "Criticality is almost mandated by the Bayesian brain," says Friston. ›

170,000

kilometres of nerve fibres

PREYING ON YOUR MIND

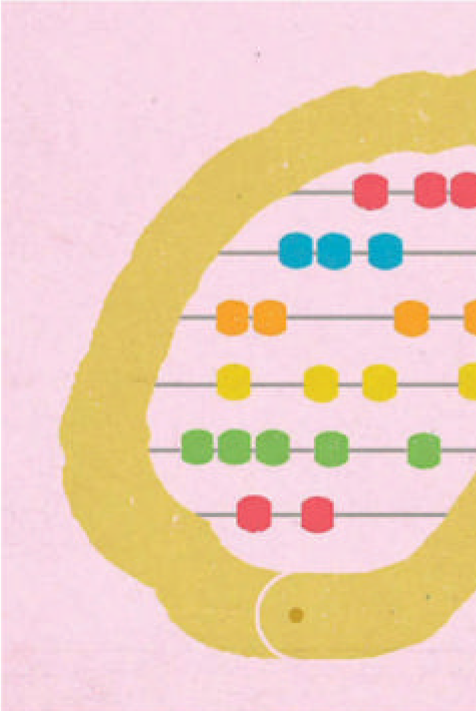
As your mind flits from thought to thought, it may seem as if dozens of sensations and ideas are constantly fighting for your attention. In fact, that's surprisingly close to the mark; the way different neural networks compete for dominance echoes the battle for survival between a predator species and its prey, and the result may be your wandering mind.

Mikhail Rabinovich at the University of California in San Diego and Gilles Laurent, then at the California Institute of Technology in Pasadena, were the first to notice this strange dynamic. They were studying the neuronal activity in the antennal lobe – the insect equivalent of the olfactory bulb in the mammalian brain – as locusts experienced different odours. Rabinovich expected the activity to flatline when they got used to each smell, but he was wrong. "Even when the scent stimulus was constant, the activity of the principal neurons in the antennal lobe changed with time," he says.

Looking closely, Rabinovich noticed that the pattern of activity was not random, but similar to the form described by mathematicians Alfred Lotka and Vito Volterra in the early 20th century. The Lotka-Volterra equations, also known as predator-prey equations, are a key ecological tool for predicting fluctuations in populations of interacting species. A predator near-exhausts its supply of prey, and so starves while its prey recovers, and the cycle starts again.

ANUP SHAH/NATUREPL.COM

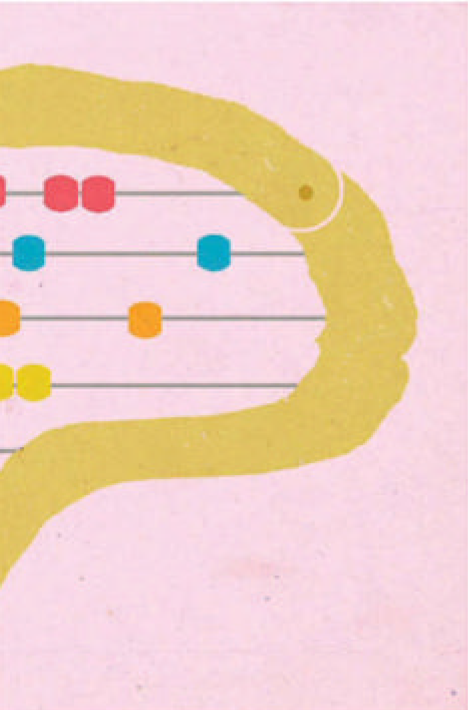
Rabinovich dubs such perpetual fights "winnerless competitions" and he says they occur in the brain as well. Here, though, the fight is not between just two competitors, but between multitudes of cognitive patterns. None ever manages to gain more than a fleeting supremacy, which Rabinovich thinks might explain the familiar experience of the wandering mind. "We can all recognise that thinking is a process," he says. "You are always shifting your attention, step-by-step, from one thought to another through these temporary stable states."



DAN PAGE

People with psychiatric conditions might benefit from the work. In the past, conditions like attention-deficit hyperactivity disorder (ADHD) were studied by looking at quick snapshots of neural activity. But Rabinovich's work gives neuroscientists a tool to make sense of the brain's responses as they evolve with time, potentially explaining why the attention drifts in unusual ways. Working with Alexander Bystritsky at the University of California in Los Angeles, Rabinovich has already shown that his equations can accurately describe the neuronal activity associated with both ADHD and obsessive compulsive disorder. "They are very convenient for diagnosing the disorders," he says.

> "The competing activity between brain regions resembles the perpetual fight between predator and prey"



THE SUM OF CONSCIOUSNESS

Getting to grips with consciousness may seem like a step into the unknown, or even the unknowable, but Giulio Tononi at the University of Wisconsin-Madison was not daunted.

The first challenge was to find a good definition of consciousness by boiling it down to its most essential elements. He reasoned that each moment of awareness is a fusion of information from all of our senses. An experience's colours, smells and sounds are impossible to isolate from one another, except through deliberate actions such as closing your eyes. At the same time, each conscious experience is a unique, never-to-be-repeated event. In computational terms, this means that a seat of consciousness in the brain does two things: it makes sense of potentially vast amounts of information and, just as importantly, it internally binds this information into a single, coherent picture that differs from everything we have ever – or will ever – experience.

Perhaps the best way to understand this is to consider the difference between the brain and a digital camera. Although the screen seems to show a complete image to our eyes, the camera just treats the image as a collection of separate pixels, which work completely independently from one another; it never combines the information to find links or patterns. For this reason, it has very low "integration", and so according to Tononi's theory, it isn't conscious. The brain, on the other hand, is constantly drawing links between every bit of information that hits our senses, which allows us to be aware of what we see.

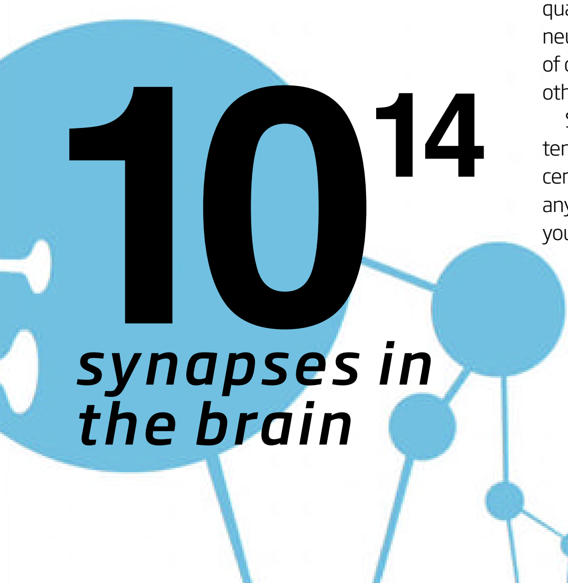
"An experience's colours, smells and sounds are impossible to isolate from one another"

Physicists haven't paid much attention to measuring how much information a physical system can hold on to and integrate, so Tononi worked out the equations himself. The result is a quantity known as "phi". "Now I could go back to neurobiology with this tentative theory: any seat of consciousness must have a high level of phi, and other systems must not," says Tononi.

Some accepted anatomical findings gel with this tentative theory. For instance, we know that the cerebral cortex is crucial for conscious experience – any damage to the brain here will have an effect on your mental life. Conversely, the cerebellum is not necessary for conscious awareness, which was something of a puzzle given that it contains more than twice as many neurons as the cerebral cortex.

When Tononi analysed the two regions using his theory, it all made sense: the cerebral cortex may have fewer neurons, but the cells are very well connected to one another. They can hold large amounts of information and also integrate it to generate a single coherent picture – the level of phi is very high. The cerebellum is more like the digital camera: it may contain more neurons than the cerebral cortex, but there are fewer interconnections and so no coherent picture – the level of phi is low, in other words.

"I've been studying consciousness for 25 years, and Giulio's theory is the most promising," says Christof Koch at the California Institute of Technology in Pasadena. "It's unlikely to be the final word, but it goes in the right direction – it makes predictions. It moves consciousness away from the realm of speculative metaphysics." (For more on consciousness, see Chapter 6, page 84.)



Lights out

Tononi's theory can also explain what happens when we fall asleep or are given an anaesthetic – through experiments he has shown that the level of phi in the cerebral cortex drops as our consciousness fades away.

This makes sense when we consider all of the ideas emerging from the field of computational neuroscience. The cerebral cortex is home to many of the highly interconnected "rich club" hubs, which may explain why it is so good at integrating incoming information. Neural signals zip freely through these interconnections to generate conscious experiences. Fall asleep, though, and the neural signals within the cerebral cortex slip further away from the critical point vital for neural communication. The physical interconnections remain, but traffic no longer flows through them. The Bayesian brain loses its ability to make sense of the world around it – all of the thoughts engaged in the brain's winnerless competitions fade to black.

The various strands of the computational neuroscience story come together powerfully. Are they the final word in our understanding of the brain? "They're undoubtedly flawed in some way – no one is being naive," says Beggs. Nevertheless, he and others think neuroscience is poised to become a numbers game. "We'll find out in a few years," he says. "In the meantime, it's certainly a fun journey." ■


PAWEŁ JOŃCA

Hidden depths

The vast majority of brain research is drowning in uncertainty. It's time to build a more complete understanding of the mind, says Ingfei Chen

IT'S FOUR in the afternoon when I meet John Ioannidis, but lines of fatigue are deepening under his eyes. He's exhausted with jet lag after a whirlwind tour of 20 European cities, where he's been lecturing and brainstorming with colleagues. In a corner of his office, I spot two oddly shaped bags, which hold gear for his sport of choice, épée fencing. It seems a fitting hobby for this soft-spoken professor, who is a crusader for good science.

Statistical logic and careful scrutiny of evidence are the weapons that Ioannidis nimbly wields. His previous targets have included spurious claims about drugs and other medical treatments from clinical trials backed by the pharmaceutical industry. Now his gaze has turned to the brain. Joining a growing army of critics, he has documented serious flaws in the ways that many – if not the vast majority of – neuroscience studies are designed, analysed and reported.

That should perhaps be a warning whenever we read headlines about studies capturing snapshots of the brain on "love", "fear", "religion" or "politics". It turns out that many of those colourful brain scans may offer little more than mirages, obscuring the true picture of the human mind in action.

Worse still, the problems are not just confined to a few misleading brain-scan reports. From experiments investigating the action of genes and individual molecules to studies linking brain structure to mental health, question marks are now hanging over the whole field of neuroscience. "Currently, I wouldn't put much trust in most of the literature," says Ioannidis, who is an epidemiologist at the Stanford University School of Medicine in California.

Amid these concerns, it might seem as if our understanding of the brain is set to disappear in a fog of uncertainty, and you will find many observers in the popular press who are now bashing "neuromania". But it's important not to forget the advances of the last century. And while the tough conclusions of Ioannidis and his colleagues are certainly reason to reassess our knowledge, their insights should only lead to more fruitful efforts in uncovering the mind's mysteries. "Neuroscience is moving forward," says Chris Baker of the US National Institute of Mental Health (NIMH). As the fog clears, more nuanced theories should, in time, emerge in sharp relief.

Although philosophers have long pondered the origins of thought, it was the invention of functional magnetic resonance imaging in 1991 that really sparked our love affair with neuroscience. fMRI is based on studying the flow of blood in the brain, with more blood rushing to the areas working hardest. The scans reveal bright splotches of neural activity inside people's heads as they engage in different tests of their capacity to see, feel, remember or think. We were instantly seduced by these technicolour insights. ›

92 PER CENT OF SCANS EXAMINING THE ANATOMY OF CONDITIONS LIKE AUTISM MIGHT HAVE MISSED THE TRUE ANSWER, WITH MANY REPORTING LINKS THAT WEREN'T REALLY THERE

FRANK MULLER/HOLLANDSE HOOGTE/EYEVINE

But there were always some quiet grumblings about whether transient neural activity could reveal much about complex mental processes or behaviours. But the brain-scan backlash only really exploded into public view in late 2008, when psychology researchers Edward Vul and Harold Pashler at the University of California, San Diego, published a critique of what they cheekily dubbed "voodoo correlations". The pair had been baffled by a profusion of highly implausible fMRI results strongly linking behaviours or traits to one or just a few specific areas of the cortex. Examining 53 fMRI studies, Vul, Pashler and their colleagues concluded that half of them reported untrustworthy results that were simply too good to be possible, thanks to "seriously defective" methods.

Double dipping

To understand why, first consider that a typical fMRI scan of the whole brain contains as many as 100,000 three-dimensional pixels, called voxels – a vast amount of data to analyse. Researchers use specialised software to find clusters of voxels that light up when participants view images that trigger, say, empathy or emotional responses. However, the challenge is that true signals can be obscured by underlying random fluctuations in those voxels – a bit like the static noise on an untuned TV. fMRI software tries to filter that out but it cannot work miracles, so many areas will inevitably show some increased activity simply by fluke.

Ideally, neuroimagers should use two sets of scans. One set is for identifying which voxel clusters are highly activated during the experiment. Having found these regions, you then look at them specifically in the second set of scans to confirm that the response wasn't due to random fluctuations, and then measure its size. But Pashler and Vul found that many researchers instead made the mistake of using just one data set for both the initial and final analysis, which allows the random noise to inflate an apparent link to a behavioural response or trait. Such "double-dipping" led researchers to some exciting but premature conclusions, including overly simplistic ideas about the origin of personality traits. Neuroticism, for instance, was chalked up to stronger activity in a pair of almond-shaped regions called the amygdalae, which are known to be involved in fear and other negative emotions.

Confirming that the problem was spread far and wide, Baker and colleagues at NIMH looked at all the fMRI studies published in five top journals in 2008. Of the 134 papers, 42 per cent had made double-dipping errors. The flawed method is also common in studies of single-neuron responses in animals, as well as in genetic analyses, Baker's team noted.

Neither critique went as far as overturning the broader conclusions of the studies in question. "It doesn't invalidate everything," Baker says of his work, "but it raises question marks."

The voodoo correlations study, in particular, set off an angry back-and-forth of rebuttals. One cause of criticism was that Vul and Pashler named offending studies, which some said was overly aggressive. "It came across as a little bit nasty," says fMRI specialist Russell Poldrack of the Stanford School of Medicine in California, although he admits that it got people's attention. "I don't know that a paper that was written more nicely would have necessarily had as much impact."

"We spoke frankly and just kind of had a little fun," says an unrepentant Pashler, while acknowledging that since he and Vul do not themselves do brain-scanning research, they had not needed to worry about how their next studies or grant applications would be received.

After the furore died down, many fMRI researchers realised that the critiques were essentially right. Voodoo correlations and double-dipping appear to be less common now, and the idea that you can map complex personality traits to a few specific regions like the amygdalae is increasingly considered to be "a pipe dream", says cognitive neuroscientist Tal Yarkoni, also at the University of Texas at Austin. Personality traits are now thought to be associated "with lots of different brain regions interacting in complex ways", he says.

But as researchers patched up those holes in their methods, other equally serious

Brain scans promised to pinpoint our personality traits

concerns began to emerge. A jaw-dropping study from the University of Michigan published in 2012, for instance, demonstrated that an fMRI experiment could be analysed in nearly 7000 ways – and the results could vary hugely. With so much flexibility, neuroimagers can unintentionally (or indeed deliberately) analyse their experiments in a way that yields the most favourable results. One tongue-in-cheek report showed that even a dead salmon's brain could appear to be "thinking" inside a scanner if the wrong techniques were used (see image, page 28).

The most alarming wake-up call came when Ioannidis published a paper showing that the problems run much deeper than flawed fMRI studies. Working with Katherine Button and Marcus Munafo of the University of Bristol, UK, and others, he analysed 48 review papers that collectively had scrutinised 730 studies examining the risk factors and treatments for neurological disorders such as Alzheimer's disease and chronic pain. The experiments used many different methods, including measures of cognitive functioning, gene testing and clinical trials. From this, the team estimated the odds that each study was able to detect something that was truly there to be discovered – otherwise known as its "statistical power".

The results were grim. The average overall power was about 20 per cent, largely because the number of subjects used in the experiments was simply too small for reliable results to come out of them, even if they passed the standard statistical tests. In other words, four out of five studies might have been missing the actual biological effect or mechanism sought, and therefore reported false negatives.

But that's not all. The low power delivers a double whammy of uncertainty: not only are you likely to be missing the evidence even if it's under your nose, but "if you do detect something that seems to be significant, it has a higher chance of being a false positive", Ioannidis says.

The picture was even more troubling when looking specifically at structural MRI studies that investigated the physical anatomy of the brain (as opposed to the changing neural activity that shows up in functional MRI). The average statistical power of studies linking structural abnormalities to mental health conditions such as depression or autism was a feeble 8 per cent – meaning that 92 per cent of the investigations would have failed to make true discoveries and in many cases detected something that was not really there.

Data dredging

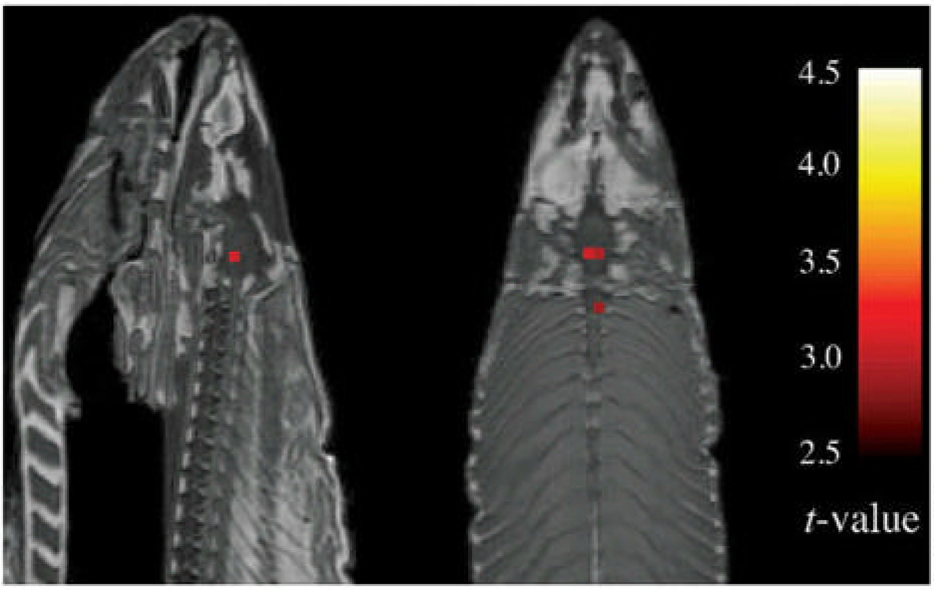
As in many fields, published studies in neuroscience tend to show more positive results than would be expected, something Ioannidis and his colleagues confirmed through further work examining bias in fMRI investigations and animal studies of neurological illnesses. Some of this bias arises simply because negative studies are not published very often. But another possibility, Ioannidis says, is "data dredging" – researchers fishing through and analysing subsets of their results until they find something favourable.

To know exactly which or how many of the reports are right or wrong would mean attempting to replicate all the findings, which usually isn't done. But based on his experience with other fields, Ioannidis thinks the vast majority of neuroscience studies published in recent years are likely to be incorrect. "Neuroscience is in serious trouble," he says.

What is to be made of this damning assessment? For a start, it does not mean ditching everything. Conclusions that have stood the test of time are more believable, and Ioannidis is not questioning textbook knowledge of brain anatomy and function. Injury from a stroke in Broca's area, for ›

THERE ARE 7000 WAYS OF ANALYSING BRAIN SCAN DATA, LEADING TO CONFUSING OR CONFLICTING RESULTS

Fishy findings: a dead salmon seems to spring to life in a scanner



CRAIG BENNETT ET AL

instance, obviously impairs the ability to speak, so we can be sure of its role in language production. Such big effects can be discerned even by studying just a small number of people, and have been corroborated by many strands of evidence.

It is probably the newer findings that we should take with a pinch of salt, particularly as neuroscientists tease apart the finer processes that are likely to underlie many complex mental tasks, behaviours or differences in personality traits. Such phenomena are much harder to measure, and because the patterns of brain activity are so faint, a lot more data must be collected before the true signal can be detected above the background noise.

Unsurprisingly, Ioannidis has ruffled many feathers, although many neuroscientists agree with the gist of his findings. The big concern is that he is being too alarmist. In 2014, a report by neuroscientist Martha Farah at the University of Pennsylvania in Philadelphia picked apart the criticisms and concluded that whilst they have some validity, they should not cast doubt on neuroimaging as a whole. Similarly, Poldrack is concerned that the ideas may be "spun into this kind of global nihilism that all of neuroscience is bullshit". Certainly, no one should be saying that. Many fMRI findings have held up over time, including observations that the frontal cortex is always activated during short-term recall and that the hippocampi are active during sleep, perhaps as they work to consolidate memories.

"I wouldn't keep doing science if every time I found something, I later found that it was unreliable," Poldrack says. While there are certainly problems, he adds, "many of us are doing what we can to try to address them". But some researchers worry that if governments get the wrong message, they may starve labs of funding, killing revolutionary research.

For his part, Ioannidis is adamant that transparency is the best way to keep the public's confidence in science. "I don't like hiding things under the carpet. I prefer to identify issues and solve them."

And he does have a prescription to cure many of those ills. For example, bigger sample sizes – such as in rigorous multi-centre studies – are often the most obvious way to increase statistical power when looking at small, hard-to-detect effects. Alternatively, for some research questions, studying a few subjects can still produce reliable results, if you gather enough data from each person. Increasing the size of fMRI studies can be challenging, however, because it costs around $500 per hour to use a machine, though arguably the funds are better spent on larger but fewer studies.

Another approach is to encourage brain scientists to disclose their data and replicate others' findings and so weed out some of the false positives. For instance, in 2010, Poldrack and several colleagues launched the web-based Open fMRI Project, which lets investigators upload their raw data sets so that others can reanalyse and validate their results. Replication is a thankless task, though, since researchers don't get promoted for being right or confirming ideas – they get promoted for publishing intriguing new results.

If all this seems like a struggle, neuroscientists may take heart from genetics research, which faced a similar upheaval a

$4.5 BILLION – THE FUNDING FOR AN INITIATIVE TO PROBE THE BRAIN'S CIRCUITS

decade ago after a flood of small studies overemphasised the role of particular genes in disease and personality traits. Now, with much bigger studies and consistent rules for reporting and sharing data, that field has gone from a replication rate of 1 per cent to more than 90 per cent reliability, Ioannidis says.

Indeed, a couple of large initiatives are already tackling these challenges. In the $40 million Human Connectome Project, neuroscientists across a dozen institutions are building a detailed wiring diagram of the brain's circuitry (see "The greatest map of all", page 10). They are scanning a large sample – 1200 people – using fMRI and a technique called diffusion imaging, and the data will be openly shared. It promises to give us our best view yet of the way the brain's anatomy shapes thought and behaviour.

A SCEPTIC'S GUIDE TO NEUROMANIA

While the neuroscientist's toolkit comes into question (see main article), there are also many common pitfalls in the way the results are interpreted to explain complex traits and behaviours.

For instance, you will often read about differences in brain activity or structure that appear to be linked to psychopathic tendencies, with studies showing that convicted murderers have reduced activity in areas associated with empathy when they see images of people suffering. Defence lawyers might use this as evidence that a defendant had diminished responsibility, and some pundits have even pondered whether it might be possible to identify people who are more likely to commit a crime. But there are probably plenty of people who show similar quirks in the brain scanner, with no criminal intentions. (Indeed, doctors are thought to tone down their own empathic response to pain to help them manage a patient's distress.) And differences in a murderer's brain may be the result of their past brutality, not the cause.

Similar "neurocentric" arguments are sometimes used when talking about drug abuse as a "brain disease". There is no doubt that addictive substances do create long-lasting changes to our neural circuity, but as psychiatrist Sally Satel and clinical psychologist Scott Lilienfeld point out in their 2013 book *Brainwashed*, this view can devalue many other factors, including stress, the influence of friends, and access to drugs. In this way, it might distract addicts from psychological strategies such as avoiding cues that trigger a craving. Satel and Lilienfeld also point out that placing all the blame on the brain's circuits could diminish people's belief in their own self-control – about 80 per cent of addicts do manage to kick the habit.

Brain science clearly has big potential for medicine and the law. But it is crucial to realise that our neurology need not rule our fate. David Robson

Building bridges

The BRAIN Initiative, meanwhile, is getting $4.5 billion of US government funding to develop techniques that will pick out the finer circuits in the brain, bridging the gaps between studies examining single neurons and the large-scale fMRI maps. That will include rethinking or refining existing techniques, such as "optogenetic" methods that allow you to control neuronal activity with pulses of light, as well as inventing entirely new technologies.

All this may mean we will finally be able to appreciate the complexity of the brain. Jack Gallant at the University of California, Berkeley, for instance, points out that there is so much more for us to see if only we pay attention to the bigger picture. At the moment, it's as if we've been peering at the brain through a lousy microscope, he says – partly due to the fact that most MRI data is thrown away to focus on a few selective results. "We're missing huge things," he says.

Consider our understanding of face recognition – a knotty task for the brain, given just how much our expressions can vary. Typical fMRI experiments would compare just two conditions, such as showing volunteers pictures of faces versus places. Based on such investigations, neuroscientists used to think that one region of the brain – the so-called fusiform face area (FFA) – uniquely responds whenever a person sees a face. But the story has grown more complicated as further research turned up a network of other regions that cooperate to recognise faces.

And as neuroimaging grows more sophisticated, so too does our view of the brainscape. Gallant's experiments, for instance, collect hours of brain-scan data from a few subjects as they watch movie trailers, which allows the team to track the brain's changing reaction to an immensely wider range of stimuli. The researchers then skip some of the usual processing steps that lead to data loss, so that they can draw as much meaningful data as possible from the experiment.

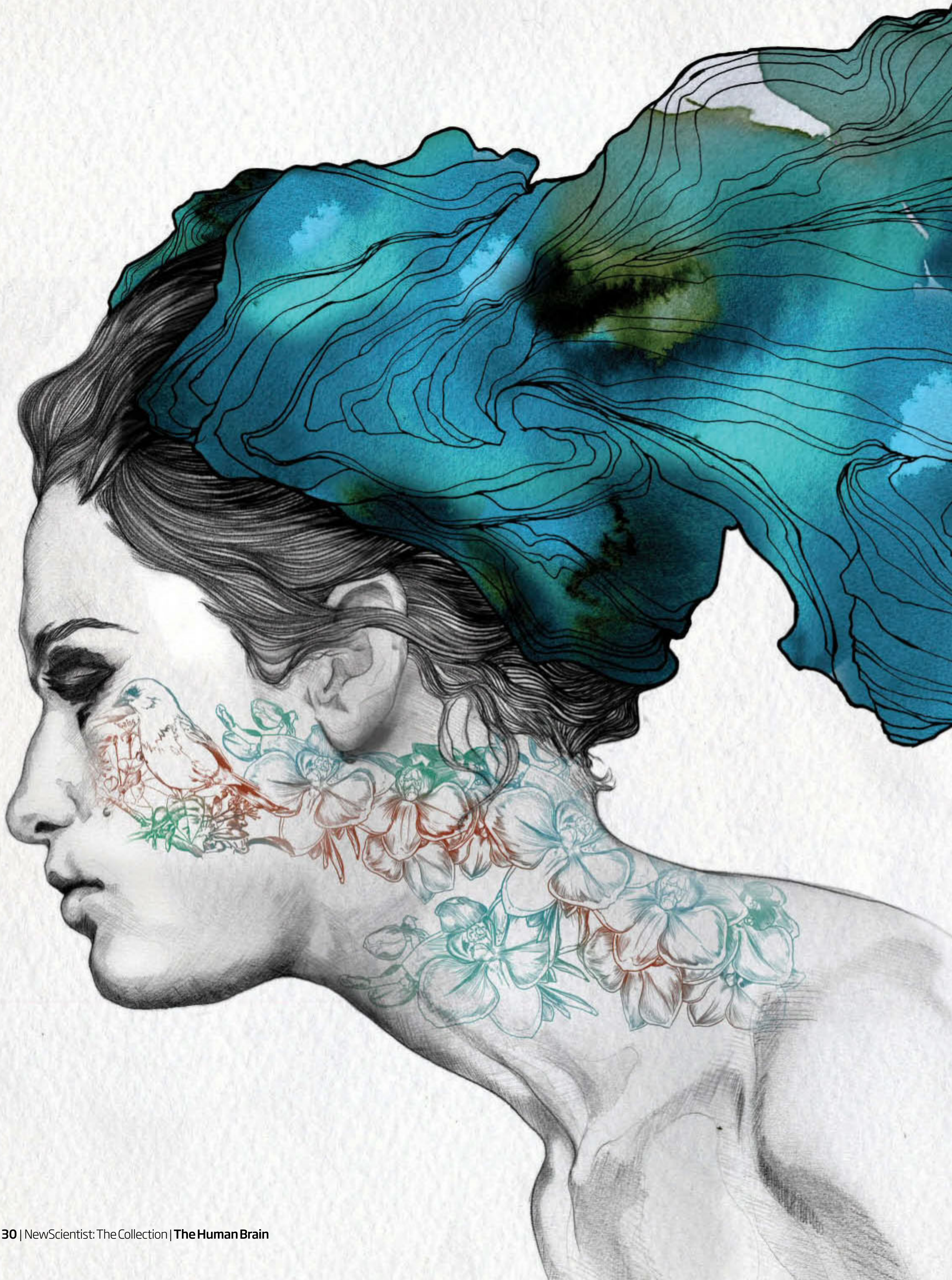
Their results show the FFA to be even more intricate than previously imagined, suggesting that it can be subdivided into three separate areas. While these all respond to faces, each is also involved in processing different categories of other objects, such as flags, crucifixes and snakes – making the FFA something like a Swiss Army knife for visual recognition. That doesn't mean the initial view of the "face area" was wrong. It was just incomplete, Gallant says. (Although others point out more studies will be necessary to confirm that the same principles apply to the average brain.)

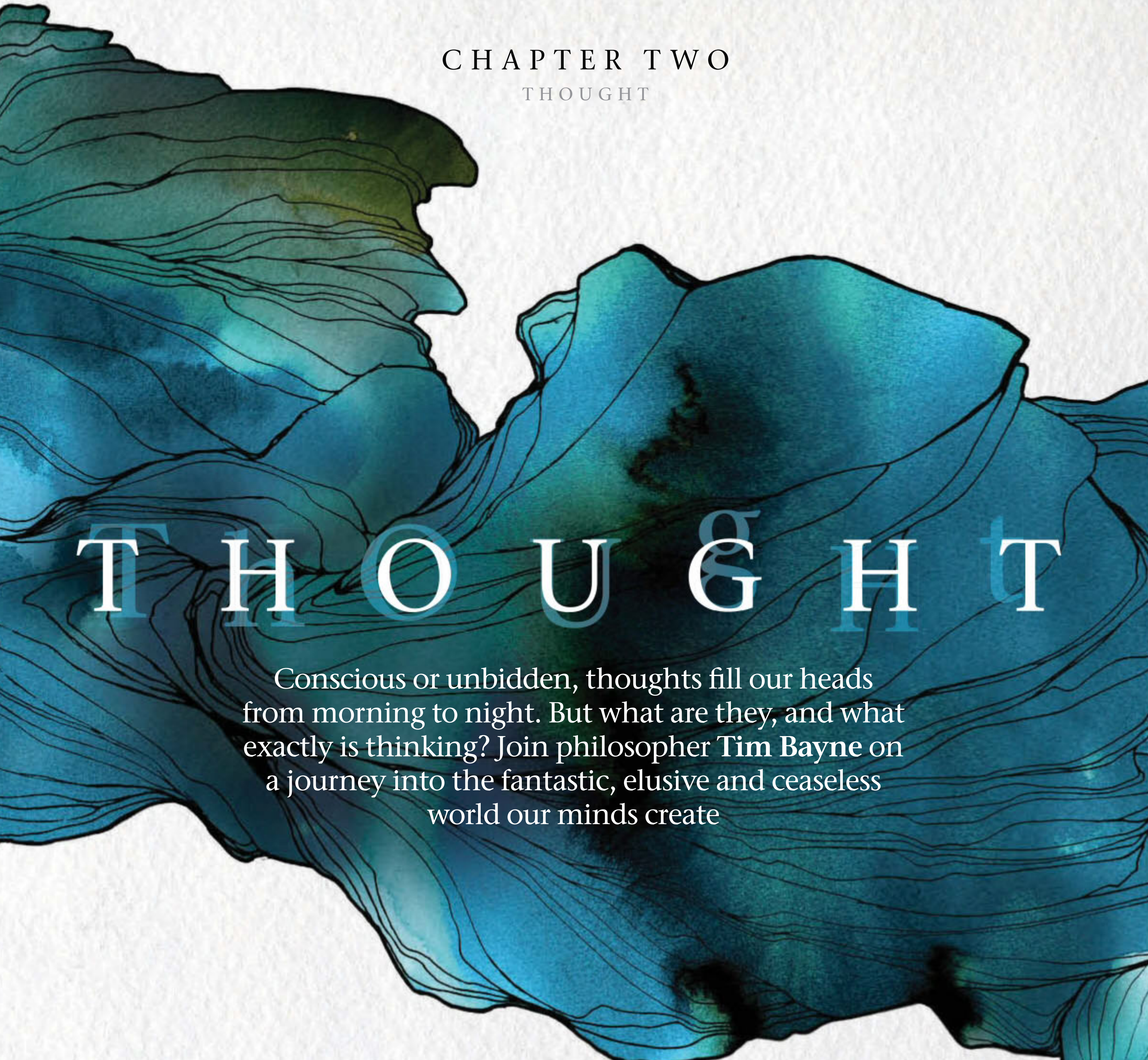
Such deepening complexity in the understanding of the brain is to be expected as one's microscope gets better and better. But Gallant says it just goes to show that we are still at the tip of the iceberg when it comes to the prevailing theories. Even with all the work on visual perception, for instance, no one can yet build a robot that sees like a human, let alone a machine that accurately recognises people. And phenomena like emotions or moral judgement are even murkier.

Will the understanding come eventually? Gallant remains an optimist, pointing out that fMRI was invented only 20 years ago. Back then, nobody knew how best to design the experiments and analyse the vast data they generated, but he thinks the lessons of past mistakes, such as double-dipping, will be learned. The study of the brain just gets better all the time, he says.

Even the épée-fencing Ioannidis agrees that our understanding of the brain will eventually correct itself where wrong. But the question is, how quickly? "If it takes several years for something to be refuted, that could be a real waste of effort." As he points out, "the brain is more complex than almost any other system".

Few questions are as profound as the mysteries between our ears, and there is no doubt that solving them will need the finest tools wielded with the greatest skill. ■





THOUGHT

Conscious or unbidden, thoughts fill our heads from morning to night. But what are they, and what exactly is thinking? Join philosopher Tim Bayne on a journey into the fantastic, elusive and ceaseless world our minds create

TRY, if you can, to imagine a life without thought. For a human being it wouldn't be much of an existence. Thoughts fill our every waking moment, and whether they are insightful, banal, playful or bizarre, there is no denying that thinking comes naturally to us. We might say that thought is to human beings what flight is to eagles and swimming is to dolphins.

But it is one thing to think and quite another to understand the nature of thought. Just as eagles fly without any grasp of aerodynamics and dolphins swim without understanding fluid mechanics, so most of us think without having any insight into its nature. Thinking may be commonplace, but it is quite rare to think about thought itself.

So what is thought? That is a surprisingly difficult question to answer. Neuroscience, psychology, philosophy and other disciplines have approached it from their various perspectives, but thought has not received as much sustained attention as it deserves.

Perhaps part of the explanation for this is that thought is an extremely varied and complex phenomenon. We can think about an incredible variety of things: objects, people, places, relationships, abstract concepts, the past, the future, real things and imaginary things. We can think about nothing at all, and even think about thought itself.

The exercise of thought is also elusive, although there are some things we can say about it. We use thought to solve problems and invent things – but how much control do we have over it? And is there a limit to what we can think of?

To make some progress with these ›

GABRIEL MORENO

questions we first need to make some distinctions, because the term "thought" can refer to three quite different features of mental life.

In one sense, thought refers to a type of mental event. To think of something is to bring it to mind in some way. In another sense it refers to a certain kind of mental faculty. Just as there are faculties associated with perception and language, so too there is a mental faculty – or perhaps faculties – associated with the capacity to think. And in a third sense it refers to a certain kind of mental activity. Just as you can be engaged in the activity of looking for something or listening to something, so too you can be engaged in the activity of thinking about something.

Let's first consider thought as a mental event. What are thoughts, and what distinguishes them from other kinds of mental events, such as perceptual experiences and bodily sensations?

Suppose you are having a bonfire. You can see the flames and feel the heat. These are purely perceptual events. You may also find yourself wondering what would happen if the wind changed direction, or how combustion works. These events are prompted by your perceptual experience, but they are not themselves forms of perception. They are thoughts.

More than a feeling

Although the distinction between perception and thought is intuitive, no one has been able to characterise it unequivocally. One way is to argue that thoughts involve the deployment of concepts, whereas sensory states do not. It is possible to see a bonfire without possessing the concept of a bonfire, but impossible to think about it. However, this view is contentious. For one thing, some theorists argue that concepts are implicated in both thought and perception. And it has proved difficult to say precisely what concepts are.

Another way to distinguish thought from perception is by their conscious character: "what it's like" to think about a bonfire is very different from what it's like to perceive a bonfire. But here too we run into difficulties. Although everyone agrees that thinking about a bonfire is subjectively different from perceiving one, pinning down why is tricky.

The issue is further complicated by the fact that thoughts are often unconscious. Consider when you are trying to solve a problem, and something simply comes to mind, or you sleep on it and find that it is miraculously solved in the morning. So you can't just rely on their conscious character to distinguish thoughts from other mental events.

How about thought as a mental faculty? A useful starting point is René Descartes's description of thought as a "universal instrument which can be used in all kinds of situations". What did he mean?

Consider, again, the difference between perceiving and thinking. In order to perceive, say, an apple, there must be a causal connection between you and it. Light must be reflected from it and be processed by your visual system. No such connection is required to think about an apple. You can think about one whenever you want, whether or not it is there. This is what allows the faculty of thought to be used "in all kinds of situations".

Another feature of thought that Descartes points us to is its scope. Perception only provides access to a limited range of things. Vision can tell us that an apple is red or that it is falling, but only a creature with the power of thought is able to appreciate the fact that it originated in western Asia or that it has

BRIAN SHUMWAY/GALLERYSTOCK

THOUGHT EXPERIMENTS

Sometimes an experiment is impossible. But that doesn't necessarily stop us from doing it – in our heads. Such thought experiments are one of the most impressive demonstrations of the power and scope of human thought.

The ancient Greeks knew about thought experiments in mathematics. Today they are most common in physics. Galileo described the first, which dealt with the speed at which stones of different sizes would fall when dropped.

The most famous is Schrödinger's cat, which demonstrates the implausibility of a certain interpretation of quantum mechanics using a classic *reductio ad absurdum* (see page 36). Erwin Schrödinger was later proved right in a real-world version of the experiment.

Einstein performed another famous one at age 16, when he imagined himself running alongside a beam of light. This flight of fancy, he later said, sowed the seed for special relativity.

A vivid imagination was also important to Kary Mullis, who shared a Nobel prize in chemistry for inventing a way of copying DNA. He did it, he said, by imagining himself "down there with the molecules".

Thought experiments can also help us explore moral issues. The trolley problem, for instance, asks whether would you act to avert an accident that is about to kill 10 people if your deliberate intervention would save the 10, but intentionally kill 1 other person.

Thought isn't always a reliable guide to reality, however. In 1935, Einstein, Nathan Rosen and Boris Podolsky imagined the properties of two "entangled" particles. They used the absurdity of the outcome to claim that quantum theory must be incomplete. However, we've since developed the technology to do the experiment for real, and in this case reality turns out to be truly absurd.

Sometimes thought leads nowhere, as in considerations of what happens to information absorbed by a black hole. In 2004, Stephen Hawking conceded a bet in the face of "proof" that information is not destroyed by the black hole. It turns out he gave in too soon: the question is still wide open.

Nonetheless, "thought experiments are incredibly useful for distilling the essential elements of a situation", says Dave Wineland of the National Institute for Standards and Technology (NIST) in Boulder, Colorado. Wineland won the Nobel prize in physics in 2012 for his experimental work in quantum physics. Despite our impressive array of experimental abilities, thought experiments can still challenge and improve our understanding of the world, he says. Michael Brooks more genes than a human. We can think about objects that are far removed from us in space and time, about the concrete and the abstract, about the past and the future, and about what does and what does not exist. The reach of human thought may not be completely unlimited (more on this below), but there is no doubt that it vastly outstrips the reach of perception.

A final feature of the faculty of thought is its integrative nature. It enables us to relate one state of affairs to another and appreciate connections between them.

Consider a famous episode in the history of medicine. While working at a hospital in Vienna in the 1840s, physician Ignaz Semmelweis noticed that the incidence of childbed fever was much higher in one maternity ward than another. He also noticed that this ward was staffed by medical students who performed autopsies. This led him to wonder whether the students might be contaminating the women with "cadaverous material". He tested this hypothesis by requiring the students to wash their hands with calcium hypochlorite – known to remove the smell of corpses – before visiting the maternity ward. This led to a dramatic drop in deaths from childbed fever.

"Much of the value of thinking comes from our ability to organise thoughts"

Semmelweis's discovery, which laid the foundations for the germ theory of disease, required two acts of integration: not only did he make a hitherto-unnoticed connection, he also thought of a way of testing the resulting hypothesis.

We make use of the problem-solving powers of thought on a daily basis. Whether planning a holiday, attempting to juggle work and children, or just trying to figure out the best way to get from A to B, we spend much of our lives thinking about the relationship between events.

Let us now turn to thought as a mental activity. In other words, let us consider thinking.

Although thoughts can occur in isolation, it is perhaps more common for them to come in trains. There are two types of trains of thought. Sometimes thoughts are related associatively: one thought naturally and effortlessly leads to another, like a game of word association. For example, thoughts of Switzerland might trigger thoughts of skiing which might lead to thoughts of snow which might lead to thoughts of Christmas... and so on. Associative thinking is familiar from daydreams and other forms of reverie.

Although there is a certain delight to be had in following this kind of train of thought, the power of thinking arguably resides in something more systematic: the fact that it enables us to use evidence and logic. Indeed, the term "thinking" is sometimes reserved for this activity (see "Thought experiments", left).

Consider the chain of thought "Socrates is a human", "all humans are mortal" and "Socrates is mortal". The components are inferentially connected, for if the first two are true then so too is the third.

Much of the value of thinking comes from our ability to organise thoughts into coherent trains to "see" what follows from what. In other words, much of our interest in thinking concerns reasoning.

There is a certain kind of delight to be had in following an undirected train of thought

The nature of thought

Having distinguished various aspects of thought, we can now turn our attention to the nature of thought. What is it?

It used to be believed that thought required some kind of non-physical medium – a soul or an immaterial mind. Modern theorists typically reject this in favour of a materialist account, according to which thought involves only physical processes.

There are three main motivations for this. The first is because it can account for correlations between states of the brain and states of thought. From the mild changes that follow from drinking

caffeine to the more radical ones that result from brain damage, it is clear that the state of the brain is intimately correlated with our capacity to think.

A second motivation is its ability to account for the causal role of thoughts in the world. Thoughts are both caused by physical events and are the cause of them. Seeing a train pull into the station might lead you to think "time to go", which leads you to pick up your luggage and board the train.

Third, the materialist account of thought does justice to the continuity of nature. We assume that humans evolved from animals that lacked thought. Although we cannot rule out the possibility that this involved the emergence of some kind of non-physical medium, it is more plausible to assume that the evolution of thinking creatures can be fully explained by changes in the structure of physical systems.

None of these reasons is decisive alone, but taken together they provide a strong case for the physicalist conception of thought. So how might thoughts manifest as physical phenomena in the brain?

For most of human history, thought has been essentially private, accessible only through speech and behaviour. There are various theories about how thoughts arise (see "Thinking like a computer", right). But developments in "brain decoding" are letting researchers study thought more directly.

Mental arithmetic

Using fMRI, neuroscientists are starting to be able to use information about a person's brain states to determine what they are thinking. In one study, volunteers were asked to choose between two options – "add" or "subtract" – before being presented with two numbers on which to perform their chosen operation. The researchers were able to tell with 70 per cent accuracy whether the subjects had decided to add or subtract, thereby reading their hidden intentions. Other researchers have had similar success working out what people are looking at, or even what they are dreaming about, from their brain activity alone (for more on this, see "The I in dreaming", page 124).

Although impressive first steps, it is worth emphasising the limitations of decoding studies. First, the range of thoughts that participants are told to entertain is artificially restricted. In the add/subtract study, there were only two possibilities. In the real world the range of thoughts is not constrained like this, and thus the task of interpreting a person's brain activity in everyday life will be vastly more difficult.

Brain decoding also requires a lot of advance preparation, mapping correlations between people's thoughts and their brain activity. Researchers cannot read thoughts that are not already included in their database. Brain imaging is thus still a long way from decoding the language of thought, let alone designing a machine that can read people's thoughts.

"For most of history, thought has been private, accessible only through speech"

One hotly contested question about the nature of thought is the role that language plays. There is a wide range of opinion. One end of the spectrum is that we think in language. At the other is the view that language has no role in thought other than to allow us to communicate our thoughts. The truth is likely to lie somewhere in the middle.

One way into this debate is to consider what kinds of thoughts non-human animals can entertain. Researching this is difficult, but there are at least three domains in which evidence of animal thought has been found: numbers, social relations and psychological states.

Many species have some capacity to track mathematical properties. In one study, rats were trained to press a lever when they heard two tones and a different lever when they heard four. They were trained to do the same in response to flashes of light. When presented with one tone and one flash, they pressed the first lever, indicating that they had understood the stimulus as "two events". In response to two tones and two flashes of light, they pressed the other lever.

A number of species can also compare quantities quite accurately. In one experiment, chimpanzees were given a choice of two trays of chocolate chips. On each tray were two piles – a 3-chip pile and a 4-chip pile, say, or a 7-chip pile and a 2-chip pile. The chimps were thus faced with the problem of determining which tray had the most chips overall. Although

THINKING LIKE A COMPUTER

There are many theories that try to explain how thought can arise from a material object such as a brain. One of the most successful is the computational theory of thought (CTT), which envisages thinking as being like the workings of a computer.

CTT concerns the nature of both thoughts and thinking. In a nutshell, it proposes that thoughts are sentences in a "language of thought", and that thinking involves transitions between these sentences governed purely by their "formal properties", not their meaning.

Let's unpack that a bit. A formal property is a property that something has by virtue of its physical form. The formal property of a word is its shape, not its meaning. The English word "monkey" and the French word "singe" differ in their formal properties but mean the same thing.

What does it mean to say that thoughts are sentences in a language of thought? Consider the thought "Marcel has a monkey". Just as the sentence itself is built up out of linguistic symbols that have meanings, CTT holds that the thought is built up out of "thought symbols", each of which carries a distinct meaning. One symbol will refer to Marcel, another to monkeys, and a third to the relation "having".

CTT explains thinking by appealing to the formal properties of these symbols. It posits a mechanism that is sensitive to the formal properties (whatever they are) and implements a set of rules about how to manipulate these symbols without knowing what they mean. Thought thus operates much like an automated address reader for letters. Although the machine doesn't know anything about Mr Smith or Mr Jones, it is able to ensure that their mail gets to them because it is sensitive to the formal differences between Smith and Jones.

Tim Bayne

they struggled when the quantities were very similar, they were generally good at choosing the right tray.

Chimps can also grasp simple fractions. When shown half a glass of milk, they are able to point to half an apple and ignore three-quarters of an apple in order to gain a treat.

Overall, the evidence suggests that a number of species can represent quantities up to three in exact ways and larger quantities in approximate terms. These representations are thought-like in so far as they are stimulus-independent and systematic.

A second domain in which there is evidence of animal thought concerns social rank. Some of the most intensive research on social cognition has been done on female baboons, whose complex social world involves a two-tiered hierarchy. Families are ranked relative to each other, and females within each family are too.

This ranking – which is fluid – plays a pivotal role in baboon society, and it is no surprise that baboons have complex representations of their social world. For example, a baboon may be more startled by a sequence of calls that represents a subordinate threatening a dominant baboon from a different family than it is by a sequence of calls that represents an equivalent conflict within a family, even when the difference in overall rank order is identical.

There are a number of ways in which a baboon's understanding of its social world has thought-like features. First, social status is not directly obvious in the environment, and keeping track of it requires the deployment of a theory about it. Second, it appears to be somewhat open-ended: a baboon can represent a great number of possible relations between members of her troop including ones that are unexpected. These features provide good justification for describing the baboon's representation of its social world as a form of thought.

A third area in which thought-like representations have been found is in the understanding of psychological states. Primates, at least, seem to be able to determine what others can see – and thus, perhaps, what they know – on the basis of what they are looking at. They will follow the gaze of others to locate the object of their attention and will remove food items from the line of sight of other animals. In experiments, subordinate chimpanzees will only take food items that dominant chimps cannot see – dominant chimpanzees typically take all the food and punish subordinates that challenge them – suggesting they understand the connection between seeing and knowing.

Unlike other animals, humans are born into a social world of other thinkers

PATRICK ZACHMANN/MAGNUM PHOTOS LEFT: GABRIEL MORENO

State of mind

There is also evidence that primates can monitor their own states of mind. In a series of studies, monkeys learned to perform a test that required them to discriminate between two shapes. When they answered correctly they received food; when they got it wrong they got nothing, and were obliged to wait a while for the next trial, which they didn't like to do. The monkeys learned that by pressing a button they could opt out of a test and move immediately to the next. The monkeys' use of the opt-out suggested that they were assessing how difficult each test was, for they opted out only on difficult trials.

It seems clear that non-human species use thought-like processes in a number of situations. Even so, they do not come close to matching the range and sophistication of human thought. What accounts for the uniqueness of human thought? The answer appears to be related to language.

Consider the following experiment involving Sheba, a chimpanzee trained to use numerals to represent items. Sheba was offered two plates of food, one large and one small. To obtain the larger plate, she had to point to the smaller one. ›

> *"Do we control our thinking, or is it something that just happens to us?"*

Although she understood the rule she wasn't able to overcome her instinct to point towards the larger plate – until the plates were covered and numerals representing the number of treats were placed on top of them.

The use of symbols allowed Sheba to transcend her normal abilities and do something much smarter: disengage her thought from perception. This "decoupling" is a striking feature of human thought, and may be facilitated by (and perhaps even require) the use of symbols, especially language.

Another example of the transformative power of symbols is provided by a study of chimpanzees trained to use plastic tags to represent sameness and difference. A pair of cups might be associated with a red triangle (sameness) whereas a cup and a shoe might be associated with a blue circle (difference).

Once the chimps had grasped this idea they could then – and only then – go on to appreciate higher-order relations of sameness and difference. They understood that two pairs, such as cup-cup and cup-shoe, have the relation of difference. The researchers suggest that the tags enabled the chimps to perform this task because they could transform a higher-order task into a simpler one of determining whether the symbols associated with each pair were the same.

As the philosopher Andy Clark has remarked, "experience with external tags and labels thus enables the brain itself… to solve problems whose level of complexity and abstraction would otherwise leave us baffled."

Language facilitates thought in other important ways. It is a tool that allows us to augment our powers of thought. By putting thoughts into language we are able to take a step back and subject them to critical evaluation. There is good reason to suppose that much distinctively human thought involves, or is at least enabled by, language.

Another distinctive feature of human thought is that it occurs in a social environment. We are born into a community of thinkers, and we learn to think by being guided by those who are experts. Indeed, childhood is an extended apprenticeship in thinking. We learn both what to think and how to think.

Perhaps most importantly of all, cultural transmission allows the best thoughts of one generation to be passed on to the ones that follow. Unlike other species, whose cognitive breakthroughs usually have to be rediscovered anew by each generation, we are able build on the thoughts of our ancestors. We inherit not just the contents of their thoughts, but also methods for generating, evaluating and communicating thoughts.

What thinking involves

Another key question that arises from considering thought as an activity concerns the kind of control we have over it. Is thinking an intentional and controlled activity, or is it largely passive? Do we control it, or is it something that just happens to us?

Sometimes thought is controlled by the application of a rule. Mathematical and logical operations, for example, are rule-based, and philosophers have invented many other systematic "thinking tools" to help them think more clearly (see "Tools for thought", right). But this is an unusual kind of activity, and most episodes of thinking involve no rule.

Suppose that I ask you why democracies tend not to wage war against other democracies. (It is often said that democracies have never waged war on one another but that is not true.) If you have not already considered this question, you may need to think about it.

What precisely does that involve? If your experience is anything like mine,

TOOLS FOR THOUGHT

"Thinking is hard." So says Daniel Dennett at the start of his recent book *Intuition Pumps and Other Tools for Thinking*. As a philosopher, he speaks from experience.

But just as artisans don't have to go about their business with their bare hands, so thinkers don't have to work unaided. Over the centuries, philosophers have invented a range of handy tools to make thinking a bit easier. Some are useful only in very specific circumstances, such as calculus or probability theory. Others are more broadly applicable. Here is a selection of Dennett's favourite thinking tools

REDUCTIO AD ABSURDUM

Literally, reduction of an argument to absurdity. The trick here is to take an assertion or conjecture and show that it leads to preposterous or contradictory conclusions. Homeopathy's claim that water has a "memory" of substances that were once dissolved in it can be challenged in this way by pointing out that tap water has had millions of different substances dissolved in it.

OCCAM'S RAZOR

Don't invent a complicated explanation for something if a simpler one will do. This is only a rule of thumb but it has proved extremely useful in science, such as when heliocentrism swept away an elaborate system of epicycles to explain the movement of the planets. (Not to be confused with Occam's broom, which is the intellectually dishonest trick of ignoring facts that refute your argument in the hope that your audience won't notice.)

STURGEON'S LAW

Named after sci-fi author Ted Sturgeon, who felt that his genre was unfairly maligned by critics. "They say '90 per cent of it is crud'," he complained. "Well, they're right… but 90 per cent of everything is crud." This is a useful tool when criticising a discipline, school of thought or art form. If you can't land a punch on the good 10 per cent, leave it alone.

"SURELY" AND RHETORICAL QUESTIONS

Whenever you encounter these in a text, stop and think. The author usually wants you to skate over them as if the claim is so obvious as to be beyond doubt, or the answer self-evident. The opposite is often the case.

Graham Lawton

you simply put the question to yourself... and wait for something to spring to mind. Sometimes nothing much happens; on other occasions, your unconscious comes up with something intelligible. Either way, there is no rule that you can consciously follow in order to generate the required thoughts.

On the whole, thinking often doesn't seem to extend much beyond putting questions to yourself and waiting for your unconscious to answer. The role of consciousness in such cases seems to be that of a minder whose job is to ensure that one's train of thought doesn't wander off topic.

We are, however, surprisingly poor at keeping our mind-wandering tendencies in check. In one study, people were asked to read a passage in their heads and monitor themselves for "zoning out". They were interrupted at random to check whether they were still reading the passage. It turned out that the participants zoned out a lot and, what's more, were generally not even aware that they had.

In fact, a significant amount of thought is undirected – that is, not aimed at any specific goal or problem. This kind of thought takes many forms, ranging from simply wandering away from a task to the spontaneous, unbidden thoughts that pop into your head during rest or routine chores.

JODIE GRIGGS/FLICKR SELECT/GETTY

Until recently, undirected thought was seen as a useless and wasteful aspect of our internal mental lives. But research now suggests that it is a normal and even necessary aspect of thought. Brain activity during mind-wandering is reminiscent of that seen when people are deliberately engaged in creative thinking. It may be that, paradoxically, undirected thought is when we get our best thinking done.

There is also evidence that attempting to control the direction of a stream of thought can be counterproductive. In a famous study, psychologist Daniel Wegner asked participants not to think about white bears for a 5-minute period. He found that this group reported more thoughts about white bears than did a second who had been instructed to think about white bears.

The limits of thought

So although we have some conscious control over the direction of our thoughts, it is far from unlimited. And if we have relatively little control, perhaps we also have relatively little responsibility for what we think.

Nonetheless, the potential of human thought is clearly very great. It is not limited in the way our physical and perceptual abilities are. We cannot see or visit distant tracts of space and time, for example, but we can think about them.

Are there limits to what our minds can grasp? The idea that certain aspects of reality are beyond us might at first seem implausible. After all, there doesn't seem to be any aspect of the world that we cannot think about. Is there any reason to take the possibility of cognitive limits seriously?

There is. Given that the machinery of human thought is part of our biology, there is every reason to suspect that it suffers from the kinds of bugs and blind spots that constrain other biological systems. It is doubtful whether chimpanzees possess the ability to think about quantum mechanics, for example. Perhaps that is one of the limitations of lacking language. But if there are parts of reality that are inaccessible to other thinking species, why should we assume that no part is inaccessible to us?

It is one thing to grant that some aspects of reality lie beyond our grasp, but quite another to identify what they might be. Is it possible to demarcate the borders of human thought?

The question might seem absurd. You might argue that if a certain thought is unthinkable then we can't think about it, let alone know that it is unthinkable. But there is nothing paradoxical about attempting to determine where the limits lie. The key involves distinguishing thinking about a thought from actually thinking it. Just as we can know what we don't know – the known unknowns – so too we might be able to think about what we cannot think: the thinkable unthinkables, you might say.

Wherever the boundaries of human thought might lie, there is no doubt that we are very far from having reached em. There are thoughts – deep, important and profound thoughts – that no human being has yet entertained. Thought has taken us a long way; who knows where it will lead. ■

Not thinking of white bears... not thinking of white bears... damn

PLAINPICTURE/ROBERT HARDING/THORSTEN MILSE

Most of us talk to ourselves throughout the day, but what is this inner speech and how does it shape our thoughts and decisions? Psychologist **Charles Fernyhough** listens in

Life in the chatter box

IT CAN happen anywhere. I can be driving, walking by the river or sitting quietly in front of a blank screen. Sometimes suddenly, sometimes gradually and imperceptibly, I become conscious of words that no one else can hear, telling me things, guiding me, evaluating my actions. I am doing something perfectly ordinary – I am thinking – and it takes the form of a voice in my head.

If you ask people to reflect on their own stream of consciousness, they often describe experiences like this. Usually termed inner speech, it is also referred to as the inner voice, internal monologue or dialogue, or verbal thought. But although philosophers have long been interested in the relationship between language and thought, many believed that inner speech lay outside the realms of science. That is now changing, with new experimental designs for encouraging it, interfering with it and neuroimaging it. We are beginning to understand how the experience is created in the brain; its subjective qualities – essentially, what the words "sound" like; and its role in processes such as self-control and self-awareness. The voice in our head is finally revealing its secrets, and it is just as powerful as you might have imagined.

Much of modern research has been inspired by the long-neglected theories of L. S. Vygotsky, a Russian psychologist whose career unfolded in the early days of the Soviet Union. Vygotsky only studied psychology for about 10 years before his untimely death from tuberculosis in his late thirties – a fact that has led some to call him "the Mozart of psychology". Starting with observations of children talking to themselves while playing, Vygotsky hypothesised that this "private speech" develops out of social dialogue with parents and caregivers. Over time, these private mutterings become further internalised to form inner speech.

If Vygotsky was right, inner speech should have some very special properties. Because it develops from social interactions, it should take on some of the qualities of a dialogue, an exchange between different points of view. Vygotsky also proposed that inner speech undergoes some important transformations as it becomes internalised, such as becoming abbreviated or condensed relative to external

DANIEL STOLLE

speech. For instance, when hearing a loud metallic sound outside at night and realising that the cat is to blame, you probably wouldn't say to yourself, "The cat has knocked the dustbin over". Instead, you might just say, "The cat", since that utterance contains all the information you need to express to yourself.

Partly because Vygotsky's work was suppressed by the Soviet authorities, it was a long time before his ideas became well known in the West, and even longer before researchers tested whether people actually report these qualities in their inner speech. In the first such study, conducted in 2011 at Durham University, UK, my colleague Simon McCarthy-Jones and I found that 60 per cent of people report that their inner speech has the to-and-fro quality of a conversation.

Eavesdropping on thoughts

So-called "self-report" methods have their limitations, not least that people are being asked to comment retrospectively on their inner experience. Another method, offering a richer picture of people's thoughts during a particular time period, was developed by psychologist Russell Hurlburt at the University of Nevada, Las Vegas. It involves participants being trained to give very detailed descriptions of their own inner experience in response to random cues from a beeper. Such studies have shown that people often report a train of thought unfolding more quickly than circumstances ought to have allowed, and yet not seeming rushed, which could be taken as evidence for the compression of sentences that Vygotsky postulated.

Vygotsky's theory also suggests some possibilities about the way inner speech is created in the brain. If it is derived from external speech, as he proposed, both might be expected to activate the same neural networks. Sure enough, long after his death, fMRI studies have linked inner speech to the left inferior frontal gyrus, including a region called Broca's area, which is known to be important for speech production.

Quite how much our inner and outer speech overlap remains a matter of debate. According to one view, inner speech is just external speech without articulation: the brain plans an utterance, but stops short of kicking our muscles into action. If that is the case, our internal voice should resonate with the same qualities of tone, timbre and accent as our ordinary external speech. ›

"Dramatic difficulties can come from brain damage that silences the inner voice. One such individual reported a lack of self-awareness after her illness"

There are some hints that this may be the case. In their lab at the University of Nottingham, UK, psychologists Ruth Filik and Emma Barber recently asked participants to read limericks silently in their heads. One was:

There was a young runner from Bath,
Who stumbled and fell on the path;
She didn't get picked,
As the coach was quite strict,
So he gave the position to Kath.

The other limerick read:

There was an old lady from Bath,
Who waved to her son down the path;
He opened the gates,
And bumped into his mates,
Who were Gerry, and Simon, and Garth.

Importantly, some of the participants had northern English accents, with short vowels (pronouncing "Bath" to rhyme with "Kath"), while the others had the long vowels of a southern accent ("Bath" rhyming with "Garth"). By tracking the volunteers' eye-movements, the researchers showed that reading was disrupted when the final word of the limerick did not rhyme in that volunteer's accent – when a southerner read "Bath" then "Kath", for instance. Although this study suggests that inner speech does indeed have an accent – and presumably other qualities of our spoken voice – one concern is that the inner speech we produce when reading is not necessarily the same thing as our everyday, spontaneous inner speech, which means that more naturalistic studies are needed.

So much for the subjective qualities of inner speech. What, if anything, does it actually do? Vygotsky proposed that words in inner speech function as psychological tools that transform the task in question, just as the use of a screwdriver transforms the task of assembling a shed. Putting our thoughts into words gives them a more tangible form which makes them easier to use. It may also be that verbal thought can allow communication between other cognitive systems, effectively providing a common language for the brain.

One of Vygotsky's most enticing predictions was that private and inner speech give us a way of taking control of our own behaviour, by using words to direct our actions. While driving up to a roundabout in busy traffic, for example, I'll still tell myself, "Give way to the right", especially if I've just been driving overseas. Knocking out the systems responsible for inner speech should therefore impede our performance on certain tasks that require planning and control, offering a powerful test of the hypothesis.

Such experiments typically require participants to repeat a word to themselves out loud to suppress their verbal thoughts while they perform a task (a technique known as articulatory suppression). Using this set-up, Jane Lidstone, one of my colleagues at Durham University, looked at the performance of children aged 7 to 10 on a planning task known as the Tower of London, which involves moving coloured balls around between three sticks of differing lengths in order to match a given pattern. Lidstone found that children performed worse if they had to repeat a word out loud, compared with trials in which they instead tapped repetitively with one of their feet. Similar findings have emerged from studies with adults. Alexa Tullett, now at the University of Alabama in Tuscaloosa, and Michael Inzlicht of the University of Toronto in Canada gave student participants a classic test of control known as the Go/No-Go task, which required them to press a button the moment they saw a yellow square pop up on the screen, but to remain still when they saw a purple square. It is a considerable test of impulse control, and, as predicted, the students were less accurate during articulatory suppression, compared with when they were doing a spatial task. Although experiments like these seem artificial, they allow researchers the kind of control over conditions that good science demands to test something like self-control.

Pep talks

So we know that inner speech has a role in regulating behaviour, but could it also have a role in motivating it? The research on children's private speech (Vygotsky's precursor of inner speech, remember) shows that it frequently has an emotional or motivational flavour. Athletes often give themselves pep talks before, during and after performances. In our study of the quality of inner speech, McCarthy-Jones and I found that two-thirds of students reported using internal speech that either evaluated their behaviour or served to motivate it.

Inner speech may even help us to become aware of who we are as individuals. Some philosophers have proposed that awareness of inner speech is important for understanding our own mental processes, an aspect of what psychologists call metacognition. Children typically do not become aware of their own inner speech until around age 4, although it is uncertain whether that shows their inability to reflect on their own thought processes, or the fact that inner speech is not yet fully internalised by that age. At Mount Royal University in Calgary, Canada, psychologist Alain Morin has found that people who use inner speech more often show better self-understanding. "Inner speech allows us to verbally analyse our emotions, motives, thoughts and behavioural patterns," he says. "It puts to the forefront of consciousness what would otherwise remain mostly subconscious."

While researchers are still gathering the evidence, these results certainly suggest that the voice in the head is important to many cognitive processes. But what about people who, for various reasons, don't talk to themselves in the usual way? As you might expect, deaf people who communicate in sign language often talk to themselves in sign too. People with autism, meanwhile, who often have problems with linguistic communication, seem not to use inner speech for planning, although they do use it for other purposes such as short-term memory. A more dramatic difficulty comes from damage to the language areas of the brain, which can silence some people's inner voices. One such individual, neuroanatomist Jill Bolte Taylor, reported a lack of self-awareness after a stroke that damaged her language system – supporting Morin's view that verbal thinking may be important for self-understanding.

Lending an ear to the differences between people might also tell us more about the dark side of inner speech, following a growing understanding that our internal monologue is not always beneficial to our well-being. When we worry and ruminate, we often do it in words, and our inner speech may contribute to anxiety and depression by keeping thoughts in the head that would be better off discarded. Inner speech may play its biggest role, however, in an experience that is often associated with other forms of mental disorder. People with certain psychiatric diagnoses (particularly schizophrenia), and also a small minority of people who do not have a mental illness, report the experience of hearing a person speak when there is no one present. Voice-hearing, or auditory verbal hallucination, is an enigmatic phenomenon whose cognitive and neural bases are not yet well understood. One prominent theory proposes that it occurs because the individual produces an utterance in inner speech that they do not recognise as their own. The result is that a bit of speech that was actually self-generated becomes attributed to another person: an alien voice.

Various lines of evidence converge to support this view. An early observation was that people who hear voices produce very slight activation in their articulatory muscles when their voices occur. Cognitive behaviour therapy to treat voice-hearing often focuses on blocking the phonological loop, by articulatory suppression or listening to music, so that the rogue inner speech cannot be generated. But the phenomenon of voice-hearing is undoubtedly more complicated than this. McCarthy-Jones, now at Macquarie University in New South Wales, Australia, notes that "while inner speech appears to be the basis of some voices, others are actual or mutated memories of earlier life-events (often traumatic ones)". Many researchers, particularly those associated with the worldwide Hearing Voices Movement, now believe that voices have important meanings for the individual, and therefore that they need to be understood rather than suppressed.

"According to one view, our inner voice should resonate with the same tone, timbre and accent as our normal speech"

A shower of words

There is much more we need to learn about inner speech's roles in our thinking and behaviour. Some insights may come from people who, without any disability, don't report any inner speech at all. For some of these people, it may be that inner speech is present, but that it is so condensed and abbreviated that it no longer seems very like language. It will also be interesting to note the consequences when people try to suppress their inner speech (and indeed all conscious thought) through varieties of meditation.

One thing we can be sure about is that inner speech takes many forms. Some will be good for explicit self-regulation and motivation; others will be closer to a kind of deep thinking with no particular sound quality. In fact, understanding inner speech better will help us to be clearer about what we mean by the nebulous term "thinking", and in this way make progress with some long-standing philosophical problems about how language, cognition and consciousness work together.

When I think about my own inner speech, I keep coming back to Vygotsky's ideas about "condensation". Sometimes I catch myself in the middle of a full-blown argument with myself, debating things from different points of view. Most of the time, though, the experience is more fragmentary: thoughts and feelings that are close to being put into language, but are not yet quite the kind of speech you would hear spoken out loud. Vygotsky likened this transition of thought into speech to "a cloud shedding a shower of words". Condensed or expanded, this rich internal dialogue must hold clues to understanding the distinctively creative, flexible properties of human thought. ■

CHAPTER THREE

INTELLIGENCE

WHAT IS INTELLIGENCE?

A century of clashes and discoveries has upended assumptions and revealed fascinating paradoxes. Intelligence is definitely not what most of us had imagined, says Linda Gottfredson

WHAT DO IQ TESTS MEASURE?

A century ago, British psychologist Charles Spearman observed that individuals who do well on one mental test tend to do well on all of them, no matter how different the tests' aims, format or content. So, for example, your performance on test of verbal ability predicts your score on one of mathematical aptitude, and vice versa.

Spearman reasoned that all tests must therefore tap into some deeper, general ability and he invented a statistical method called factor analysis to extract this common factor from the web of positive correlations among tests. This showed that tests mostly measure the very same thing, which he labelled the general factor of intelligence or "g factor". In essence, g equates to an individual's ability to deal with cognitive complexity.

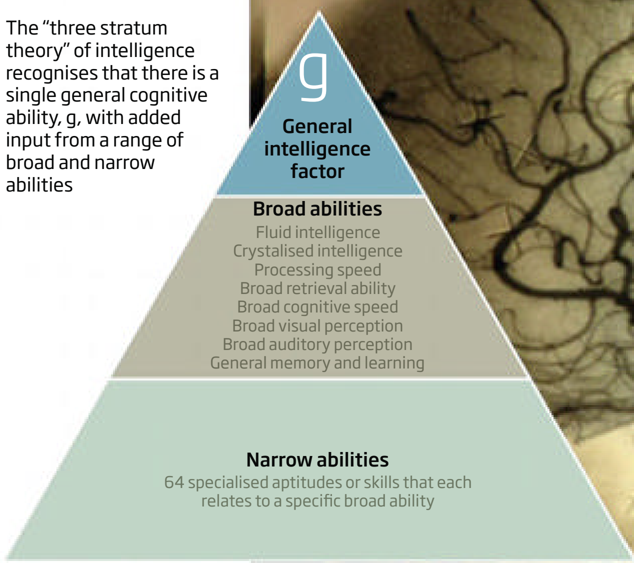
Spearman's discovery lay neglected in the US until the 1970s, when psychologist Arthur Jensen began systematically testing competing ideas about g. Might g be a mere artefact of factor analysis? No, it lines up with diverse features of the brain, from relative size to processing speed. Might g be a cultural artefact, just reflecting the way people think in western societies? No, in all human groups – and in other species too – most cognitive variation comes from variation in g.

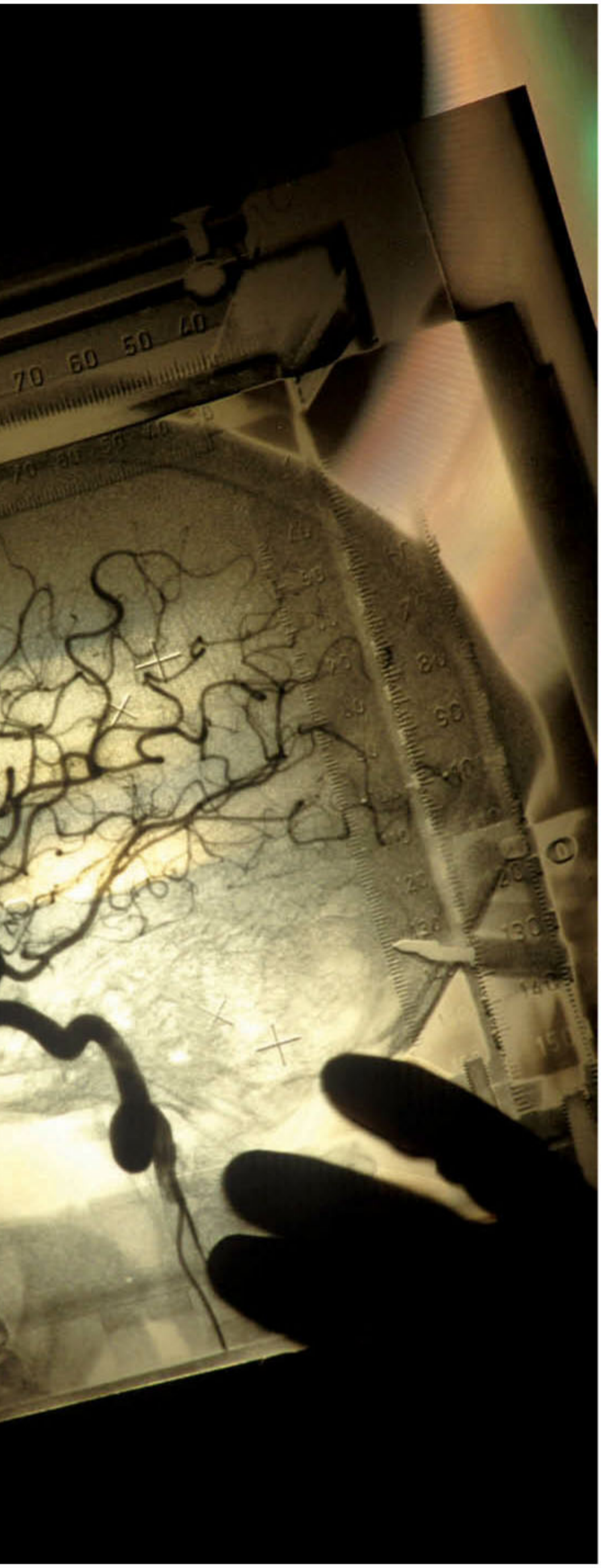
Jensen's analyses transformed the study of intelligence, but while the existence of g is now generally accepted, it is still difficult to pin down. Like gravity, we cannot observe it directly, so must understand it from its effects. At the behavioural level, g operates as an indivisible force – a proficiency at mentally manipulating information, which undergirds learning, reasoning, and spotting and solving problems in any domain. At the physiological level, differences in g probably reflect differences in the brain's overall efficiency or integrity. The genetic roots of g are even more dispersed, probably emerging from the joint actions of hundreds if not thousands of genes, themselves responding to different environments.

Higher g is a useful tool, but not a virtue. It is especially handy when life tasks are complex, as they often are in school and work. It is also broadly protective of health and well-being, being associated with lower rates of health-damaging behaviour, chronic illness, post-traumatic stress disorder, Alzheimer's and premature death.

Higher g helps an individual get ahead socioeconomically, but it has little connection with emotional well-being or happiness. Neither does it correlate with conscientiousness, which is a big factor in whether someone fulfils their intellectual potential.

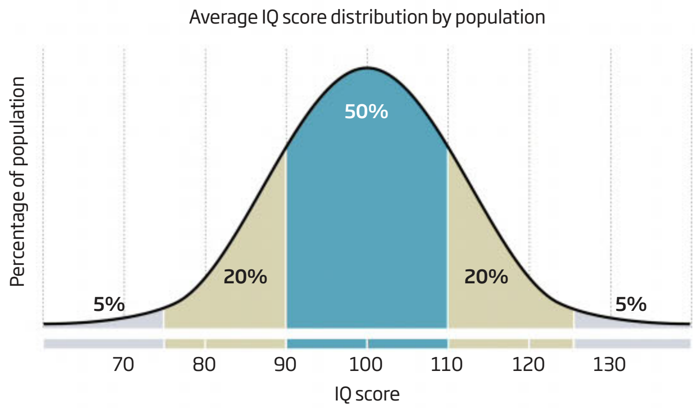
The "three stratum theory" of intelligence recognises that there is a single general cognitive ability, g, with added input from a range of broad and narrow abilities





JOE MCNALLY/GETTY

QUANTIFYING INTELLIGENCE



The first intelligence quotient (IQ) test was born of a desire to help the most vulnerable. In 1904, the French Ministry of Education commissioned psychologist Alfred Binet to find a practical way to identify children who would fail elementary school without special help. Binet assembled 30 short, objective questions on tasks such as naming an everyday object and identifying the heavier of two items. A child's performance on these, he believed, would indicate whether their learning was "retarded" relative to their peers. His invention worked and its success spawned massive intelligence-testing programmes on both sides of the Atlantic.

Organisations turned to IQ tests to screen large pools of applicants: military recruits for trainability, college applicants for academic potential and job applicants for employability and promotability. The tests were eagerly adopted at first as a way to select talent from all social levels, but today their use can be considered contentious, partly because they do not find equal amounts of intelligence everywhere.

Nevertheless, intelligence testing continues because it has practical value. Many colleges, employers and the armed services still use paper-and-pencil or computer-based intelligence tests to screen large groups of applicants. The gold standard, however, is the orally administered, one-on-one IQ test, which requires little or no reading and writing. These include the Stanford-Binet and Wechsler tests, which take between 30 and 90 minutes and combine scores from areas such as comprehension, vocabulary and reasoning to give an overall IQ. These batteries are used to diagnose, treat or counsel children and adults who need personal or academic assistance. Ability testing is governed by detailed ethical standards and professionally administered tests must meet strict criteria including lack of cultural bias and periodic updating. In fact, IQ tests are the most technically sophisticated of all psychological tests and undergo the most extensive quality checks before publication. ›

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Alfred Binet invented the IQ test to identify those schoolchildren most in need of help

WHAT MAKES SOMEONE SMART?

Intelligence tests are calibrated so that, at each age, the IQ average score is 100 and 90 per cent of individuals score between IQ 75 and 125. The typical IQ difference between strangers is 17 points and it is 12 between full siblings. So what makes some people smarter than others? And how can we change our score?

OLDER AND WISER

The brain is a physical organ and no less subject than any other to ageing, illness and injury. The normal developmental trajectory is that aptitude at learning and reasoning – mental horsepower – increases quickly in youth, peaks in early adulthood, and then declines slowly thereafter and drops precipitously before death. The good news is that some important abilities resist the downturn.

Some IQ researchers distinguish between tests of fluid intelligence (gF) and crystallised intelligence (gC). The first assess on-the-spot learning, reasoning and problem solving; the second assess the crystallised fruits of our previous intellectual endeavours, such as vocabulary in one's native language and broad cultural knowledge. During youth, gF and gC rise in tandem, but they follow different trajectories thereafter. All gF abilities decline together, perhaps because the brain's processing speed slows down with age. However, most people's gC abilities remain near their personal peak into old age because they reside in the neural connections that gF has laid down over a lifetime of learning and practice. Of course, age-related memory loss will affect an individual's ability to recall, but exactly how this affects intelligence is not yet known.

This has practical implications. On the positive side, robust levels of gC buffer the effects of declining gF. Older workers are generally less able to solve novel problems, but they can often compensate by calling upon their larger stores of experience, knowledge and hard-won wisdom. But gC can also disguise declines in gF, with potentially hazardous results. For example, health problems in later life can present new cognitive challenges, such as complex treatments and medication regimes, which individuals with ample gC may appear to understand when actually they cannot cope.

There are ways of slowing or reversing losses in cognitive function. The most effective discovered so far is physical exercise, which protects the brain by protecting the body's cardiovascular health. Mental exercise, often called brain training, is widely promoted, but it boosts only the particular skill that is practised – its narrow impact mirroring that of educational interventions at other ages. Various drugs are being investigated for their value in staving off normal cognitive decline, but for now preventive maintenance is still the best bet – avoid smoking, drinking to excess, head injuries and the like.

Overall size of the brain, relative to the body, correlates with IQ

Intelligence requires integration of sensory and other information

Learning and experience can increase the size of specific brain areas

High IQ is associated with faster mental processing speed

Volume of the cortex, the brain's grey matter, correlates with IQ

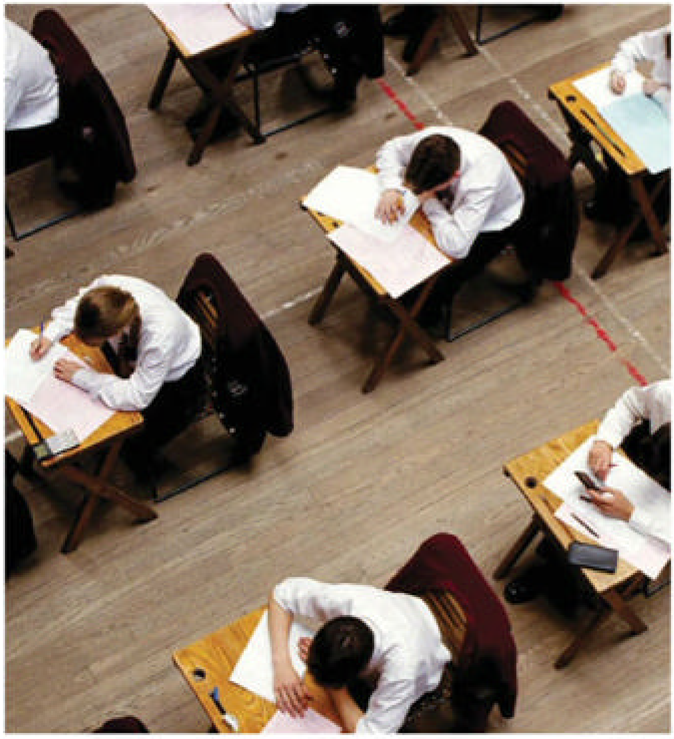
Volume of tissue linking the brain's hemispheres correlates with IQ

DIFFERENT TYPES OF INTELLIGENCE

Consider the engineer's superior spatial intelligence and the lawyer's command of words and you have to wonder whether there are different types of intelligence. This question was debated ferociously during the early decades of the 20th century. Charles Spearman, on one side, defended the omnipotence of his general factor of intelligence, g. On the other, psychologist Louis Thurstone argued for seven "primary abilities", including verbal comprehension (in which females excel) and spatial visualisation (in which males excel). Thurstone eventually conceded that all his primary abilities were suffused with the same g factor, while Spearman came to accept that there are multiple subsidiary abilities in addition to g on which individuals differ.

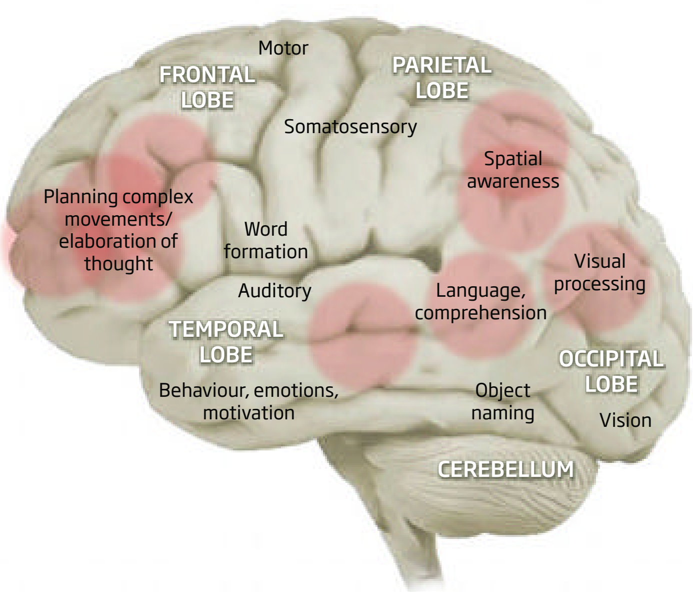
This one-plus-many resolution was not widely accepted until 1993, however. It was then that American psychologist John B. Carroll published his "three stratum theory" based on a monumental reanalysis of all factor analysis studies of intelligence (see diagram, page 42). At the top is a single universal ability, g. Below this indivisible g are eight broad abilities, all composed mostly of g but each also containing a different "additive" that boosts performance in some broad domain such as visual perception or processing speed. These in turn contribute to dozens of narrower abilities, each a complex composite of g, plus additives from the second level, together with life experiences and specialised aptitudes such as spatial scanning.

This structure makes sense of the many differences in ability between individuals without contradicting the dominance of g. For example, an excellent engineer might have exceptional visuospatial perception together with training to develop specialist abilities, but above all a high standing on the g factor. The one-plus-many idea also exposes the implausibility of multiple-intelligence theories eagerly adopted by educators in the 1980s, which claimed that by tailoring lessons to suit the individual's specific strength – visual, tactile or whatever – all children can be highly intelligent in some way.



"Intriguingly, the heritability of intelligence is less than 30 per cent before children start school, rising to 80 per cent among adults"

Intelligence is distributed across many areas of the brain and people with the highest IQ tend to have increased volume in a network of regions (shaded) including key language areas



NATURE AND NURTURE

Each of us is the embodiment of our genes and the environment working together from conception to death. To understand how these two forces interact to generate differences in intelligence, behavioural geneticists compare twins, adoptees and other family members. The most compelling research comes from identical twins adopted into different homes – individuals with identical genes but different environments – and non-kin adopted into the same home – unrelated individuals sharing the same environment. These and other studies show that IQ similarity most closely lines up with genetic similarity.

More intriguingly, the studies also reveal that the heritability of intelligence – the percentage of its variation in a particular population that can be attributed to its variation in genes – steadily increases with age. Heritability is less than 30 per cent before children start school, rising to 80 per cent among western adults. In fact, by adolescence, separated identical twins answer IQ tests almost as if they were the same person and adoptees in the same household as if they were strangers.

The surprising conclusion is that most family environments are equally effective for nurturing intelligence – the IQ of an adult will be the same almost regardless of where he or she grew up, unless the environment is particularly inhumane.

Why do the shared environment's power to modify IQ variation wane and genetic influences increase as children gain independence? Studies on the nature of nurture offer a clue. All children enter the world as active shapers of their own environment. Parents and teachers experience this as their charges frustrate attempts to be shaped in particular ways. And increasing independence gives young people ever more opportunities to choose the cognitive complexity of the environments they seek out. The genetically brighter an individual, the more cognitively demanding the tasks and situations they tend to choose, and the more opportunities they have to reinforce their cognitive abilities.

Given that an individual's ability to exploit a given environment is influenced by their genetic endowment, and given that "better" family environments tend not to produce overall increases in IQ, it is not surprising that attempts to raise low IQs by enriching poor school or home environments tend to disappoint. Narrow abilities can be trained up but g apparently cannot. This makes sense if g is an overall property of the brain. That does not mean intensive early educational interventions lack positive effects: among other things they may reduce rates of teenage pregnancy, delinquency and school dropout. Besides, even if we cannot boost low intelligence into the average range, we do know how to help all children learn more than they currently do and achieve more with the intelligence they have. ■

Identical twins are a natural laboratory in which to study how intelligence develops

LEFT GETTY, BACKGROUND DOUG CORRANCE/GETTY

The intelligent approach to IQ

Worldwide, IQs have risen by up to three points per decade over the past century. At 80, **James Flynn**, the man this increase is named after, explains its implications and the effects of sex, culture and attitude on intellectual achievement

Our IQs have risen. Does this mean we are getting smarter?
Our brains have no more potential at conception, but because we have done different "mental exercise" throughout our lives, our brains would look different at autopsy, just as a weightlifter's muscles look different from a swimmer's. Our ancestors were just as good as we are at practical intelligence, at dealing with everyday life. But we have developed the mental skills needed to deal with the demands of the modern world.

Does that mean we should revise our definition of intelligence?
Once we understand how our minds have changed, I leave it to you whether you want to say we are "more intelligent". There is no doubt that we need a new approach to the study of intelligence.

If one individual is better than average on one important cognitive skill, they tend to be better on all of them. Society, on the other hand, may change so as to demand enhancement of one important skill – say, the ability to use logic to deal with abstract symbols – but make no extra demands on the expansion of our everyday vocabulary. Writing the cognitive history of the 20th century, of how our minds have changed over time, is quite different from measuring how much one person's cognitive skills are superior to another's.

You caused a bit of stir talking about gains in women's IQ.
Women have gained on men over the past generation, to the point where they now equal or slightly surpass men. I don't think the advantage that women are showing is a genetic advantage for intelligence; I suspect it's down to extra mental exercise. Girls are more likely to use their mind in school than boys are. But at university, they really are two or three points below men, and that's because more marginal women, IQ-wise, qualify for university.

How come?
A girl with an IQ of 100 thinks of herself as university material and has the marks. A boy with the same IQ hates school and doesn't have the marks. So you're much more likely to find girls with an IQ below 110 in university than boys. Even so, females do better than males at university.

"If we didn't investigate because it was politically incorrect, we'd never know"

What about the infamous remarks by Larry Summers, when he was president of Harvard University, that women have less innate ability than men for science and mathematics?
This is a perfectly respectable hypothesis. Every hypothesis should be tested. He remarked that at the highest level of pure mathematics, women are under-represented. My answer is that if there is a difference, it's not cognitive but temperamental.

I'm convinced from my research that women can use logic just as well as men. It could be that thanks to the testosterone of males and the greater proclivity of women to be interested in human beings, there will always be fewer women in pure mathematics. Who knows?

I have an open mind. When I lecture on this, I say Summers was wrong to think that women are less gifted cognitively.

It's a sensitive issue. Why tackle it?
We need to know. And if people like me didn't investigate it because it was politically incorrect, we never would know. It's not accidental that I'm the one who's overwhelmingly brought this evidence to bear on the gender issue. A lot of other people were too scared to go into it.

When feminists say to me that this is a great difficulty, I say, do you want women to be as competitive and soulless as men? I mean, is your ideal human being someone who neglects their family and kids and works 16 hours a day to be a corporate executive? You can't have it both ways.

Do these differences in outlook exist between cultures too?
Yes. If you came home and told your Irish father [Flynn is Irish American] you'd made the football team, he'd be over the moon. If you told that to a Jewish parent, they might forbid you to play football. And if I came home with a good report card, my father would give me perfunctory praise. A Chinese parent, the kid knows he's over the moon.

In my book *Asian Americans,* I wrote that Chinese Americans who had come to America before 1950 as children, or had been born in the US, had IQs no higher than whites – they just outperformed them like crazy. That is, they could drop seven points on whites and still get the SAT scores and grades to get into Berkeley. A Chinese American with an IQ of about 93 looked as intelligent as a white at 100, in terms of their educational and occupational profile. Like women, Chinese are more adjusted to formal education. They don't skip class; they hand homework in on time; they don't get suspended.

What implications does the "Flynn effect" have for the use of the death penalty?
In the US I'm going to be executed rather than exonerated if I have an IQ above 70 – because below that is where they deem "significant limitations", such as problems with literacy or social skills, set in. For 10 years I have been trying to educate judges about the Flynn effect and the need to restandardise IQ tests every generation or so. If I was tested in 1976 with an IQ test from 1948, it has been inflated by 28 years of IQ gains, which means that an IQ of 67 could be returned as one of 75.


GRAHAM TURNER/THE GUARDIAN

Have you succeeded in changing things?
At the beginning, I faced enormous resistance. Today, almost everyone who defends capital offenders is aware of my work. Given how conservative the judicial profession is, I'm not discouraged. I hope that before I die, I will see more progress.

You're now 80, but you're still working pretty much full time?
I teach four-fifths of the time, two courses, and I have a lot more time for my writing than I did when I was department head.

Doesn't this run counter to the material in your new book about the "dark" side of old age?
No, that is about analytical people losing more ground in old age. Most IQ tests divide skills into four categories – analytical skills, verbal skills, working memory and perceptual speed. Disturbingly, those who are most above the average analytically have the deepest fall-off between the age of 65 and 88. Retirement age is what really sets things off.

Why do people decline after they retire?
Let's imagine that high-performance analytical brains are like high-performance cars: in old age, they need more servicing than the average car. It could be that evolution has not geared the high-performance analytical brain to keep its tone in old age, neuronally. Or it may be that most highly intelligent people mainly use analysis at work, and when they retire, they lose an analytical exercise advantage over the average person. But there's a bright spot for verbal skills: for people who are well above the mean, verbal facility decays slower.

How are you holding up?
Oddly enough, I don't really feel I have fewer new ideas or am able to do less analysis than I could at 20. I do find my working memory has slipped a bit. I've remained intensely active. I still run.

What do the next few years hold for you?
I'm on a crusade to salvage university education. I looked at students at a very good US university, one of the top 10, and found that only about 1 in 5 could do any critical thinking outside their major subject. Universities are in a position to correct this; every department could run a course that gave them these key tools. And I've just finished a little book on climate change. This seems to be an issue that any educated person would want to have an independent opinion on. ■

Are we getting stupider?

There are signs that our century-long rise in intelligence has gone into reverse, finds **Bob Holmes**

IN DENMARK, every man is liable for military service at the age of 18. Nowadays, only a few thousand get conscripted but all have to be assessed, and that includes doing an IQ test. Until recently, the same one had been used since the 1950s. "We actually have the same test being administered to 25,000 to 30,000 young men every year," says Thomas Teasdale, a psychologist at the University of Copenhagen.

The results are surprising. Over this time, there has been a dramatic increase in the average IQ of Danish men. So much so that what would have been an average score in the 1950s is now low enough to disqualify a person from military service, Teasdale says.

The same phenomenon has been observed in many other countries. For at least a century, each generation has been measurably brighter than the last. But this cheerful chapter in social history seems to be drawing to a close. In Denmark, the most rapid rises in IQ, of about 3 points per decade, occurred from the 1950s to the 1980s. Scores peaked in 1998 and have actually declined by 1.5 points since then. Something similar seems to be happening in a few other developed countries, too, including the UK and Australia.

So why have IQ scores been increasing around the world? And more importantly, why does this rise now seem to be coming to an end? The most controversial explanation is that rising IQ scores have been hiding a decline in our genetic potential. Could this possibly be right? Do we face a future of gradually declining intellectual wattage?

There's no question that intelligence – as measured by IQ tests, at least – has risen dramatically since the tests were first formalised a century ago. In the US, average IQ rose by 3 points per decade from 1932 to 1978, much as in Denmark. In postwar Japan, it shot up by an astonishing 7.7 points per decade, and two decades later it started climbing at a similar rate in South Korea. Everywhere psychologists have looked, they have seen the same thing.

This steady rise in test scores has come to be known as the "Flynn effect" after James Flynn of the University of Otago in New Zealand, who was one of the first to document the trend (see "The intelligent approach to IQ", page 46). Much has been written about why this has been happening. There may be a cultural element, with the rise of television, computers and mobile devices making us better at certain skills. The biggest IQ increases involve visuospatial skills. Increasing familiarity with test formats may also play a role.

The general view, though, is that poor health and poor environments once held people back, and still do in many countries. Wherever conditions start to improve, though, the Flynn effect kicks in. With improved nutrition, better education and more stimulating childhoods, many people around the world really have become smarter.

We have, after all, changed in other ways: each generation has been taller than the previous one, probably because nutrition has improved. So although height is thought to have an even larger genetic component than intelligence – taller parents tend to have taller children – the environment matters too.

If better nutrition and education have led to rising IQs, the gains should be especially large at the lower end of the range, among the children of those with the fewest advantages in their lives. Sure enough, that's what testers usually see. In Denmark, for example, test scores of the brightest individuals have hardly budged – the score needed for an individual to place in the top 10 per cent of the population is still about what it was in the 1950s. "It was the bottom end that was ›

OLIVER JEFFERS

"More people are developing their potential, but that potential may be declining"

moving up. The top end hardly moved at all," says Teasdale.

If social improvements are behind the Flynn effect, then as factors like education and improved nutrition become common within a country their intelligence-boosting effects should taper off, country by country. "I've been predicting for some time that we should see signs of some of them running out," says Flynn. And those signs are indeed appearing. It seems we are seeing the beginning of the end of the Flynn effect in developed countries.

Similarly, the increases in height are also tapering off. But IQ scores are not just levelling out but appear to be declining. The first evidence of a small decline, in Norway, was reported in 2004 (see chart, below). Since then a series of studies have found similar declines in other highly developed countries including Australia, Denmark, the UK, Sweden, the Netherlands and Finland. Should we be worried? Not according to Flynn and Teasdale. The evidence remains sparse and sometimes contradictory, and could just be due to chance.

A good education is one of the factors that help boost IQ scores

Underlying decline?

Even if they are not down to chance, such small declines could be attributable to minor changes in social conditions such as falling income or poorer education, which can easily be reversed, says Flynn. But these are invented hypotheses for a very small phenomenon, he points out. "You'd want to be pretty certain that phenomenon was actual before you scratch around too hard for causes."

There is a more disquieting possibility, though. A few researchers think that the Flynn effect has masked an underlying decline in the genetic basis of intelligence. In other words, although more people have been developing closer to their full potential, that potential has been declining.

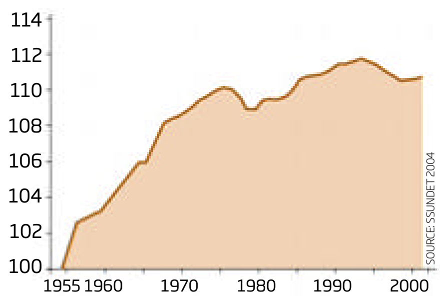
Most demographers agree that in the past 150 years in Western countries, the most highly educated people have been having fewer children than is normal in the general population. The notion that less educated people are outbreeding others is far from new, as is the inference that we are evolving to be less intelligent. It's even the theme of a 2006 film, *Idiocracy*.

"This is a claim that has been made for over a century now, and always with the most horrific prediction of what might happen if we don't stop it," says Bill Tucker, a historian of psychology at Rutgers University in Camden, New Jersey. This idea led to the extensive eugenics programme in the US, with its forced sterilisations, which in turn helped inspire the "purity" policies of Nazi Germany.

This unpleasant history, though, doesn't mean there is no genetic decline, some argue. Richard Lynn of the University of Ulster, UK, a psychologist whose work has often been controversial, has tried to calculate the rate of decline in our genetic potential using measured IQ values around the world in 1950 and 2000. His answer: a bit less than 1 IQ point, worldwide, between 1950 and 2000. If the trend continues, there would be another 1.3 point fall by 2050. Even if he is right – and it's a big if – that is a tiny change compared with the Flynn effect. Would small declines like this even matter?

A score to settle

The rise of average IQ scores of military conscripts in Norway has slowed and started to reverse. Similar patterns are seen in a few other countries



Yes, argues Michael Woodley, a psychologist at Free University of Brussels (VUB) in Belgium. This kind of evolution would shift the bell curve of intelligence, he claims, and a small shift can lead to a big drop in the number of high scorers. For example, if mean IQ fell from 100 points to 97, it would almost halve the number of people who score above IQ 135. "It's a leverage effect," Woodley says.

Would this really matter? People who score highly in IQ tests are not always the most successful in life. In any case, with so many confounding factors, it is far from clear whether the "evolving to be stupid" effect is real. For example, it has been suggested that caesarians allow more bigger-brained babies to survive than in the past.

A definitive way to settle this issue would be to look at whether gene variants associated with higher IQs are becoming less common. The trouble with this idea is that so far, despite huge effort, we have failed to find any specific gene variant linked to significantly higher IQs in healthy individuals.

"Boy, a lot of investigators have spent a lot of time looking for that stuff, with some pretty big samples and sophisticated methodology," says Ronald Yeo, a psychologist at the University of New Mexico in Albuquerque. "Of course it doesn't mean that there aren't genes that are important. It's just there are so many of them and they each have so little effect."

PATRICE NORMAND/PICTURETANK

Yet Woodley thinks his team has found clear evidence of a decline in our genetic potential – and he claims it is happening much faster than Lynn's calculation suggests. Instead of relying on fertility estimates, Woodley looked at a simple measure: reaction time. Quick-witted people, it turns out, are exactly that: smarter people tend to have quicker reaction times, probably because they process information more quickly.

Back in the 1880s, the polymath Francis Galton measured the reaction times of several hundred people of diverse social classes in London. A few years ago, Irwin Silverman of Bowling Green State University in Ohio noticed that the reaction times Galton recorded – an average of about 185 milliseconds between seeing a signal and pushing a button – were quite a bit quicker than the average of more than 250 milliseconds in modern tests, which began in the 1940s.

Woodley's team reanalysed Silverman's data, factoring in the known link between reaction time and intelligence. When they did this, they found that reaction times had indeed slowed over the century, by an amount corresponding to the loss of one full IQ point per decade, or more than 13 points since the Victorian era.

Critics have been quick to attack Woodley's analysis, arguing that Galton may not have measured reaction times in the same way as later investigators. If Galton's apparatus had a button with a shorter range of motion, for instance, then he would have measured shorter reaction times. What's more, Silverman points out that there is no obvious downward trend in the post-1940 data, as there should be if Woodley is right.

In a detailed response published in June 2014, Woodley maintains that today's brains remain slower even after accounting for all these other explanations. But even if he's right about reaction times, the correlation between IQ and reaction time is not an especially strong one: reaction time explains only about 10 per cent of the variation in IQ.

"Probably every generation moans about the new generation being less intelligent, and every upper crust moans about the lower classes out-breeding them," says Kevin Mitchell, a neurogeneticist at Trinity College Dublin in Ireland. "The basic premise is that IQ levels are dropping. And I don't see any evidence for that, which is why I find the whole debate a bit odd."

Trouble ahead

The coming decades should provide a definitive answer. If what we are seeing in countries like Denmark is merely the end of the Flynn effect, IQ scores should stabilise in developed countries. If Woodley and his colleagues are right, we should see a continuing decline.

Even if we are evolving to be more stupid, it is far from clear whether we need to worry about it. Flynn thinks the problem may just take care of itself, as societal improvements such as better healthcare and more promising employment options bring down fertility rates in every stratum of society.

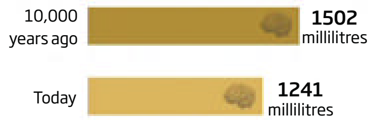
But don't breathe a sigh of relief just yet. In the longer term, there may be an even more fundamental threat to our intelligence. We humans mutate fast – each of us has 50 to 100 new mutations not present in our parents, of which a handful are likely to be harmful, says Michael Lynch, an evolutionary geneticist at Indiana University in Bloomington. In the past, harmful mutations were removed as fast as they appeared, because people unlucky enough to inherit lots of them tended to die young, before they had children. Now, things are different. Fetal mortality, for example, has declined by 99 per cent in England since the 1500s, Lynch says.

This means that populations in developed countries are accumulating harmful mutations. Over tens of generations, Lynch has calculated, this will lead to a large drop in genetic fitness. With so many genes contributing to brain function, such a decline might well drag down our brainpower, too. The only way to stop that might be to tinker with our genomes. Given our ignorance about the genetic basis of intelligence, and the ethical complexities, that is a long way off.

Coming back to the short-term, though, there is an obvious option for those concerned about intelligence levels. "If you're worried about it, the answer is what the answer has always been," says Mitchell. "Education. If you want to make people smarter, educate them better. That won't make everybody equal, but it will lift all boats." ■

Shrinking brains

Average volume of European female brain



Are humans evolving to be dumber? A few researchers argue that this has happened over the past century or so (see main story), but it could have been going on for much longer. One thing is certain: our brains have been shrinking for at least 10,000 years. An average European woman today, for example, has a brain about 15 per cent smaller than that of her counterpart at the end of the last ice age.

It has been suggested that with the rise of agriculture and towns, and increased division of labour, people could survive even if they weren't as smart and self-sufficient as their hunter-gatherer ancestors. But smaller doesn't necessarily mean wimpier, says John Hawks, an anthropologist at the University of Wisconsin in Madison. Brains are costly to operate, so evolution is likely to favour increased efficiency. Modern brains might do just as much with a smaller package, Hawks thinks.

CHAPTER FOUR

MENTAL HEALTH

Down with dementia

The dream of living to a ripe old age becomes a nightmare if your mind disintegrates en route. Yet there has been some much-needed good news about this condition, finds Liam Drew

MY PATERNAL grandfather died shortly before I was born. The man my father's stories conjured up was physically and mentally tough: a first world war veteran who was boisterous with his drinking buddies and, at home, an old-fashioned head of the household.

But beside those tales sat his life's sad, unelaborated footnote; that he ended his days demented and degraded.

When I ask directly, my dad recalls his father sitting silently for hours, endlessly nursing an empty tea cup, oblivious to all. But my parents prefer not to go into detail. My mum says: "People just didn't talk about dementia 40 years ago."

Today, though, we talk about dementia a lot. With life expectancy continuing to rise and the baby-boomer population bulge standing on the cusp of old age, Western countries face what is sometimes called a looming tsunami of dementia. Such is the urgency that in December 2013 London hosted the first G8 summit on the subject, where the world's eight richest countries agreed to coordinate their research efforts against the problem.

The epidemic will place huge strain on healthcare systems; in the UK, the annual cost of caring for someone with this condition is more than the average salary. And on a personal level, the prospect of a long life loses its appeal if it ends this way.

But wait a minute. All the gloomy predictions have been based on a central assumption that people will continue to develop dementia at the same rate as they always have. It is a reasonable assumption – age is the primary risk factor for dementia – but it may well be wrong. There is emerging evidence that the dementia rate in developed countries has fallen.

Since the average age of the inhabitants of Western countries is rising, this may not be enough to stop the total number of people with dementia from increasing. So we still need to plan accordingly at the societal level. But our individual chances of succumbing appear to have decreased. For once, this is a good-news story about dementia.

The search is now on to uncover what has driven these trends, so that they can be maintained and maybe even amplified. "I think this gives some basis for cautious optimism," says Kaare Christensen, an epidemiologist at the University of Southern Denmark in Odense, who led some of the research. "There seems to be huge potential for further progress – if we don't destroy it."

How well our minds function in old age is a major determinant of our quality of life. A small decline in cognitive abilities is an almost inevitable part of ageing. For most people this is a gentle downward turn in mental agility, frustrating but with no great impact.

If this fall-off is more than usual for someone's age, but not enough to interfere with their day-to-day living, it is classed as mild cognitive impairment. This is a high-risk state for progression to dementia.

Dementia is a general breakdown of the intellect and personality, with disintegration of memory, attention and emotional control. Of all the diseases linked to ageing, for me this is the most fearsome. It is degrading for the person concerned and heartbreaking for those around them.

About two-thirds of dementia cases are caused by Alzheimer's disease, in which neurons die off amid distinctive clumps of protein. The next most common form is vascular dementia, caused by deterioration of

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> "How well our minds function in old age is a major determinant of our quality of life"

the brain's blood vessels and often involving minor strokes. There are other, less common subtypes, plus a growing belief that dementia at very old ages typically involves a mix of different forms of disease.

What's always been known is that the risk of dementia rises markedly with age – seemingly inexorably. Very few cases occur before the age of 60, and between 60 and 70 the condition is still restricted to an unlucky 1 per cent or so. After this point, though, the odds worsen significantly: about 5 per cent of 70 to 80-year-olds are affected, and beyond 80 the risk rises ever more sharply (see graph, page 54).

The logic has always seemed inescapable: the more 80-year-olds there are around, the more people there will be with dementia. The number of people with dementia globally is often predicted to triple by 2050.

Unequivocally good news

But over the past few years there have been hints that the actual numbers didn't fit this picture. Research suggested that dementia was on the retreat. The studies weren't conclusive, though – either they were too small or their findings statistically borderline.

The picture has now changed. In 2013, leading medical journal *The Lancet* published two studies involving thousands of people, which definitively challenge the orthodoxy.

One compared two surveys of dementia numbers in the UK, done 20 years apart. The first, from 1994, led to the conclusion that there were about 650,000 people with the condition. With the increase in average age of the population over the intervening years, the repeat survey – which used exactly the same tests and definitions – should have found nearly 900,000 people with dementia. But the count came up over 200,000 short. Looking at how the illness affected specific age groups, it appeared that people were developing dementia later in life (see chart, page 54).

The finding came as a welcome surprise to Carol Brayne, the epidemiologist at the University of Cambridge who led the study. "It has been a very positive experience," she says. The editorial that *The Lancet* ran to accompany the paper described the findings as "unequivocally good news".

The other study looked at the health of two groups of Danish people in their mid-90s, born a decade apart, in 1905 and 1915. The nonagenarians were asked to complete a battery of physical and mental tests. While the two groups had similar physical health, those born in 1915 markedly outperformed ›

"Modern life, with its constant multimedia inputs, may be much more stimulating than it was 50 years ago"

the earlier-born in cognitive tests. "They were not stronger, but they were smarter," says Christensen, who led the study. "The two papers complement each other beautifully."

The big question, naturally, is why things changed. Neither study was designed to uncover the reasons behind any trends, but we can make educated guesses. The main suspects are long-term trends of rising prosperity, education, and better health; all these things seem to be good for the brain.

The idea that learning and thinking could ward off the physical diseases that bring on dementia has been controversial. "It was very fringy in the beginning," says Yaakov Stern, a neuropsychologist at Columbia University in New York, who has spent the last 25 years investigating this idea.

His interest was sparked in the 1980s, when a colleague claimed that more highly educated professionals were less likely to develop Alzheimer's disease. Sceptics thought there must be other explanations – perhaps these groups simply performed better on the cognitive tests used to diagnose Alzheimer's, or maybe the low income that goes hand in hand with lack of education was linked with other risk factors.

But these possibilities were ruled out by further studies, and the notion began to gain support that intellectual activities create a resilience to age-related decline across brain networks. Such "cognitive reserve" helps the brain to keep functioning despite mild physical deterioration, so the theory goes. "Just because you have pathology doesn't mean the brain says 'I'm going to drop dead,'" says Stern. "The brain says 'I'm going to do the best I can.'"

Happily for the cognitive reserve theory, populations did become better educated over the first half of the 20th century in many Western countries – including the UK and Denmark – through improved access to education and repeated increases in the school-leaving age. Both Brayne and Christensen think education is probably one part of the explanation for their findings.

Could this trend continue? The school-leaving age in the UK, for instance, has risen further since the people in the British study were at school. And in recent decades growing numbers of people have gone on to higher education. It remains to be seen if this will drive further improvements or whether, perhaps, there might be an upper limit on the protection afforded by early-life education.

Of course, for many of us it is too late to do anything about our schooling. But cognitive reserve is not just set by formal education. It is also affected by the mental demands of our jobs and our intellectual activities throughout life. "Cognitive function is modifiable right across the life course," says Marcus Richards, an epidemiologist with the UK Medical Research Council's Unit for Lifelong Health and Ageing in London. "It's never too late to take control of protecting it."

This idea has been seized upon by firms that produce "brain training" computer games. There is no question that practising a computer task makes you better at that task, as any gamer will tell you. But it remains uncertain whether such skills can help brain function in general, as the adverts claim, nor do we know how long any benefits might last.

The first study to show that a computer game could lead to benefits beyond the console appeared in 2013. A game designed to help people get better at multi-tasking enhanced their powers of attention and working memory for at least six months. But before placing any faith in such an approach, bigger and longer studies are needed, ideally ones that also measure rates of dementia.

In the meantime, there are less controversial – and arguably more enjoyable – ways of building your cognitive reserve, like taking up mentally taxing hobbies such as the card game bridge, or playing a musical instrument. A full social life may also protect against dementia, according to several studies.

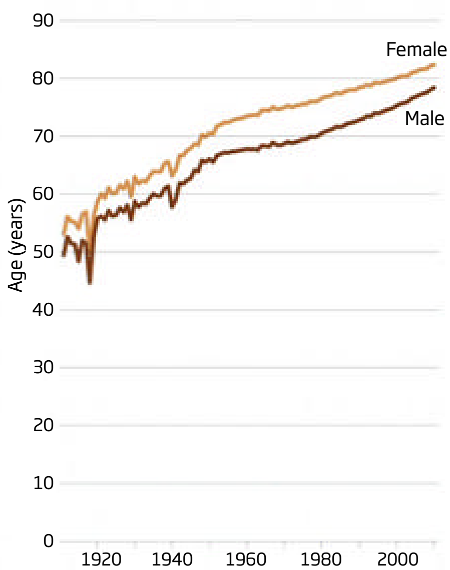
Just existing in the modern world – with its mobile phones and constant multimedia inputs – may be much more intellectually stimulating than it was 50 years ago. "Life now is very cognitively demanding for everybody," says Stern.

But mental stimulation is not the brain's only input – there are also its physical inputs, in the form of oxygen, energy and nutrients, delivered by the blood supply. Animal research has shown that healthy blood vessels are critical for good cognitive function in later life, minimising the risk not just of vascular dementia but the other forms too. "It would

Dementia curveball

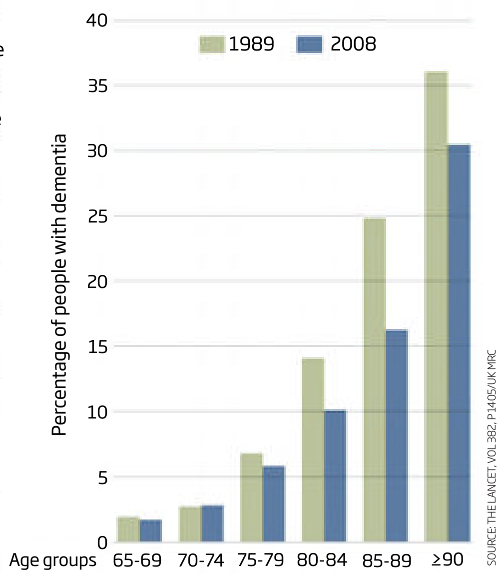
Life expectancy at birth in England and Wales

The steady increase in life expectancy has led to widespread predictions that there will soon be a sharp upsurge in the number of dementia cases...



Dementia prevalence

...but a recent study casts doubt on those predictions, as the rate of dementia among over-65s has fallen over the past 20 years



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be unreasonable not to think that vascular factors played a role," says Brayne.

Certainly rates of heart and vascular disease have been falling in Western countries since the 1970s, probably due to a mix of factors, including better awareness of the risks of smoking, high cholesterol and sedentary lifestyles, and the wider use of drugs to control blood pressure. One study that hinted at falling dementia rates – before the recent research in *The Lancet* – compared people's brain circulation with MRI scans, and found that later-born people had healthier blood vessels.

As the advice in the UK's National Dementia Strategy puts it: "What's good for the heart is good for the brain." The take-home messages are not new: don't smoke, try to stay in shape, and keep an eye on your blood pressure and cholesterol levels. But the recent evidence is providing more incentive than ever to pay heed.

What's more, the benefits of exercise have not only been shown in observational studies – where people who happened to be more active had less dementia – but also in randomised trials, the best kind of evidence. In other words, people asked to do more exercise had less intellectual decline as they aged.

There is, however, another very important factor affecting the health of our blood vessels, and that is what we eat. At the start of the 20th century, malnutrition was widespread in the UK – almost half the men called up to serve in the first world war were found not fit to serve for this reason. People suffered from a lack of vitamins and other micronutrients, as well as a general shortage of calories.

Diets improved markedly over the following decades, thanks to rising prosperity levels and public health measures such as free school meals. Thankfully child malnutrition is now rare in the UK. But could we use diet to improve our brain health still further?

Fish appeal

The most promising nutrients to target would be the antioxidant vitamins C and E, the B vitamins and folate, and omega-3 fatty acids, abundant in fish. But while observational studies show that eating too little of these substances heightens the risk of dementia, randomised trials of adding extra to the diet, in the form of supplements, haven't shown benefits. Such trials have limitations, though, says Richards; few last longer than a couple of years, while "people are accumulating these dietary exposures over decades".

Still, at the moment most researchers are reluctant to recommend anything other than the standard heart-healthy nutritional advice. That is a Mediterranean diet, rich in fruit and vegetables, with plenty of fish and not too much red meat or high-calorie junk food.

For what gives most concern is dietary excess rather than deficiency. Unlike people born in the first half of the 20th century, later generations have famously got themselves overweight. And today the West is suffering unprecedented levels of diabetes, which also predisposes people to dementia, according to recent research. Some even talk of Alzheimer's being a form of "brain diabetes".

As no one knows the relative contributions of all the possible factors that could explain why dementia rates have fallen – diet, education, health – it is impossible to confidently predict future disease rates. Yet it is likely that rising obesity and diabetes will affect future trends and that, says Richards, is something dementia researchers are watching with "nervous anticipation".

For the most pessimistic, the upsurge in these twin risk factors means we should not say that dementia rates are falling, merely that they fell between the two observed generations. For these reasons, and also simply because people are living longer, healthcare systems must be ready. "We still need a society which is adapted to cope with a lot of old people, and a lot of old people with some cognitive impairment," says Brayne. "That message doesn't go away because our paper shows an age-specific reduction."

Which may explain why the recent studies in *The Lancet* didn't get much attention at the G8 dementia press conference I attended at the launch of the summit in London: they might dilute the message that more research funding is needed as a matter of priority. Dementia research is certainly neglected compared with other conditions, in relation to the number of people they affect, and the promise of greater funding that emerged at the summit is essential.

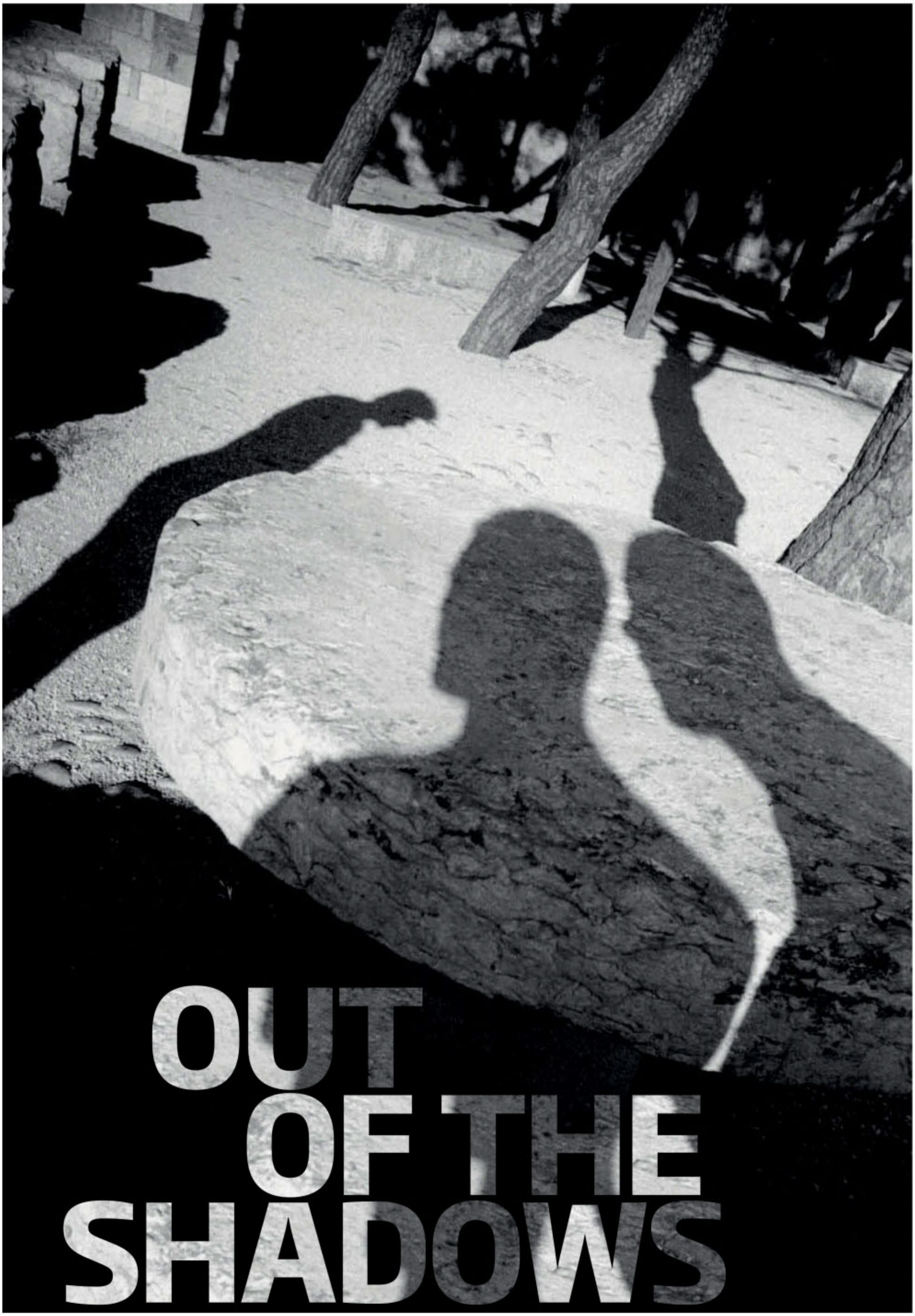
Yet the new studies suggest that researching preventative measures could be a sound investment. For while we may not get to choose when, where and to whom we're born, we do have some control over how we live.

My granddad, born in 1898, had barely any schooling, fought in the first world war and endured the austerity of the second. Born in 1977, I've had over two decades of education and a pretty comfortable life. On the other hand, while he dug graves for a living, I spend my work day mainly sitting down.

Still, since researching this article, I have felt more hopeful about my odds of enjoying a healthy and independent old age. I like the thought that it's within my power to improve those odds. Lately, when possible, I've even been walking instead of taking tube trains, and putting a bit more effort into eating enough fish and vegetables.

It's one thing if my body suffers the consequences of an unhealthy lifestyle – quite another if my mind does too. ■

MEYER/TENDANCE FLOUE



OUT OF THE SHADOWS

There are gentler ways of helping people with schizophrenia to reclaim their lives than fighting their delusions with drugs, says **Clare Wilson**

"I WAS trembling all the time. I couldn't shave. I couldn't wash. I was filthy," says Peter Bullimore. "I had become the archetypal schizophrenic. People would write on my windows: 'Schizo out' and I had one member of the public slash my face."

Today, that period of Bullimore's life is long behind him. He runs a mental health training consultancy in Sheffield, UK, and travels the world giving lectures on the subject.

You might think that Bullimore's turnaround is thanks to a wonder drug that has brought his schizophrenia under control. On the contrary: it was the side effects of his medication that had brought him so low. Instead, he opted for a seemingly radical course of action – he was slowly weaned off his medications and started a new type of therapy.

Bullimore's experience may be an extreme case, but we have long known that the drugs used to treat schizophrenia are very far from ideal. The downsides have always been seen as a necessary price to pay for relief from the condition's devastating symptoms, but now that idea is being called into question. Not only are the side effects of these drugs worse than we thought; the benefits are also smaller. Although people need to be taken off their drugs slowly and carefully to avoid a relapse, it looks as though outcomes are better in the long run if medication is kept to a minimum.

Now, there is growing interest in less damaging ways of helping people with the condition – including talking therapies and even forms of brain training. "People are starting to think differently about schizophrenia," says Max Birchwood, a psychologist at the University of Warwick in the UK. "Attitudes are definitely changing."

Since it was first described by European psychiatrists in the late 19th century, schizophrenia has often been seen as the most fearsome of all mental illnesses. Those affected usually start behaving oddly in their teens or 20s: hearing voices or seeing things that aren't there, often coupled with paranoid delusions, such as that members of their family want to kill them. These periods of psychosis may come and go unpredictably over the years, and they can be life-wrecking; 1 in 10 people with schizophrenia commits suicide.

Bullimore was 29 when it first hit. Ostensibly his life was on track: he ran a manufacturing business and was married with three children. But during a period of stress and overwork, things started to go badly wrong. He became convinced that cars were following him, and heard voices calling him a pervert. He saw the horror-film character Freddy Krueger looking back at him from mirrors. "It was a very frightening time," he says.

After a particularly terrifying hallucination one night, the next day, Bullimore smashed his business partner over the head with a telephone, then went home and curled up in a chair. "I stopped there for three weeks," he says. "All the voices were really, really bad."

The causes of schizophrenia are frustratingly mysterious. A long-standing theory is that the strange symptoms stem from a person's inability to distinguish between their own thought processes and inputs from the outside world. The imagined voices often say things the person could plausibly be thinking themselves, for instance (see "Life in the chatter box", page 38). But that doesn't so neatly explain the hallucinations and delusions, nor the memory and concentration difficulties that often come with schizophrenia.

Many genes that raise the risk of schizophrenia have been discovered, most of which seem to affect brain development or functioning – suggesting that the condition arises when something goes wrong with the brain's wiring as it develops and matures during adolescence. The prevailing theory is that the problems lie in neural networks that use the brain chemical dopamine, in part because drugs such as LSD and amphetamines, which can cause symptoms of psychosis, are known to raise dopamine levels.

Until the 1950s, there was little that doctors could do for someone like Bullimore, other than lock them up in an asylum and sedate them with strong tranquillisers called barbiturates. But then a new class of drugs was developed that proved helpful in treating people in the grip of acute psychosis. These ›

"I saw Freddy Krueger looking back at me from mirrors"

"I saw Freddy Krueger looking back at me from mirrors"

> *"Therapists can now accompany patients into their private hell using virtual reality"*

antipsychotics, as they became known, could calm people who were distressed or shouting, without knocking them out like tranquillisers did. The drugs were found to block dopamine signalling, bolstering the theory that overactivity of these pathways caused schizophrenia.

As wider use of antipsychotics allowed people with schizophrenia to live in the community rather than a psychiatric hospital, they are often credited with bringing an end to the often inhumane asylums. But right from the start these drugs were known to have unpleasant side effects.

Mental fog

The most obvious effects were physical: the slowing down and stiffening of movements. After a few weeks on the drugs, some people start to get strange tics and spasms of their face muscles. But the biggest complaints are about the way the drugs affect a person's thoughts. Antipsychotics seem to slow down people's thinking, worsening the memory and concentration problems caused by the condition itself. "My head was clouded and I couldn't think," remembers Bullimore. A recent study has confirmed suspicions that long-term use actually shrinks the brain.

They can also make people feel both unhappy and highly agitated, a potentially lethal combination, says psychiatrist David Healy, head of the North Wales Department of Psychological Medicine, Bangor, UK. His study of historical records from a Welsh mental hospital showed that 100 years ago people with schizophrenia were no more likely to kill themselves than the general population. This suggests it is modern drugs that cause schizophrenia's high suicide rate, he says. "They can produce some of the most uncomfortable experiences a human can have."

Yet the potential side effects were seen as the necessary cost of controlling a dangerous illness. Scores of trials had shown that after a person's initial psychotic breakdown had been brought under control, if they stopped taking their medication they were at higher risk of relapse.

Those studies were short, though, typically lasting from months to a year, with the longest being two years. Now for the first time there has been long-term follow-up of a randomised trial comparing people who reduced their use of antipsychotics with those who continued their treatment. The findings have sent shock waves through the world of psychiatry.

In this Dutch study, while the people assigned to the dose-reduction group initially had a higher relapse rate, after two to three years, the people who stayed on their drugs had "caught up", and after seven years differences between the two groups were statistically insignificant (see graph, right).

More importantly, those in the dose-reduction group had more than double the chance of achieving what psychiatrists call "functional recovery" – 40 versus 18 per cent.

In other words, even though they might have occasional symptoms, they could hold down jobs and look after themselves. "That's what's meaningful to the patient," says Lex Wunderink, a psychiatrist at Friesland Mental Health Services in Leeuwarden, the Netherlands, who led the study. Wunderink speculates that this ability to function independently is being hampered by the dopamine-suppressing effects of antipsychotics.

As the case against the drugs mounts, some are beginning to question whether the dopamine theory itself is right. After all, there has never been strong evidence that people with schizophrenia have overactive dopamine signalling, says Joanna Moncrieff, a psychiatrist who has written a polemic against antipsychotics called *The Bitterest Pills*. Along with others, Moncrieff believes antipsychotics may simply be another version of the tranquillisers used back in the 1950s. "If someone's preoccupied by their psychotic symptoms, if you can dampen down their thinking, they lose interest in their delusions," she says.

Today, there are rival theories about the causes of psychosis. Some cases may be caused by an autoimmune reaction to certain proteins on the surface of brain cells. Other research implicates different brain chemicals, including glutamate and serotonin. Several compounds that boost glutamate signalling in the brain have reached early clinical trials, although it is too soon to say if they will pass the larger trials needed to prove their worth.

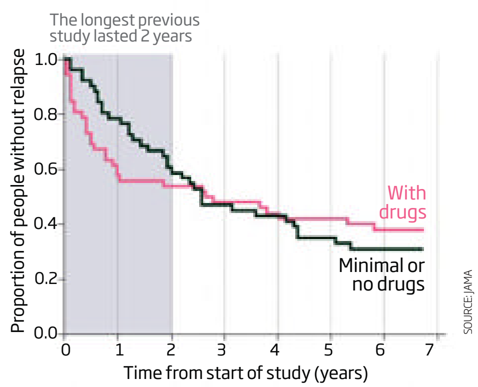
In the meantime, the problems with antipsychotics are leading to growing interest in a range of alternatives to medication. The most promising are talking therapies like cognitive behavioural therapy (CBT), which aims to train people in new ways of thinking. CBT is often used for depression and anxiety to combat negative thought patterns, but psychiatrists have been sceptical about its usefulness for schizophrenia. "People say CBT can't possibly work – schizophrenia is an intrinsic brain disorder," says Birchwood, who helped pioneer CBT. "How can talking therapy change anything to do with the brain?" Yet many studies have shown it to be useful.

There are at least two possible explanations. For starters, people are more likely to descend into psychosis if they are stressed and unhappy – as Bullimore did. "It's a very stress-sensitive disorder," says Birchwood. Many of the talking therapies help people cope better

What makes a recovery?

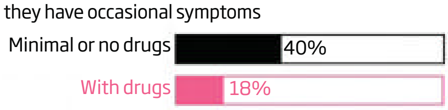
People with schizophrenia are often forced to take antipsychotic drugs for the rest of their lives

Short-term studies had suggested that drugs reduce the risk of relapse – but a recent paper indicates that the longer-term picture is different



Life without drugs

What's more, people weaned off the drugs have a greater chance of a "functional recovery" – the ability to hold down a job and look after themselves, even if they have occasional symptoms



with everyday problems, such as family arguments, reducing the stress that could trigger a breakdown.

Another benefit of talking therapies is that, while unable to eliminate the voices and hallucinations, they do help people feel less disturbed by them. One goal of CBT is to help people realise the voices don't have any power over them. "That enables them to disengage from the voices," says Birchwood.

Rather than CBT, Peter Bullimore received help from informal group therapy that explored the psychological origins of his troubles. Bullimore was sexually abused from the age of 5. "The voices would repeat what the abuser had said," he says. "This was an area of my life I hadn't dealt with."

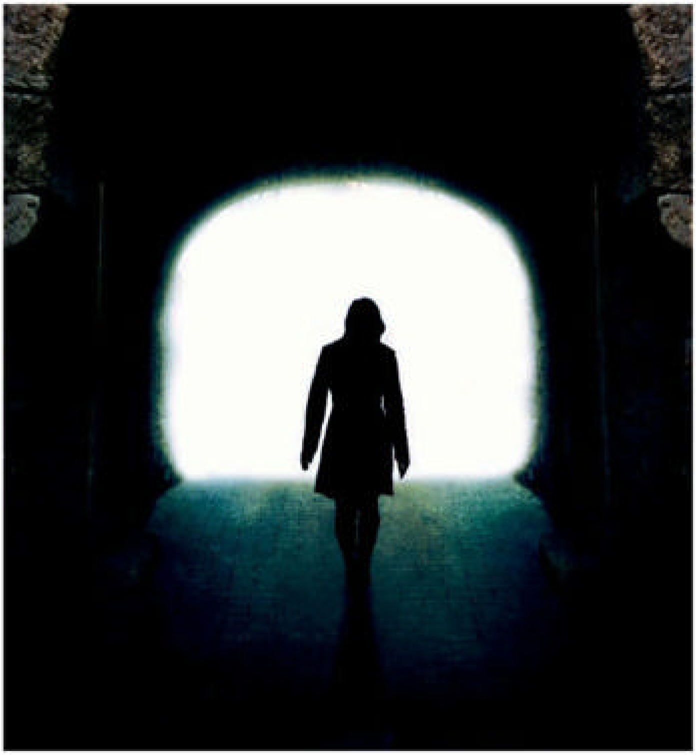
And it may be possible to enhance the power of talking therapy with a new computer-based technique designed specifically to combat aggressive voices, which looks promising from a small pilot study. Patients were helped to make a computer avatar that "embodies" the voice in their head. Sitting in another room, the therapist then had their speech digitally altered so they could be the voice of the avatar, speaking to the patient through the computer monitor. "We accompany the patient into their own private hell," says Julian Leff, a psychiatrist at the Institute of Psychiatry in London, who designed this approach.

Over several sessions, the patient was encouraged to stand up to the avatar, while the therapist made it become less aggressive in response. The approach helped 15 out of 16 people in the study, who found that it reduced the frequency and intensity of the voices. Three people even reported that they stopped hearing the voices altogether. "What they learn to do with the avatar they can then do outside the sessions," says Leff.

A different approach is to target the memory and concentration problems that plague people with schizophrenia. Once done with pen and paper, there are now several "brain training" computer programs in trials that are marketed specifically for this condition. Typically they comprise a range of tasks designed to improve people's mental skills in a variety of ways, particularly memory, attention and logical reasoning.

At the least, this should help people stay in work or education – but the benefits may be even greater. Some think the cognitive problems could lie behind the psychosis, perhaps because they lead people to mix up external sensations with their own thoughts. Carefully targeted brain training programs could reverse the core symptoms of psychosis if the illness is caught early enough, says Sophia Vinogradov at the San Francisco Medical Center. She says a small study done by her group has shown that brain training for people in the early stages of schizophrenia reduced psychotic symptoms.

See the light: therapy helps people to escape their demons



MOHAMAD ITANI/PLAINPICTURE

The turning tide

It is much too soon to say whether brain training can indeed reverse psychosis, but talking therapies have certainly been shown to reduce relapses. NICE, the agency that produces clinical guidelines for the UK National Health Service, recommends that talking therapies should be offered to all those with schizophrenia, in addition to antipsychotic drugs. The British Psychological Society has now also launched a report calling for greater access to talking treatments. Unfortunately, it is cheaper and easier to just dole out the tablets. "Most [health] trusts have not invested sufficiently in training to deliver these services," says Birchwood.

And many doctors think the evidence favours the continued use of antipsychotics. "Nobody would say that antipsychotics are perfect, but they are effective in preventing relapse," says David Taylor, head of pharmacy at the Maudsley Hospital in London, the UK's largest psychiatric teaching hospital. While the seven-year Dutch study suggests that people do better in the long-term without medication, that needs replicating before it changes practice. "It is something that needs more investigation," he says. In Taylor's experience, people can avoid some of the worst side effects by switching medicines. "They can usually find a drug which is reasonably well tolerated," he says.

And when it comes to people in the throes of a severe psychotic breakdown, Taylor says antipsychotics are the only option. "Acute psychosis is not a pleasant condition. It's extremely frightening and debilitating," he says. "The more rapidly those symptoms can be relieved the better."

Indeed, most of those who favour alternative treatments agree drugs are unavoidable at such times. But subjecting people to a lifetime of compulsory antipsychotics seems to be on the way out. The tide is already turning in some parts of the world, with Finland minimising drug use and New York experimenting with such a policy. The Finnish scheme's success is gaining worldwide attention, and it seems likely that other countries will follow their lead.

There are also efforts to give people who hear voices practical support to continue with their lives, such as sheltered accommodation or supported employment. "It is possible for people to have ongoing symptoms and yet hold down a job," says Birchwood.

It's a transformation that would be welcomed by Bullimore. These days he still hears voices, although now they are quieter and are usually friendly, or at least neutral. He sometimes hears his dead mother giving guidance, for instance, and another voice helped him write a book. "That was my creative side," he says. "My relationship with my voices has changed. It has woken me up to a new world." ■

Depression that resists every treatment is on the rise, but luckily the key to a cure may already be in our hands, says **Samantha Murphy**

Rebuilding broken brains

ONE OF Vanessa Price's first chronic cases involved a woman we'll call Paula. Paula came to the London Psychiatry Centre, where Price is a registered nurse, after two years of unrelenting depression. First she stopped seeing her friends. Then she stopped getting out of bed. Finally, she began cutting herself. Sessions with a psychiatrist didn't help, neither did medication. In fact, they made it worse. Paula had joined the ranks of people diagnosed with treatment-resistant depression.

The steady rise in this diagnosis over the past two decades reflects a little-known trend. The effectiveness of some antidepressant drugs has been overstated, so much so that some pharmaceutical companies have stopped researching them altogether.

The stubborn nature of these cases of depression has, however, spurred research into new and sometimes unorthodox treatments. Surprising and impressive results suggest that we have fundamentally misunderstood the disorder.

In fact, the new research has opened the door to thinking about depression not as a single condition but as a continuum of illnesses, all with different underlying neurological mechanisms, which may hold clues to lasting relief. This promise has sparked a renaissance in drug development not seen since the 1950s.

Depression is an illness whose brutality is matched only by its perverseness. Estimates vary, but it is likely that close to one in six of us can expect to struggle with it at some point in our lives. The symptoms are cruel – including insomnia, hopelessness, loss of interest in life, chronic exhaustion and even an increased risk of ailments such as heart disease. Depression also leads people to cut themselves off from others, a tendency exacerbated further by the continuing stigma surrounding the condition, thought to deter over half of depressed people from seeking treatment. Untreated, depression can lead to suicide; the World Health Organization estimates there is one suicide every 40 seconds. These factors all contribute to the WHO's assessment of depression as the leading cause of disability in the world.

What causes people to become depressed? The dominant theory is that depression results from a chemical imbalance in the brain, with the neurotransmitter serotonin as the prime suspect. Many trials have linked depression to low levels of serotonin, something that was thought to disrupt the brain's ability to pass messages across synapses, the tiny gaps between neurons.

Mysterious decline

The theory was that a boost in serotonin should return neural signalling and mood to normal levels. The first drug based on the serotonin hypothesis – fluoxetine, better known as Prozac – was launched in the late 1980s, and nearly all subsequent antidepressants have operated on the same general principle: keep levels of serotonin high by preventing the brain from reabsorbing and recycling it.

Although such drugs remain the go-to tools for lifting depression, however, they seem to be getting less effective (see "False dawn", page 62). Clinical trials in the 1980s and 1990s indicated that these drugs would help 80 to 90 per cent of depressed people go into remission. But studies in the 2000s showed that standard antidepressants work only in 60 to 70 per cent of people, a decline that was underscored in 2006 when the National Institute of Mental Health (NIMH) in Bethesda, Maryland published the results of a massive, nationwide clinical trial. Unlike many pharmaceutical trials – which often screen out certain participants – this was the first to measure the effectiveness of antidepressants in a population representative of the real world. The results were disquieting: few of the 2876 participants fully recovered without switching to or in many cases adding other medications.

What can explain this apparent decline in the potency of antidepressants? Perhaps the drugs themselves were never quite as effective as claimed. To approve a given antidepressant, the US Food and Drug Administration only requires two large-scale studies to verify that the drug is superior to a placebo. However, pharmaceutical companies are under no obligation to supply the FDA with every study they have conducted; only the positive ones.

When David Mischoulon, director of psychiatry research at Massachusetts General Hospital in Boston, sifted through previously unpublished data from pharmaceutical trials, he says he found many more negative results than positive ones: a high percentage of studies showed that the drugs were only slightly better than the placebo. "Now we think it's more in the neighbourhood of 50 per cent of people who may respond to a given antidepressant," Mischoulon says. So the rise of treatment-resistant depression might be a reflection of the time it has taken doctors to see that reality reflected in their clinics.

The next question then is why – could the drugs' failure be down to a problem in our ›

"After 15 sessions of magnetic stimulation, getting out of bed began to seem like a good idea to Paula"

understanding of the underlying mechanism? After all, untreatable depression wasn't the only inconsistency to cast doubt on the serotonin hypothesis. A 2007 study, for example, showed that serotonin levels in the brains of depressed people not receiving treatment were double those in volunteers who were not depressed.

In the wake of this confusion, several pharmaceutical companies decided to stop their work on mood disorders altogether. GlaxoSmithKline – the company that makes the well-known antidepressants Paxil and Wellbutrin – announced in 2010 that it would halt research into depression.

Without new drugs to help the growing number of people whose depression seemed incurable, clinicians found themselves in a bind. "We got used to telling our patients to hang in there," says Carlos Zarate, a neurobiologist who directs research on mood disorders at the NIMH. While they waited for a drug to start working, doctors relied on intense and frequent therapy to ensure depressed people didn't lose their jobs or attempt suicide. That strategy wasn't always effective. "I felt like a failure," Paula says. After nothing worked, she took an overdose of sleeping pills. It wasn't that she wanted to die, she says; she simply didn't care if she lived or not.

Last resort

Desperate to help their charges, some frustrated clinicians began to look for new therapies. Their investigations were all over the map: electrical and magnetic brain stimulation, and a veterinary tranquilliser known as ketamine. But they worked.

After drug treatment and behavioural therapy failed, what saved Paula was a groundbreaking therapy called repetitive transcranial magnetic stimulation (rTMS). It was the stuff of movies. Paula would put a cap on her head and sit under a big machine for about 20 minutes while a brief electric current passed through a small coil positioned a few inches above her left temple, creating a fleeting high-intensity magnetic pulse.

After 15 sessions, Paula stopped wanting to hurt herself. Getting out of bed began to seem like a good idea. When her friends dragged her to a concert, she was surprised to find herself enjoying it. "That would have been unthinkable before," she says.

Price was surprised. "I have to be honest, I was dubious," she says. "But I am absolutely stunned by the results." Price and her team have now treated 99 people there using rTMS, of which 64 per cent made a full recovery.

Price's experience is reflected in a growing body of research over the past few years, which finds that rTMS seems particularly effective against treatment-resistant depression. In one study, it benefited 12 out of a group of 28 people for whom nothing else had worked. And a review of 18 studies found that people with treatment-resistant depression who were given rTMS were five times more likely to go into remission than those receiving a sham treatment.

At the moment, rTMS treatment is not cheap. In the UK, the procedure is not available on the National Health Service, so the people treated at Price's clinic have to shell out around £8000. Australia's Medical Services Advisory Committee have decided there is insufficient evidence that rTMS works and so have declined to fund such treatments.

In the US, some clinicians have turned to a more affordable option that shows similar promise: cranial electrical stimulation. It simply involves delivering a tiny current with two electrodes strapped to the head using a sweatband. Unlike rTMS equipment, which is bulky, this device is roughly the size of a deck of cards and is available with a prescription.

Stephen Xenakis, a doctor who is also a retired general and a former adviser to the US Department of Defense, uses the device not only on his patients, but also on himself. He asks his patients to use it for 20 minutes at a time, twice a day. "Sometimes this can help in ways that the medications don't," he says. "The thing I've seen it help most with is insomnia and anxiety", conditions which both fuel, and are fuelled by, treatment-resistant depression.

But the most promising option in terms of convenience could be the drug ketamine. As early as 2000 a study of eight people with long-standing, untreatable depression suggested that a single dose of ketamine, given intravenously, would almost immediately lift symptoms.

Several studies have replicated the results. In a clinical trial involving 72 participants, researchers from the Icahn School of Medicine at Mount Sinai in New York found that people who'd failed to respond to any other treatments experienced relief from suicidal thoughts when given ketamine intravenously for 40 minutes. Zarate says that a growing body of research suggests the drug could work for 60 per cent of patients. "Some people go into remission within a day," he says, and can remain free from depression for up to 10 days.

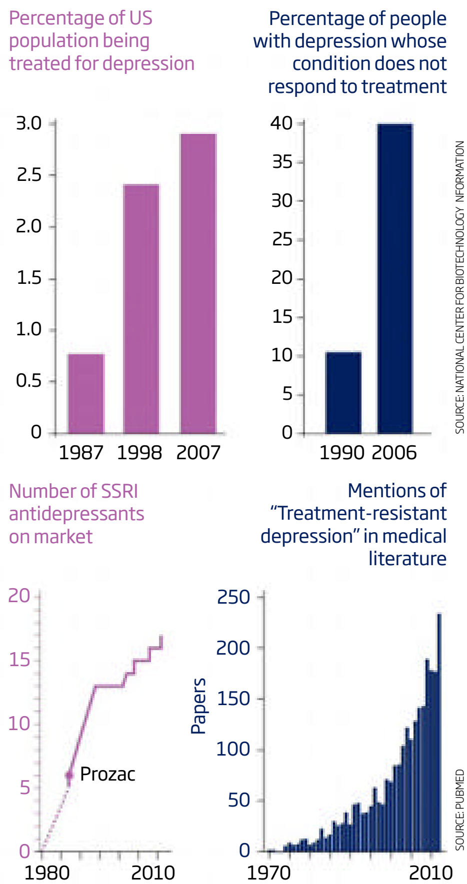
But what mechanisms might explain the success of a seemingly unrelated group of treatments where traditional ones had failed? When researchers began to piece together the results, the link they found was glutamate.

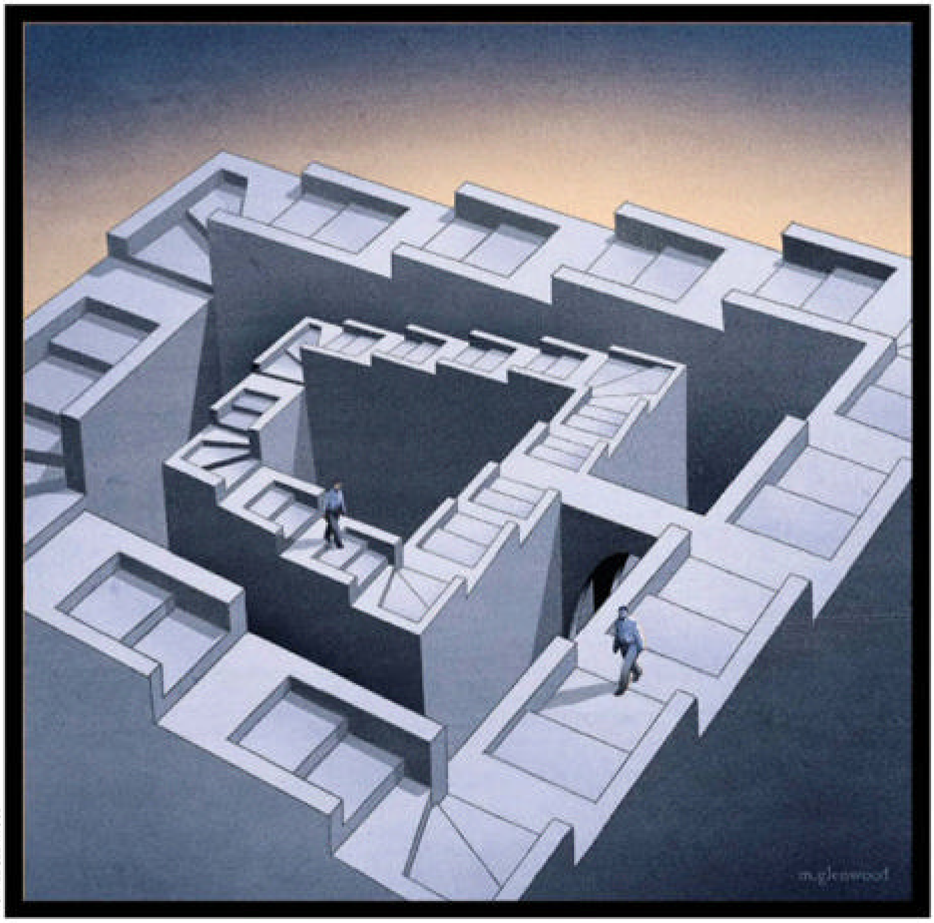
Glutamate is the most dominant stimulatory neurotransmitter in the brain, playing a key role in learning, motivation, memory and plasticity. Some researchers think that levels of glutamate, like serotonin, are too low in the depressed person's brain.

But that's where the similarity ends. Rather than simply aiding in the transport of messages between neurons, glutamate may be a factor in helping the brain's neurons repair themselves. This would dovetail with a theory of depression that has gained a significant following in recent years: that depression causes some dendrites – message-relaying "fingers" at the ends of neurons – to shrivel. The synapses become like broken bridges, with messages unable to cross between the affected neurons. Among other evidence to

False dawn

New antidepressants that boost serotonin levels looked promising when launched in the 1980s. But since then, depression appears to have become more common and more stubborn

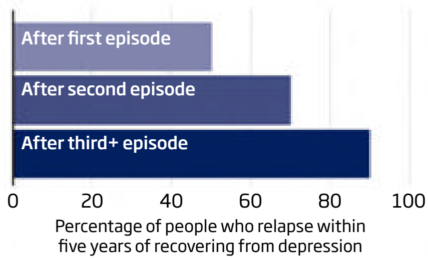




MICHAEL GLENWOOD

High risk

The risk of relapse increases substantially with every episode of depression, a possible clue to an underlying physical mechanism



SOURCE: KELLER MB AND BOLAND RJ/PSYCHIATRY

support this theory is the finding that each successive episode of depression seems to leave people more vulnerable to a subsequent episode (see graph, right).

The ketamine trials were the first clue that glutamate might help. Ketamine sets off a complex chain reaction. First, it blocks the specific receptors that glutamate binds to, releasing a tide of the chemical into synapses. That leads to an increase in a protein called brain-derived neurotrophic factor which, animal studies show, causes the dendrites to sprout new spines, helping them to receive messages from neighbouring neurons.

When Ronald Duman of Yale University injected rats with ketamine, he saw a burst of glutamate in rodents' prefrontal cortex – along with a fast increase in the formation of new synapses. Other studies show that rTMS also raises glutamate levels to cause similar structural effects.

Instead of enabling a broken brain to pass on messages in spite of damage, then, glutamate may be teaching a depressed brain how to rebuild itself. The feeling, Zarate says, is that in some cases, depression may be better explained as a disorder of neuron structure than being due to a chemical imbalance. But that doesn't necessarily mean serotonin is out of the picture.

"I don't think we were wrong," says Mischoulon. "I think we didn't have the whole story." The *Diagnostic and Statistical Manual of Mental Disorders*, the bible of psychiatry in the US, already subdivides depression into categories, including postnatal and bipolar, but it considers their underlying neurophysiological mechanisms to be the same. The new research could change that. "We're now thinking that there are probably a wide continuum of illnesses lumped together under the heading of depression," he says, with either glutamate or serotonin as the culprit.

New beginnings

If so, how will individuals know which type of depression they have? One way to find out would be to see which drugs are effective. "If you don't get a response from ketamine the first day, you probably never will," says Zarate. Work to develop a diagnostic test is already under way. "We're trying to identify certain factors in the blood associated with certain subtypes of depression," says Mischoulon. Brain scans are another possibility: these can already show whether a person will respond better to talk therapy or medication.

All this research is still very much in its infancy, but well before biomarker tests arrive, there should be a raft of new medications that exploit glutamate to combat depression. At least five companies have been working on ketamine derivatives. One example is GLYX-13, which is showing promise in clinical trials. Several pharmaceutical companies are also developing pills and intravenous drugs, the first of which should be with us within a couple of years. Zarate says some pharmaceutical companies are even focusing on glutamate drugs for first line use rather than as a last-resort treatment for depression.

One tantalising possibility remains. If glutamate affects neuroplasticity, could that lead to lasting structural changes in the brain? George Aghajanian at Yale, whose seminal work inspired all the ketamine investigations, says that in people predisposed to recurring depression, ketamine may help neurons permanently maintain new and thicker connections. In recent work on rats, he found that the drug, when combined with other compounds, "leads to long-term structural repairs in the brain", he says. But whether the same is true in humans will require much further study.

Whatever the future holds, glutamate – and the new possibilities it has raised – has at least enabled us to start thinking about depression in a different way. That is rare in the troubled waters of psychiatry. ■

SUSAN KAY/MILLENNIUM IMAGES

Fits of rapture

Why do bliss and ecstasy sometimes accompany epileptic seizures? The answer might shed light on religious awakenings, joy and the sense of self, says **Anil Ananthaswamy**

IT WAS one of the most profound experiences of Fyodor Dostoevsky's life. "A happiness unthinkable in the normal state and unimaginable for anyone who hasn't experienced it... I am then in perfect harmony with myself and the entire universe," he told his friend, Russian philosopher Nikolai Strakhov. What lay behind such feelings? The description might suggest a religious awakening – but Dostoevsky was instead describing the moments before a full-blown epileptic seizure.

Those sensations seem to have informed the character of Prince Myshkin in Dostoevsky's novel, *The Idiot*. "I would give my whole life for this one instant," the prince says of the brief moment at the start of his epileptic fit – a moment "overflowing with unbounded joy and rapture, ecstatic devotion, and completest life".

For a long time, the novelist was thought to be exercising his artistic licence and exaggerating this "ecstatic aura", rather than accurately representing a real phenomenon. Most epileptic attacks are terrifying, after all, and many people with epilepsy would give a lot not to experience another. But as more and more people with the condition have come forward reporting the same feelings, there has been a renewed interest in this "Dostoevsky syndrome" – and neuroscientists are now on the hunt for the cause.

Besides explaining those feelings of bliss experienced by Dostoevsky and other people with "ecstatic epilepsy", their investigations could also open a window on self-awareness more generally. The question is, are there safe ways we could all be transported to similar states of being?

Epileptic seizures are broadly divided into two groups: generalised and focal. In generalised seizures, electrical discharges overwhelm the outer layer of the brain, the cortex, and often lead to loss of consciousness. Ecstatic seizures seem to be of the second kind. In focal or partial epilepsy, the electrical storm is confined to a small region of the brain and the person usually remains conscious. This type of seizure can turn into a generalised one if the errant electrical signals spread.

Despite Dostoevsky's famous accounts, records of ecstatic feelings among other people with epilepsy have been scarce – perhaps because this kind of seizure is rare, but also because people are reluctant to divulge such personal feelings. "I think that they are probably underestimated," says Fabienne Picard, a neurologist at the University Hospital in Geneva, Switzerland. "Because the emotions are so strong and strange, maybe they feel embarrassed to speak about them; maybe they think the doctor will find them mad."

Picard's interest in the subject was piqued when she came across Dostoevsky's writings while making the film *Art & Epilepsy*. She soon realised that some of her patients were having very similar experiences. "When they really explained their feelings, it was incredible," says Picard. "It was very close to Dostoevsky's descriptions."

Unbelievable harmony

As Picard cajoled her patients to speak up about their ecstatic seizures, she found that their sensations could be characterised using three broad categories of feelings. The first was heightened self-awareness. For example, a 53-year-old female teacher told Picard: "During the seizure it is as if I were very, very conscious, more aware, and the sensations, everything seems bigger, overwhelming me." The second was a sense of physical well-being. A 37-year-old man described it as "a sensation of velvet, as if I were sheltered from anything negative". The third was intense positive emotions, best articulated by a 64-year-old woman: "The immense joy that fills me is above physical sensations. It is a feeling of total presence, an absolute integration of myself, a feeling of unbelievable harmony of my whole body and myself with life, with the world, with the 'All'," she said.

When I met another one of Picard's patients, a 41-year-old Spanish architect, she talked of that same connectedness. "You are just feeling energy and all your senses," she said. "You take in everything that is around, you get a fusion."

As Picard began looking for the neurological origin of the disorder, such descriptions pointed her towards the insula – a region of the cortex that is of growing interest to scientists studying consciousness. It is buried inside the fissure dividing the frontal and parietal lobes from the temporal lobe, and its main function seems to be to integrate "interoceptive" signals from inside the body, such as the heartbeat, with "exteroceptive" signals such as the sensation of touch.

There is also evidence that the processing of these signals gets progressively more sophisticated looking from the back of the insula to the front. The portion of the insula closest to the back of the head deals with objective properties, such as body temperature, and the front portion, or anterior insula, produces subjective feelings ›

RUSLAN KRIVOBOK/RIA NOVOSTI

Dostoevsky described his seizures as "unthinkable happiness"

"BRAIN STIMULATION TRIGGERED A PLEASANT FLOATING SENSATION AND A 'SWEET SHIVER' IN THE PATIENT'S ARMS"

of body states and emotions, both good and bad. In other words, the anterior insula is responsible for how we feel about our body and ourselves, helping to create a conscious feeling of "being". This led Bud Craig at the Barrow Neurological Institute in Phoenix, Arizona, to argue that this part of the brain is the key to "the ultimate representation of all of one's feelings – that is, the sentient self".

Mapping ecstasy

The altered self-awareness that Picard's patients experienced would certainly implicate the anterior insula in ecstatic epilepsy – but more direct evidence was difficult to come by. Over the past few years, Craig, Picard and their colleagues have managed to find a few people with ecstatic epilepsy who agreed to have their brains imaged during seizures. The researchers injected the patients with "nuclear tracers", which accumulate in different parts of the body and are detected using a device called a gamma camera. Areas with higher blood flow absorb more of the tracer, and the scans revealed increased blood flow – which is assumed to reflect higher neuronal activity – at or near the anterior insula during seizures.

But such imaging studies cannot be conclusive because they cannot pinpoint the hyperactive regions precisely. It takes about 30 seconds for active brain regions to absorb the tracers, but seizures usually spread rapidly to many different regions, making it difficult to locate their origins with certainty.

More concrete proof didn't come until March 2013. I was visiting Picard in her office in Geneva at the time, when she received an email from Fabrice Bartolomei, a neurologist at Timone Hospital in Marseille, France. Bartolomei's surgical team had implanted electrodes inside the brain of a young woman suffering from epilepsy with episodes of ecstatic seizures. Bartolomei's message read, "We have explored the patient… The stimulations in the anterior insula trigger a pleasant sensation of floating and chills." Picard shot off a quick reply: "I'm so happy!"

Bartolomei's patient was a 23-year-old woman. She started having seizures when she was 15, and stopped going to school as a result. She also had a difficult personality with aggressive, sociopathic tendencies. Even so, before her seizures rendered her unconscious, they always began with moments of ecstasy, much like Dostoevsky's.

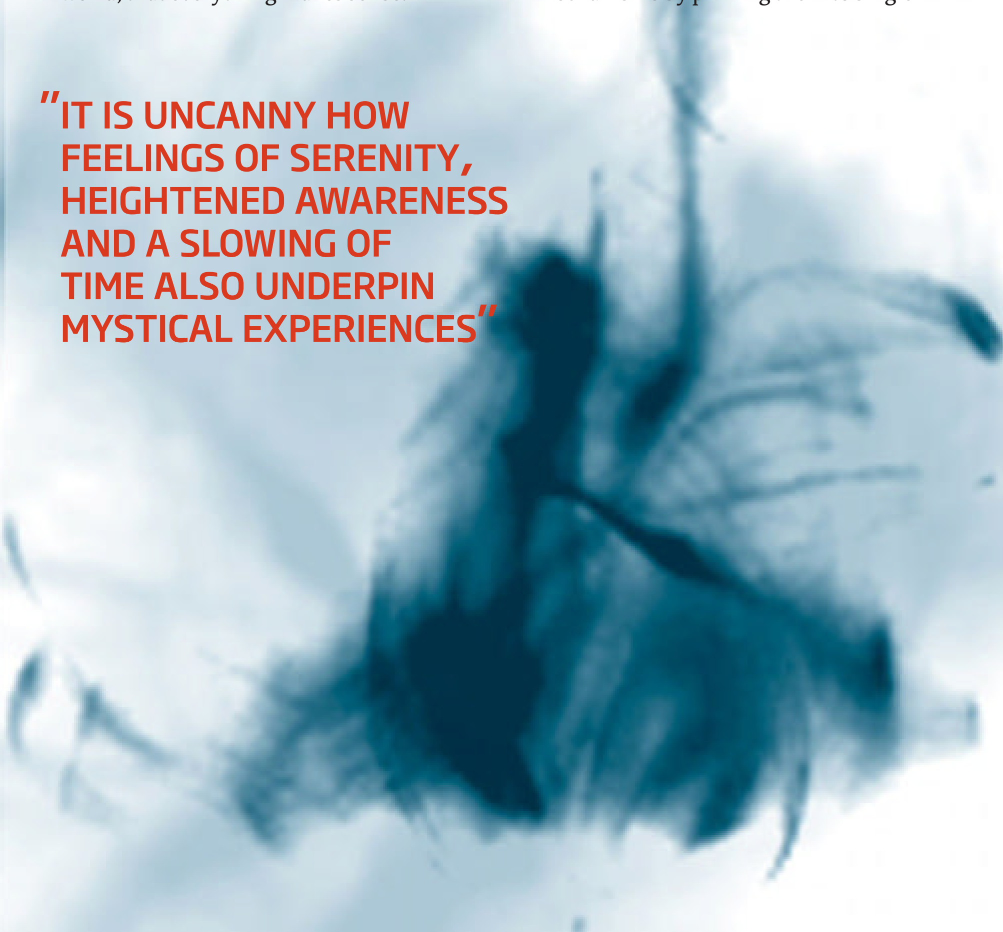
Because drugs were not effective in treating the woman's epilepsy, she gave Bartolomei the go ahead to insert electrodes into her brain to find the focus of the seizures and possibly surgically remove the tissue that was setting off the attacks. Bartolomei's measurements suggested that the seizures began in the temporal lobe but spread to the anterior insula in less than a second – supporting the idea that hyperactivity in this region was triggering the blissful feelings that preceded the generalised seizure.

Next, Bartolomei used the electrodes to stimulate the young woman's brain in specific places. The technique allows surgeons to double-check that they have found the cause of the seizure, and helps prevent them damaging or cutting away any key brain tissue. It is also the best way to determine the function of different brain regions. Much of what we have learned about the brain has come from people who have undergone this kind of exploration while conscious.

Unfortunately, the procedure can be uncomfortable, which caused Bartolomei's patient to become aggressive. But when the electrode in the anterior insula was activated, her feelings changed. "I feel really well with a very pleasant funny sensation of floating and a sweet shiver in my arms," she said. These sensations were identical to the ecstatic aura that usually accompanied her epilepsy, she said. Based on these tests, Bartolomei suggested surgery, but the woman opted against it. The experiences nevertheless gave Picard some much needed evidence of the anterior insula's role in ecstatic seizures.

More studies will be needed to confirm the effect, but Anil Seth, a neuroscientist at the University of Sussex in Brighton, UK, is impressed by these findings. "The fact that the direct electrical stimulation of the insula does elicit these kinds of feelings is pretty compelling," he says. He studies people with depersonalisation and derealisation disorders, which are associated with a dysfunctional or underactive insula, and they describe the world as being drained of sensory and perceptual reality. In a way, a hyperactive insula during ecstatic seizures produces the opposite effect, he says.

Investigating how abnormal activity in the anterior insula leads to disorders like ecstatic epilepsy might also help scientists establish how this region creates our normal experience of self-awareness. Picard's patients reported feelings of certainty – the sense that all is right with the world – which would seem to fit with a theory that the anterior insula is involved in predicting the way the body is going to feel in the next instant. Those predictions are then compared with actual sensations, generating a "prediction error" signal that might help to determine how we react to a changing environment. If the prediction error is small, we feel good, if it is large we feel anxious. It is possible that the electrical storm in the anterior insula may be disrupting the comparator mechanism, causing there to be no prediction error. As a result, the person is left feeling as if nothing is wrong with the world, that everything makes sense.



"IT IS UNCANNY HOW FEELINGS OF SERENITY, HEIGHTENED AWARENESS AND A SLOWING OF TIME ALSO UNDERPIN MYSTICAL EXPERIENCES"

Besides the sense of expanded awareness and certainty, people like Dostoevsky have also recorded the strange sense that time is slowing down during their seizures. This might reflect the way the insula samples our senses. Craig argues that the anterior insula usually combines interoceptive, exteroceptive and emotional states to create a discrete "global emotional moment" every 125 milliseconds or so – dividing our feelings into separate frames, like a film reel. He posits that a hyperactive anterior insula may generate these global emotional moments faster and faster, leading to a sense that time is slowing.

Under fire

It is uncanny how these feelings of serenity, heightened awareness and a slowing of time also underpin apparent religious experiences. Have mystics over the ages been having ecstatic seizures? Picard's patients could see why some might attribute religious meaning to their seizures. "Some of my patients told me that although they are agnostic, they could understand that after such a seizure you can have faith, belief, because it has some spiritual meaning," she says.

Needless to say, our understanding of this crucial brain region and its role in ecstatic epilepsy is still in its early stages. Neuro-imaging studies sometimes come under fire for oversimplifying complex brain mechanisms by pinning them to single regions (for more on this, see "Hidden depths", page 24). Some might argue that the recent work on the insula is no different. Most experiences, after all, are the result of complex networks of activity.

It is important to recognise, for instance, that the insula is responsible for bad feelings as well as good, with studies showing that it is often highly active during feelings of anxiety. So it will be crucial to understand exactly what sort of activity contributes to each feeling.

That may depend on what's going on elsewhere in the brain, but a better understanding may also come with more detailed maps of the insula itself. There is some evidence that the left side is more relevant for the positive feelings in question, whereas the activation of the right-hand side may be more closely linked to negative feelings. Tellingly, some people experiencing ecstatic epilepsy report alternating pleasant and unpleasant sensations – so scanning them during a seizure might help researchers to elucidate the basis of such emotions in more detail. Researchers could then work out how the different parts of the insula interact with each other and function within broader brain networks to produce everyday experiences.

We could also gain insights into the insula's role by other means. Craig and Picard think that feelings evoked by drugs like amphetamine, ecstasy and cocaine may share many similarities with ecstatic epilepsy. These chemicals usually trigger a flush of neurotransmitters through the brain, and there is evidence that, following drug use, levels of dopamine in the anterior insula are unusually high relative to other regions. The neurotransmitter serotonin may be similarly implicated in the case of ayahuasca, a psychedelic brew long associated with shamanistic rituals in the Amazon. Again, nuclear imaging results show increased blood flow in the anterior insula about 100 minutes after consumption.

Fortunately, there may be safer ways to come close to the same feelings. Meditators often experience the time-slowing, heightened self-awareness and feelings of profound well-being that come with Dostoevsky syndrome. In 2007, Richard Davidson of the University of Wisconsin in Madison and his colleagues studied 15 expert and 15 novice meditators. They found that the deeper the meditative state, the greater the activity in the anterior insula.

If that does reflect the same "unbounded joy and rapture" that Dostoevsky's Prince Myshkin reported, it certainly doesn't come easily: the experienced meditators had logged more than 10,000 hours of practice to see these effects. You may not need to give your "whole life for this one instant", as Prince Myshkin put it – but it may not be far off. ■

A light on psychobiotics

The mind-altering effects of gut bacteria are finally being understood. This knowledge offers a new way to improve our mental health, say **John Cryan** and **Timothy Dinan**

WE HAVE all experienced the influence of gut bacteria on our emotions. Just think how you felt the last time you had a stomach bug. Now it is becoming clear that certain gut bacteria can positively influence our mood and behaviour. The way they achieve this is gradually being uncovered, raising the possibility of unlocking new ways to treat neurobehavioural disorders such as depression and obsessive-compulsive disorder (OCD).

We acquire our intestinal microbes immediately after birth, and live in an important symbiotic relationship with them. There are far more bacteria in your gut than cells in your body, and their weight roughly equals that of your brain. These bacteria have a vast array of genes, capable of producing hundreds if not thousands of chemicals, many of which influence your brain. In fact, bacteria produce some of the same molecules as those used in brain signalling, such as dopamine, serotonin and gamma-aminobutyric acid (GABA). Furthermore, the brain is predominantly made of fats, and many of these fats are also produced by the metabolic activity of bacteria.

In the absence of gut bacteria, brain structure and function are altered. Studies of mice reared in a germ-free environment, with no exposure to bacteria, show that such mice have alterations in memory, emotional state and behaviour. They show autistic patterns of behaviour, spending as much time focusing on inanimate objects as on other mice. This behavioural change is driven by alterations in the underlying brain chemistry. For example, dramatic changes in serotonin transmission are seen, together with changes in key molecules such as brain-derived neurotrophic factor, which plays a fundamental role in forming new synapses.

These findings give weight to the notion of probiotics – bacteria with a health benefit. Probiotics were first proposed by Russian biologist Élie Metchnikoff who, in the early 1900s, observed that people living in a region of Bulgaria who consumed fermented food tended to live longer. However, it now seems that certain bacteria – dubbed psychobiotics – might have a mental-health benefit, too.

Although the field of psychobiotics is in its infancy, there are already promising signs. For instance, researchers from the California Institute of Technology in Pasadena recently showed that when the bacterium *Bacteroides fragilis* was given early in life, it corrected some of the behavioural and gastrointestinal deficits in a mouse model of autism. And previous reports indicate that *Bifidobacterium infantis* is effective in an animal model of depression.

How exactly do gut bacteria influence the brain? The mechanisms are becoming clear. The bacterium *Lactobacillus rhamnosus*, which is used in dairy products, has potent anti-anxiety effects in animals, and works by changing the expression of GABA receptors in the brain. These changes are mediated by the vagus nerve, which connects the brain and gut. When this nerve is severed, no effect on anxiety or on GABA receptors is seen following psychobiotic treatment with *L. rhamnosus*.

L. rhamnosus has also been shown to alleviate OCD-like behaviours in mice.

What goes on in our gut may have profound effects on what goes on in our mind

Interestingly, this bacterium not only alters GABA receptors in the brain but has been shown to synthesise and release GABA. Other evidence supports the view that gut bacteria may influence the brain by routes other than the vagus nerve – by altering the immune system and via the manufacture of short-chain fatty acids, for example.

Just as certain genes render bacteria pathogenic, it is likely that clusters of genes within gut bacteria provide mental health benefits. However, the essential genes for effective psychobiotics have yet to be established. It may be that, in the future, the ideal psychobiotic will be a genetically modified organism containing genes from several different bacteria.

In the meantime, cocktails of bacteria are likely to be more effective than single strains in producing health benefits. For example, a 2011 study showed that a combination of *Lactobacillus helveticus* and *Bifidobacterium longum* reduced anxiety and depressive symptoms in healthy volunteers. A 2013 neuroimaging study showed that a fermented milk product containing four different probiotic bacteria was associated with the

Microbiota with personality

The transplantation of faecal microbes (FMT) from a healthy individual into a recipient has emerged as an effective treatment for life-threatening *Clostridium difficile* infection. The success of this approach has focused attention on FMT to treat gastrointestinal, immune and metabolic disorders, but could FMT be useful in treating neuropsychiatric conditions too?

Intriguingly, a 2011 study by researchers in Canada showed that anxious mice have different microbiota compared with normal mice, and that transplantation of their microbiota into the normal mice makes the normal mice anxious – and vice versa.

If such effects can be translated to humans they have marked implications for development of microbial-based therapies for mental disorders. It also means that would-be FMT donors may need to be screened for mental health issues as well as infectious disease.


SVEN PAUSTIAN/PLAINPICTURE

reduced response of a brain network involved in the processing of emotion and sensation. And certain strains of bacteria can reduce the symptoms of irritable bowel syndrome, a common stress-related disorder of the brain-gut axis. This is probably achieved through a reduction in levels of the "stress hormone" cortisol and of inflammatory molecules produced by the immune system.

These findings are promising, but we are still a long way from the development of clinically proven psychobiotics and it remains to be seen whether they are capable of acting like – or perhaps even replacing – antidepressants. At a time when prescriptions for antidepressants have reached record levels, effective natural alternatives with fewer side effects would be welcome. We have now completed a study of the gut microbiota in people with severe depression and are analysing the results. If we find consistent alterations, this will provide a strong rationale for targeting depression with a suitable psychobiotic. We have also recently completed a placebo-controlled study of *Lactobacillus brevis* in treating anxiety in healthy volunteers.

"You have more gut bacteria than bodily cells, and they are as heavy as your brain"

We must, however, sound a note of caution. Despite marketing claims to the contrary, most putative probiotics have no psychobiotic activity. Until recently, lax regulation in both the US and the European Union allowed manufacturers to make outlandish claims without supporting data. This situation is changing and will protect consumers from fraudulent marketing, but the reality is that only a small percentage of bacteria tested have positive neurobehavioural effects. Some bacteria fail to survive storage in the health food store or are eliminated by acidity in the stomach. Even if they do survive gut transit, they may be devoid of health benefits.

In the 20th century, the major focus of microbiological research was on finding ways to kill microbes via antibiotics. This century the focus has changed somewhat, with a recognition of the health benefits of bacteria, not just from an immunity perspective but from a mental health one. Today, in richer nations, the impact of stress on health is perhaps as great as the threat from harmful bacteria. Psychobiotics have enormous potential. ■

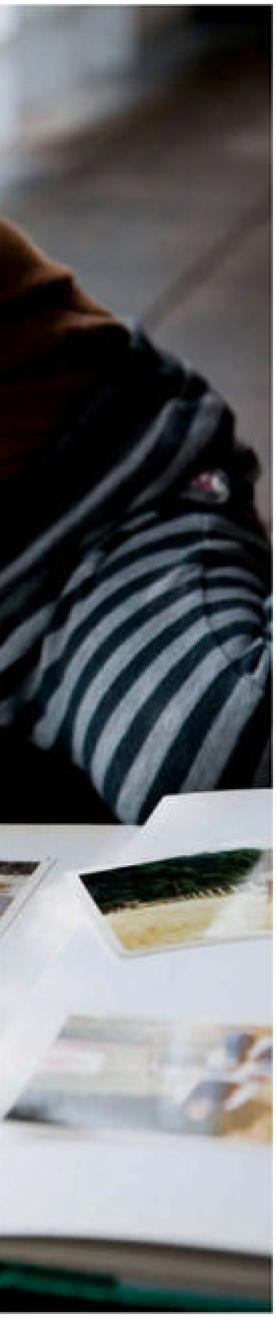
CHAPTER FIVE

AGES AND SEXES OF THE BRAIN

Our forgotten years

We remember next to nothing from the time before we go to school. Why is that, asks **Kirsten Weir**

KOHEI HARA/TAXI JAPAN/GETTY



Memories of our first few years remain sparse throughout life

WHEN my younger sister was born, I was almost 6. I woke up early the day after Christmas and asked my teenage sister where our parents were. "They're at the hospital having the baby," she said. "Go back to bed."

I remember that conversation clearly, but the actual arrival of my baby sister? Nothing. I don't recall visiting her in the hospital and holding her tiny pink hand for the first time, or my mother bringing her home and tucking her into her crib in the room next to mine.

There is nothing unusual in the failings of my early memory. In fact, "childhood amnesia", as the phenomenon is known, is universal. Most people remember nothing from before the age of 2 or 3, and memories from the next few years are sketchy at best.

This is puzzling, because in other ways children are phenomenal learners. In our first couple of years we pick up many complex, lifelong skills, like the ability to walk, talk and recognise people's faces. Yet memories of specific events in our childhood are lost to us in adult life. It's as if someone has torn the first few pages from our autobiography.

So what causes childhood amnesia? The question has troubled psychologists for more than a century, but at last we are starting to see some plausible answers. The new findings explain why some of us can remember more of our childhood than others, and even raise the question of whether it might be possible to unlock those earliest memories.

The first serious study of the problem, by the French psychologists V. and C. Henri, was in 1898. The pair found that when adults were asked about their earliest autobiographical memories, the average age at which these events occurred was just over 3 years. These findings have been confirmed by numerous later studies, which point to an average age of between 3 and 3.5 years for the very first memories. Even then, we still have notably poor recall for the following 3 years or so, at which point things start to become clearer. There is a lot of variability, however: some people seem to remember events before age 2, while others recall nothing before 6 or even 8.

Attempts to explain the phenomenon came in fits and starts in the decades after the Henris published their work. Sigmund Freud put his mind to the problem in a 1905 essay, concluding that we repress childhood memories because they are full of sexual and aggressive impulses too shameful for us to face. That idea eventually fell by the wayside, to be replaced by the view that young children just can't form explicit memories of events.

The picture changed again in the 1980s, with the first studies of children themselves, rather than investigations of adults' childhood recollections. This revealed that children as young as 2 or 3 can indeed recall autobiographical events, but that these memories fade away. The question therefore became: What causes them to disappear?

There appears to be no simple answer. "We've come to this view that there are a number of factors that coalesce to allow us to retain our memories," says Harlene Hayne at the University of Otago in Dunedin, New Zealand, who studies how memory abilities change during childhood and adolescence.

One of those factors may be the brain's anatomy. Two major structures are involved in the creation and storage of autobiographical memories: the prefrontal cortex and the hippocampus. The hippocampus is thought to be where details of an experience are cemented into long-term memory.

Broken bridge

It's here that the problem seems to lie. "We used to think the hippocampus and the surrounding cortices were well developed early on," says Patricia Bauer, who studies the development of memory during childhood at Emory University in Atlanta. But in the past 15 years or so, it has become clear that one small area of this region, called the dentate gyrus, does not fully mature until age 4 or 5. This area acts as a kind of bridge that allows signals from the surrounding structures to reach the rest of the hippocampus, so until the dentate gyrus is up to speed, early experiences may never get locked into long-term storage, Bauer says. "If the route isn't sufficiently mature to allow the information to get in, it's not going to effectively consolidate."

Hayne agrees that the brain continues to mature over a long period of development, and that this is an important step in establishing long-term memories. Yet children can still remember some events before this region is fully developed, so it can't be the be-all and end-all of childhood amnesia.

What's more, there are puzzling cross-cultural differences in the age of earliest memories. In one cross-cultural study, for example, researchers found the average age of first memories in people of European descent hovered around 3.5 years, compared with 4.8 years for east Asians and 2.7 years for Maori people in New Zealand. "Those differences cannot be explained by brain maturation alone," she says. Clearly, there

"Is it coincidental that autobiographical memories emerge at the point a child is able to give a story of their experiences?"

must be more pieces to the puzzle.

Mark Howe at City University London in the UK thinks he has come across one of the other important factors. "The thing that brings childhood amnesia to an end," he suggests, "is the advent of what we call a cognitive self." That's our sense of our own uniqueness – the understanding that the entity "me" is different from "you". This ability emerges at around 18 to 24 months of age, just before autobiographical memory begins to surface. Could it be the answer?

Over the past 10 years, Howe has explored this idea through a series of experiments. In one of his recent studies, for example, he tested whether toddlers could recognise themselves in a mirror, a well-accepted sign they have developed a sense of self. Next he showed them a stuffed lion, which he then tucked into one of several drawers in a set of cabinets. Weeks later, he brought each child back to the lab and asked if he or she remembered where the lion was napping. "The children who had a cognitive self at the time of the lion event were able to remember weeks later," he says, "whereas children who didn't have a cognitive self did very poorly."

Howe believes our sense of self helps us to organise our memories, making them easier to recall. "They become more memorable and stay with you for longer periods," he says. Yet that can't be the whole story either, since memories continue to be sparse long after the point at which a toddler can recognise his or her reflection. "The cognitive self is a necessary – although maybe not a sufficient – condition for autobiographical memory," Howe concedes.

TRUE OR FALSE?

You have heard that adorable anecdote from your childhood a million times. You can see the scene clearly in your head. But is your recollection real, or have you concocted a false memory around an oft-told family tale? "That question is the bane of memory researchers," says Patricia Bauer. In fact, says Martin Conway, you can't wholly trust any of your memories. "They always contain missing information, and I think they always contain misremembered details as well."

Unfortunately, it looks as if we are particularly susceptible to creating false memories relating to events during the period of childhood amnesia. When Harlene Hayne and her colleagues primed subjects to "recall" a childhood event that never actually happened, they were much more likely to create the false memory if they were told it happened at age 2, rather than age 10. That could have important bearings for court cases that rely on early memories, such as those investigating allegations of childhood abuse.

The magic shrinking machine

Some other factor is therefore needed to explain why memories continue to be sparse well beyond the point at which our cognitive self appears. For Hayne, the extra ingredient is the development of language skills. To investigate, she asked a group of 2 to 4-year-olds to play with a toy called the "magic shrinking machine". The kids had to place an object in the machine and perform a series of actions before an identical but smaller version of the object popped out. Hayne also recorded the words the kids could speak and understand at the time they played the game.

Then, six months to a year later, she brought the children back and asked them about the magic shrinking event. They could remember the game and re-enact aspects of it, but in no instance did they use a word to describe the machine that had not been part of their vocabulary when they first played with it – even though their vocabularies had grown by leaps and bounds in the meantime. "Their ability to describe it was really locked relative to their language at the time of the event," she says.

Further evidence came in 2010 when Martin Conway and Catriona Morrison both then at the University of Leeds, UK, published a study that again suggested the contents of our first memories depend on our first words. They asked adults to describe and date their earliest memories associated with words like "ball" or "Christmas". It turned out that the earliest memories around each cue word dated to several months after the average age at which the word is acquired. "You have to have a word in your vocabulary before you're able to set down memories for that concept," Morrison concludes (for more on this, see "Memory: The ultimate guide", page 104).

Perhaps a sense of self provides a structure around which to organise memories, and language then provides a further kind of memory scaffold, anchoring the details in a format we can call up years later. Morrison suggests that this may be because language allows a child to construct a narrative, which might help them to consolidate their memories. A 2-year-old can identify a dog, for example, but it takes until about 4 before the child can flesh out a story about their new pet. "Is it coincidental that autobiographical memory emerges at the same stage at which a child is able to give you a narrative account of an experience?" Morrison asks.

Recognising your reflection is a sign that you have a sense of self

Hayne and her colleagues have explored the importance of narrative by recording conversations between mothers and their children at various points between the child's second and fourth birthdays, noting whether each conversation included "elaborations" (richly detailed descriptions) or merely "repetitions" (which focus on just one or two aspects of the event). Ten years later, the team contacted the children and asked them about their early memories. This revealed that those whose mothers had many more elaborations than repetitions within their conversations had distinctly earlier memories than children of mothers who had a lower elaboration-to-repetition ratio. In other words, the way you talk to your kids when they are young might shape what they will remember years down the road.


ANDERS HVID/GALLERYSTOCK

MEMOIRS OF AN ELEPHANT

If our autobiographical memories only emerge once we develop language and a sense of self, does that mean humans are alone in reminiscing about the past? Some animals such as chimps, elephants and bottlenose dolphins pass the mirror self-recognition test (see main story), indicating they have some capacity for self-awareness. And they can definitely store long-term information.

But according to Catriona Morrison, animal memories are thought to be conditioned responses to stimuli rather than conscious (or self-conscious) reflection. Without language and a more sophisticated sense of self, it's unlikely our non-human cousins have autobiographical memories, Morrison says. Harlene Hayne agrees. "Most experts believe that autobiographical memory is unique to humans," she says.

This could also explain those puzzling differences between cultures. Compared with east Asian parents, European and North American parents tend to discuss the past more often with more elaborate storytelling. As a result, their children have more early memories. The Maori storytelling culture is even richer, with detailed oral histories and a strong focus on the past, leading to even earlier memories. When it comes to autobiographical memory, "early family memory sharing is important", says Qi Wang at Cornell University in Ithaca, New York, who studies the interaction of cognitive and social development.

Mental time travel

This may seem to confirm that language skills are the key to retaining childhood memories – but in fact the issue is not that clear-cut. Talking about the past doesn't just help children develop narrative skills, it also fosters development of a sense of self. "In North American culture, people are crazy about memoirs and reality TV. It's all about life stories," Wang says, so parent-child conversations in this culture tend to focus on a child's own experiences and feelings. Among east Asians, by contrast, "the past is the way for us to learn to do better in the future". Asian parents tend to use past events as teaching tools, and do not dwell on the child's feelings or role in the event. As a result, children in these different cultures have different understandings of their personal identities.

It now looks as if language and self-perception go hand in hand, and both are necessary for autobiographical memory to flourish. The findings could have a bearing on our wider understanding of the mind. For example, our capacity to plumb the depths of our past appears to be intimately linked to our ability to imagine the future. Given the ways different cultures reflect on their past, you might also expect differences in this "future time travel" – and that's exactly what Wang has found. The work might even shed light on the quality of other animals' memories (see "Memoirs of an elephant", above).

One big question remains, however: is it ever possible to reclaim memories from that period of our early childhood that is hidden from us? It is clear that very young children remember a lot in the short term. As many a parent has witnessed, toddlers can accurately describe a trip to the zoo that happened weeks earlier. But such early recollections are fragile and may never become locked into permanent storage. "The likelihood is those early memories are simply not there," Bauer says.

Hayne's subsequent work supports the idea that those early memories aren't cemented for later retrieval, even if the reminders come soon after the event. She found that the amount of information a 20-year-old remembers about the birth of his 15-year-old brother is virtually identical to the amount of information a 5-year-old remembers about his brother's birth just a month earlier. "If you plot adult next to child data, they are virtually identical," she says. She concludes that these memories aren't simply forgotten as a person ages. "The memory never got in there in the first place," she says.

Others harbour hopes of being able to recover these early memories, however. "I think they are retained but not accessible," Conway says. In his view, memories are "snapshots" of sensory experiences. As you mature, you develop language, a sense of self and other conceptual knowledge that helps you to frame those sensory snapshots and access them. If he is right, our buried memories could be excavated – if we could only find the right cues.

That's a line of reasoning that Morrison also follows. Reaching beyond traditional memory cues of words and images, she is exploring the use of smells, flavours and music for calling up ancient memories. If she and her colleagues can identify the proper tools, perhaps one day I will be able to unearth the memory of meeting my sister for the first time. "One of the things we understand as memory researchers," Morrison says, "is there's a lot more in there than we realise." ■

Into the minds of babes

Studies of psychoactive stimulants and consciousness can shine a light on how we viewed the world as an infant, finds Anil Ananthaswamy

WHAT is it like to be a bat? Philosophers of consciousness love toying with that question. We're fascinated by the possibility of minds so unlike our own. But there's a deep mystery far closer to home. Never mind bats – we barely even know what it's like to be a baby.

We've all been there, but none of us remember. As we develop into fully self-aware beings, our subjective experience of the world shifts dramatically. Once we leave infanthood behind, that early window on the world – and what it's like to look through it – is closed to us.

But research is prising open the shutters. As we learn more about how drugs can alter our consciousness, we're learning more about how our brain states relate to subjective experiences. And that's giving tantalising glimpses into our infancy.

For those who want to get inside a baby's head, Alison Gopnik, a psychologist at the University of California, Berkeley, has a few suggestions: go to Paris, fall in love, smoke four packs of Gauloises cigarettes and down four double espressos. "Which is a fantastic state to be in, but it does mean you wake up at 3 o'clock in the morning crying," she told a room of philosophers and neuroscientists at the Toward a Science of Consciousness meeting in Tucson, Arizona, in April 2014. And if that wasn't enough, Gopnik adds another ingredient to the list: psychedelic drugs. Because a baby's world might be vivid beyond adult imagination.

To get a handle on the infant state of mind, we first need to know what goes on in the brains of adults – then see how it differs in babies. Fortunately, consciousness seems to have a telltale signature. A team led by Stanislas Dehaene of the French National Institute of Health and Medical Research in Gif-sur-Yvette has found that adult conscious perception of stimuli involves a two-stage process. The first stage involves unconscious processing of, say, an image. If we look long or hard enough, then after about 300 milliseconds, the second stage kicks in, and a network of brain regions starts reverberating. The activity correlates with conscious perception: people are able to report on what they have seen. It is only when this network of frontal and parietal brain regions, dubbed the global neuronal workspace, becomes active that we have conscious access to information about what we have perceived.

"A baby's world might be vivid beyond adult imagination"

Dehaene and his colleagues recently teamed up with Sid Kouider of the Ecole Normale Supérieure in Paris, France, to look for a similar signature in babies who were between 5 and 15 months old. In the first study of its kind, the team spotted clear signs of conscious perception. But there was one important difference. In babies from 12 to 15 months old, the second stage of reverberating neural activity began about 750 milliseconds after the onset of stimulus, rather than after 300 milliseconds. And in 5-month-olds, the lag was even greater. Their brains responded after 900 milliseconds. "Babies have the same mechanism, but are just slower," says Kouider.

So, babies are aware of their environment, but, compared with adults, there's a lag. The slower reaction could be down to the prefrontal cortex, a hub for brain activity that the studies looked at. "It allows the sharing and transmission of information throughout different regions of the brain," says Kouider. And it is one of the last brain regions to mature, becoming fully developed only in late adolescence. Another slowing factor might be down to the connections between distant brain regions. In infants, the long-distance axons that carry signals in the brain don't yet have a fully formed coating of insulation called a myelin sheath. This means signals travel more slowly along the axons than they do in adults.

But there's more to the story. Kouider and Dehaene are investigating something called access consciousness – being aware enough of a stimulus to reflect on it and talk about it. Access consciousness is widely studied because researchers typically depend on subjects being able to monitor and report their experience. But some think access consciousness is just one extreme of a spectrum. Is there middle ground between being fully aware and fully unaware? Gopnik thinks so. And that is where babies find themselves, she says.

Philosopher Ned Block of New York University has a term for this middle ground. He calls it phenomenal consciousness – what ›

REBECCA GREEN

it's like to have a subjective experience such as seeing, hearing, tasting, smelling or touching something. Take vision. For Block, when we observe a complex scene, we are conscious of a lot more than we can put into words.

Of course, subjective experience is a slippery fish to study. But Block points to a new experiment that backs up his ideas. Zohar Bronfman of Tel Aviv University in Israel and his colleagues devised a test to unpick these layers of awareness. They showed subjects grids with letters in varying ranges of colours. At the start of the test, the researchers highlighted one row of letters before displaying the entire grid for 300 milliseconds. The participants were told their task was to recall a letter from the row that had been

"When we pay attention, we regress a little part of our brain to childhood"

highlighted, so they paid attention to that row more than others. But having recalled a letter from the row, they were then asked to estimate the diversity of colours either in that row or in one of the others.

Bronfman found that people were just as good at estimating colour diversity for the rows that had not been the focus of attention as they were for the ones that had. For some, this is clear evidence that there's more to conscious awareness than access consciousness – which would only account for the ability to recall individual letters.

Working with Tim Sweeny at the University of Denver in Colorado and his colleagues, Gopnik carried out a similar test with infants. They found that infants, like adults, are able to make judgements about a collection of objects without focusing on any particular one. The team showed cartoon images of two trees, each with oranges of varying sizes, to children aged 4 and 5. The children then played a game in which they had to help a hungry monkey pick the tree with the largest oranges. They chose correctly more often when comparing groups of oranges than when comparing individuals.

So young children are good at making judgements about groups. But they are less good at focusing attention on particulars. If adult awareness is like a spotlight that lets us pay selective attention to things, an infant's awareness is like a lantern, shedding diffuse light on everything around, says Gopnik. That may let them perceive many things at once.

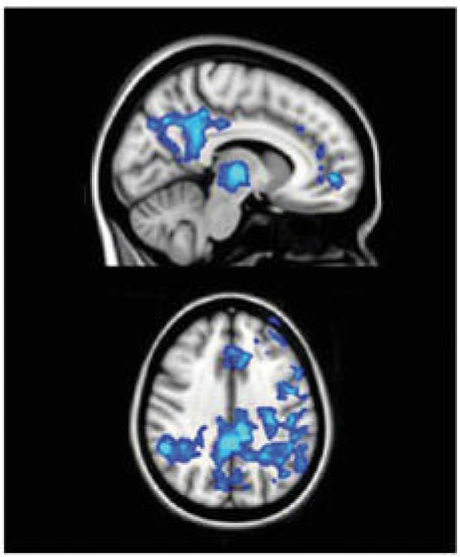
The upshot for Gopnik is that, instead of paying attention to individual things, a baby is probably picking up patterns in the bombardment of stimuli. And because they are less able to control their attention, babies are drawn to things that are rich in information. For an adult, an infant's play area can be a cacophony of colour and sound. A baby, however, is in its element.

This inability to control attention probably also means that babies are bad at shutting things out. Take a deafening pneumatic drill that has been hammering away outside your window all morning. Block notes that adults can tune out. If you're focusing on something else, for example, you may suddenly notice the drill only at midday. A baby, though, is likely to find it hard to shut out the noise to begin with. As an infant, the world may be bright and brash, with no dimmer switch.

Which brings us to the bustle of Paris, being in love, and buzzing on coffee and cigarettes. The differences between our adult experiences of the world and those of our lost early years are down to changes in the brain. But even as adults, our brains remain relatively plastic. As our attention shifts, our pliable brains shift with it, so perhaps there are ways to roll back the years, at least temporarily.

Michael Merzenich at the University of California in San Francisco and his colleagues have shown that when rats are trained to pay attention either to the frequency or the intensity of sounds, their brains rearrange themselves. When the rats were paying attention to frequency, relevant neurons were

Psilocybin disrupts hubs in the brain, rewinding them to when the ego was yet to emerge



DOI/10.1073/PNAS.1119598109

recruited to the task – but no changes were seen in nearby neurons involved with processing intensity. And vice versa.

It turns out that coffee and cigarettes can drive similar changes. The activation of certain parts of the brain for focused attention is managed by the neurotransmitter acetylcholine, which is mimicked by nicotine. At the same time, inhibitory neurotransmitters should work to stop other areas from joining the party. Unless you are drinking coffee, that is, because caffeine is thought to keep the effects of such killjoy neurotransmitters at bay, keeping your brain alert to anything and everything.

By smoking and drinking coffee you nudge your brain into a state where you're paying lots of attention – but in a wide-eyed, indiscriminate way. Being in love and travelling to new places seem to have a similar effect, says Gopnik. Under these influences, we get a more pliable, plastic brain. And that's a fair approximation of what's happening with babies, whose immature brains are more plastic overall. Being a baby is like paying attention with most of our brain. "As adults, when we pay attention, we are regressing a little part of our brain to its childhood state," says Gopnik. "We are taking a little part of us and turning that into a 2-year-old again."

Gopnik has another analogy to help us get inside the head of our infant self. Think what it's like to be totally immersed in an engrossing movie. "You are not in control, your consciousness is not planning, your self

FRANK ROTHE/GETTY IMAGES

Adults are better than young children at focusing attention and shutting out distractions

seems to disappear – that's part of what's great about being absorbed in a movie," she says. "Yet the events in the movie are very, very vivid in your awareness." Being a baby might be like being sucked into a really good movie.

It gets stranger. In infants, this expansive, along-for-the-ride experience of the world may go beyond perception. Kouider is not convinced by Block's and Gopnik's ideas about phenomenal consciousness – for him there is little to hold onto once you let go of access consciousness. But he does think that infants have a very different sense of self.

In fact, we may start life without recognisable self-awareness at all. Instead, a baby's sense of self is mixed up with its awareness of other people. That means babies may feel their own emotions and the emotions of others, without being able to tell them apart. "When the baby is having an experience, it is probably richer and much more intense, emotionally and subjectively," says Kouider.

Magical childhood

How does a baby feel the emotions of others? Probably through imitation. Smile at a baby and it smiles back. The very act of smiling is thought to induce happiness, so by imitating us, the baby feels emotions associated with those actions. The same might happen for other actions like waving or clapping. According to Kouider, we all had to figure out the boundary between ourselves and other people through social interactions. A baby learns to distinguish its own emotions from those of others by realising that it can control its own emotional state and behaviour but not that of its parents, for example.

The idea that infants might be experiencing an unbounded sense of self finds support from an unlikely source: magic mushrooms. And this also gives us another way to mimic infant consciousness. Robin Carhart-Harris of Imperial College London and his colleagues have been studying the effects of psilocybin – the active ingredient in psychedelic mushrooms – on states of consciousness. They looked at the network that connects regions in the prefrontal cortex, the cingulate cortex and the temporal lobes, among others.

"The psychedelic state offers a window into what infant consciousness is like"

Previous studies have shown that this "default mode network" is active when we are resting and when we are thinking about ourselves, and suppressed when we concentrate on a task. Carhart-Harris's team showed that psilocybin deactivates hubs in the brain like the posterior cingulate cortex and medial prefrontal cortex, as well as reducing long-range connectivity between brain regions. These hubs are like conductors of an orchestra, says Carhart-Harris. Bring on psilocybin and the conductors leave the room.

The resulting dissonance has a striking effect, disrupting our self-awareness. "It was quite difficult at times to know where I ended and where I melted into everything around me," said one of the volunteers in Carhart-Harris's study. These findings fit neatly with research that shows that the parts of the brain responsible for self-awareness are underdeveloped in infants. According to Carhart-Harris, psilocybin seems to rewind parts of the brain to when they were less organised and the ego was yet to emerge.

"One of the reasons why the psychedelic state is so interesting is that it offers a window into what infantile consciousness is like," he says. "It's the brain and mind moving back to an earlier stage, essentially, where our style of cognition is less constrained, less analytical, and more influenced by imagination and wishes, but also fears." Psilocybin also makes us emotionally volatile. Carhart-Harris is often struck by the child-like behaviour of his subjects. "One of the really notable things that you see with psychedelics is that people start to giggle," he says. "People behave in a very silly, immature way. It's quite endearing. They seem quite vulnerable."

Carhart-Harris's work on psychedelics has prompted Gopnik to rethink what it's like to be a baby. Being strung out on coffee and cigarettes may not be quite enough to explain just how bizarre infant consciousness might be. "It may be even weirder than that," she says. It might be like being on LSD, an even more powerful psychedelic than psilocybin.

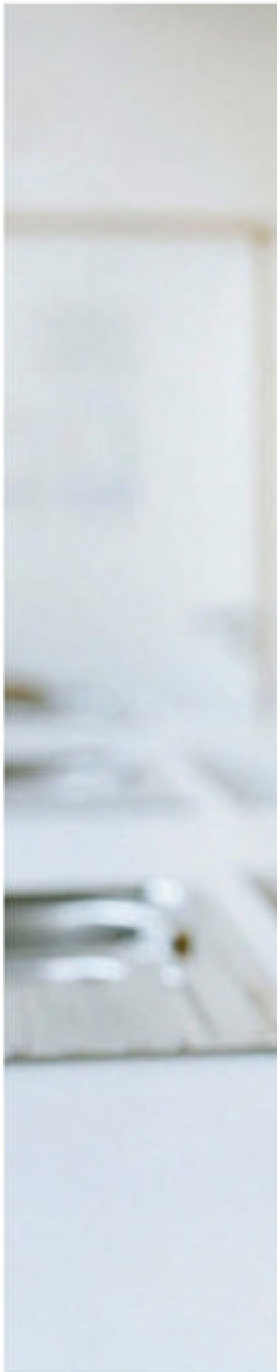
Gopnik now alerts audiences to the dangers of revisiting their past. "LSD is dangerous, nicotine is very dangerous and nothing is more dangerous than falling in love," she says. "So tea with toddlers is really the safest way to expand your consciousness." ■

AARON MCCOY/GETTY IMAGES

Babies' brains show the hallmarks of adult awareness, but there's a lag

Cognitive decline? Pah!

If you believe fading brainpower is an inevitable part of growing older, think again, say **Michael Ramscar** and **Harald Baayen**



Older and wiser: we get better at ignoring what we don't need to know

IT IS one of life's eternal mysteries: why does it get ever more difficult to recall the name of the person you were just introduced to? Surely it is a no-brainer that our cognitive powers fade as we grow older? Research seems to back this up: as we age, our scores in tests of cognitive ability decline.

Is this picture really correct? When we applied the techniques we use to study language learning to this evidence, we came to a different conclusion. In fact, counter-intuitively, many of these lower scores reflect cognitive improvement.

To illustrate the point, let's look at a test often used to measure our ability to learn and recall new information, called paired associate learning (PAL). In this test, people learn word pairs. Some are easy, *baby-cries*; others harder, *obey-eagle*. People perform worse on this task as they get older, supporting the conclusion that learning ability declines with age.

We think PAL tests paint a misleading picture of our cognitive abilities because they do not take into account prior knowledge of the words being tested, which grows with age and experience. To explain why this matters, we need to take a close look at the learning process.

The Russian physiologist Ivan Pavlov is famous for conditioning dogs to salivate at the sound of a bell. This led to a view of learning called associationism: if a cue is present, and an outcome follows, animals learn to associate them. Although humans can learn this way, the word "associate" is misleading. Our brains actually learn by making and testing predictions about the world. These are used to determine cues that are unreliable, which our brains then ignore and hence eliminate. It turns out that a dog associates a bell with food only because it has learned to ignore all other cues available to it.

We can apply this understanding of the role of elimination in the learning process to the PAL test. Results not only show that we find this test harder as we grow older but also that harder word-pairs become more difficult to learn. Why? An obvious answer is that words such as *baby* and *cries* often appear together in everyday language. This is what makes these pairs easy to remember. Meanwhile, learning nonsense pairs of words such as *obey-eagle* is hard because experience teaches us that *obey* is uninformative about *eagle* in English. This suggests a reason why older adults find PAL learning harder: they have greater experience of how words do and don't occur together.

In the past, this suggestion would have been impossible to test. There was simply no way of measuring how differences in experience might play out in learning on something like a PAL task. However, computational models enable us to estimate the connections between words based on their patterns of occurring together in billions of words of English text and speech. We used these techniques to assess the way that PAL words should behave in English. We found that as adults grow older, whether they find PAL pairs easier or harder reflects how difficult the information structure of English says they ought to be.

Traditional interpretation of PAL results assumes that all participants have equal knowledge of the words being tested. This is clearly wrong. Once we correct for the effects that increased experience can be expected to have on subsequent learning, any evidence of cognitive decline disappears. What we find instead is evidence that older people have a superior knowledge of how the English language works. In a similar vein, it is well known that as we age we get slower at discriminating real words from non-words in tests. What is less well known is that age also makes us more accurate at this task. Interestingly, people who speak two languages respond more slowly than monolingual people on similar tests, yet this is not taken as evidence that bilingualism leads to cognitive deficits. Rather, bilingual people's slower responses are thought to reflect the time it takes to search their larger "mental dictionaries".


PLAINPICTURE/MYLÈNE BLANC

This is simply because detuning our attention to irrelevant information is integral to the process we call "learning".

This observation hints at a way to overcome age-related problems with memory recall. As we age, varying the contexts of our lives more can help counteract the way our minds have evolved to continually tune out irrelevant information. This also means that, when retirement leads older people to spend most of their time in highly familiar environments, they will find it difficult to absorb the "context" that separates one memory from another. As a result, memories will become confused, even without declines in underlying brainpower.

Our research sheds similar light on another problem associated with old age: the inability to recall people's names. It turns out that names, at least in the US, have become more complex at an almost exponential rate since the 1880s. This has made the task of recognising American-English names harder over time, independent of the fact that people also learn more names as their experience grows with age. In a computer simulation, we found that simply processing the information required to recognise a name ought to take today's 70-year-olds half-a-second longer than when they were 20.

"Contrary to popular belief, neuronal loss does not play a significant role as we age"

The processes involved in forming memories and recalling names highlight how the way we learn interacts with the environment throughout our lifetimes, and shows how difficult it is to separate changes caused by learning from those of decline.

This is important. We are not arguing that the functionality of our brains stays the same as we grow older, or that cognitive decline never happens, even in healthy ageing. What we do know is the changes in performance seen on tests such as the PAL task are not evidence of cognitive or physiological decline in ageing brains. Instead, they are evidence of continued learning and increased knowledge. This point is critical when it comes to older people's beliefs about their cognitive abilities. People who believe their abilities can improve with work have been shown to learn far better than those who believe abilities are fixed. It is sobering to think of the damage that the pervasive myth of cognitive decline must be inflicting. ■

The problem of understanding the effects of prior learning on performance are unlikely to be unique to PAL and word-recognition tasks. Other psychometric tests of cognitive ability (intelligence or short-term memory, for example) also assume that the participant's prior knowledge of items being tested is irrelevant. What our research shows is that increased knowledge brings costs as well as benefits. Learning increases the amount of information that our brains have to process, which inevitably affects test performance.

Contrary to popular belief, neuronal loss does not play a significant role in age-related changes in brain structure. Rather, consistent with our findings, most of the changes that occur as healthy brains age are difficult to distinguish from those that occur as we learn. Thus, understanding the costs and benefits of learning is critical if we are to establish the facts of cognitive ageing. For example, memory experiments show that, as we age, we "encode" less contextual information, such as what we were wearing when we learned a new fact. This makes the fact harder to recall, and is seen as a sign of cognitive decline. Yet everything we know about the way our brains learn indicates that people must inevitably become insensitive to many background details as life experience grows.

PINK BRAINS, BLUE BRAINS, PURPLE PEOPLE

Some differences between men's and women's brains may be there to make us act the same. **Kayt Sukel** reports on a startling idea

SEVERAL years ago, the car I was driving was rear-ended by another at a stop sign. No one was hurt, but my passenger and I had to wait around to give a statement to the local police. Later on I asked my companion if he had noticed that the officer addressed most of the questions to him, even though I was the one who had been driving. "I think he was just afraid you were going to do the typical female thing and fall apart," he replied.

The notion that men can face adversity with stoicism while women are more likely to respond with histrionics is just one example of the gender stereotypes that permeate our culture. If my friend was right, they even persist among those who should be taking particular care to treat people equally.

Perhaps such prejudice is justified, though. After all, in recent years evidence has turned up of numerous differences between men's and women's brains, whether at the level of synapses, signalling chemicals, or gross anatomy. Brains come in hues of either pink or blue, as one researcher puts it.

But could we be overlooking an important caveat? A new theory that has sprung from research on prairie voles says that at least some of those disparities evolved not to create differences in behaviour or ability, but to prevent them. They are there to compensate for the genetic or hormonal differences that are necessary to create two sexes with different sets of genitals and reproductive behaviours.

If that sounds paradoxical, imagine comparing a chunky mountain bike with a lightweight road bike. To compensate for the mountain bike's greater resistance, you have to pedal harder to reach the same speed; one difference makes you introduce another to achieve the same output. In brain terms, while certain circuits may be shaded pink or blue, that would not stop the output, or behaviour, being a uniform purple.

Of course this "compensation theory" will not explain away all brain differences between the sexes, but it could account for some. The idea is still in its infancy and so far has largely been overlooked. If it is right, though, our innate abilities may not be so different after all.

"Compensation is a concept that most people haven't thought about and it's important," says Larry Cahill, a neuroscientist who researches human sex differences at the University of California, Irvine. "This is something we need to be paying attention to." ›

For most of history, men's and women's different roles in life were assumed to be mainly innate and unalterable. This was challenged in the west with the rise of feminism in the second half of the last century. Perhaps the different behaviours of boys and girls arose because of cultural norms: parents praising boys for romping and smashing toy cars, for instance, while expecting girls to be more reserved and play with their dolls.

Around the same time, though, new light was being shed on the biology of gender. In the womb, we all start out more or less female, until sometime between six and 12 weeks of pregnancy. Then, in male fetuses, a gene on the Y chromosome causes certain cells to make testosterone, which leads to the development of the penis and testicles. Female fetuses do not have this "testosterone bath" and so develop female reproductive organs.

But the sex hormones' influence is not limited to our gonads: they also play a key role in the brain's development, influencing the architecture of various neural circuits. As well as establishing these anatomical differences, the sex hormones presumably affect our behaviour as adults too, as their receptors have been found in many brain regions.

Understanding the ways in which male and female brains differ has become a hot topic in neuroscience, particularly in the past decade with the growth of brain scanning as a research tool. For instance, one of the most famous findings is that men seem to have a larger region of the brain thought to be involved in spatial reasoning, such as that used in a task like mentally rotating three-dimensional figures: the left-hand-side inferior parietal lobule, located just over the ear. Women, on the other hand, appear to have larger areas of the brain associated with language.

A common critique of this sort of work is that there is only a small average difference between the sexes, with more variability within each sex than between men and women as a whole. The results tell us about population averages, not individuals, in other words. Even so, any such findings tend to be seized on by the media. UK newspapers are fascinated by neuroscience, according to an analysis of their coverage of this topic over the 10 year period between 2000 and 2010. In a detailed breakdown of the stories by subject area, sex differences came eighth out of 41 neuroscience categories. As with any science stories in the media, findings tend to be exaggerated. "They want to take these results and try to spread males and females way apart on function and ability," says Cahill.

"The women had the same feelings of stress as the men but their brains were acting differently"

It is certainly true that while society has become more equal in many respects, men still outnumber women in mathematics, engineering and many areas of science. While young girls do as well in these subjects as their male classmates, they start lagging behind as they grow up and enter further education.

For instance, women make up about 20 per cent of computer science students in the US, and the same fraction of engineering students. Is it down to innate brain differences or cultural conditioning that they miss out on these well-paying sectors so crucial to today's technology-oriented society?

Research into brain sex differences has also fuelled calls to educate boys and girls separately in same-sex classes or schools, particularly in the US. It is argued that teaching methods need to be tailored to those differently hued brains.

With this sort of research having such significant implications, it is important to be aware of possible flaws. The compensation theory first caught people's attention in 2004, with the publication of a review entitled "Sex differences in adult and developing brains: compensation, compensation, compensation".

The author was Geert de Vries, who studies hormones and brain signalling systems in rodents at the University of Massachusetts in Amherst. In the 1980s he stumbled across a big sex difference in the brains of prairie voles, small rodents found in the US Midwest.

Unlike most mammals, prairie voles are monogamous and the males are devoted fathers. They spend just as much time as the females licking their pups and toting them around. Yet compared with the females, males have many more receptors in the brain for vasopressin, a brain signalling molecule that has been linked to parental care.

De Vries recalls: "When we linked this sexually [different] system to a behaviour that is spectacularly similar in males and females, I thought, 'Wait a moment, why are the sex differences opposite from the things they are doing? Could the differences be there so they can act the same?'"

The more de Vries considered the idea, the more it made sense to him. The female voles' maternal devotion was demonstrably triggered by the hormonal changes of pregnancy. The males' vasopressin circuits seemed to be compensating for the lack of pregnancy hormones. And if that kind of compensation was going on in prairie voles, could something similar also be happening elsewhere?

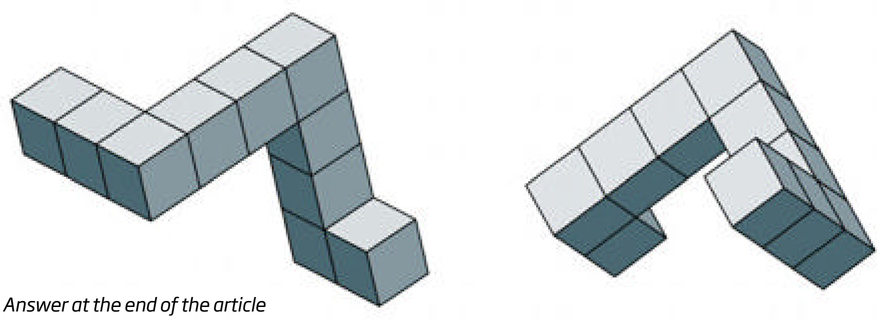
De Vries realised that the most likely candidates for compensatory circuits were those that are influenced by sex hormones or the sex chromosomes. Poring through the research literature, he found several possible compensatory mechanisms in other animals, including rats, mice and zebra finches.

While de Vries had outlined the compensation theory before, his 2004 review succeeded in bringing the idea to wider notice. One convert is Margaret McCarthy, a sex differences researcher at the University of Maryland School of Medicine in Baltimore. "Many of the sex differences we see in the brain are there to help males and females develop their different reproductive

SPACED OUT

Men tend to do better than women on tests involving spatial reasoning.

Is the shape on the right a rotated version of the one on the left?



Answer at the end of the article


JOY SALE/FLICKR/GETTY

Looks like Venus and Mars aren't so far apart after all

strategies," she says. "But those differences also carry with them some constraints. Males have high testosterone; females have cycles of various hormones. And those hormones come with costs with regards to behaviours outside reproduction."

To date, the evidence for compensation in people seems thin on the ground. But could it be going unnoticed because of the assumption that a difference in the brain always means a difference in performance?

In a 2006 review of sex difference research, Cahill cited several brain-scanning studies that had turned up differences in men and women that were not accompanied by differences in their performance.

While the mechanisms involved are unknown, Cahill thinks these could represent compensation in action, although they had not been noted as such by those who did the research.

Equal but different

For instance, in one study men and women were asked to name everyday objects in photos that were flashed up at a challenging pace. According to the PET scanner, men showed more activation in certain brain regions thought to be responsible for visual recognition, although they scored about the same as the women. The authors speculated that the men might have needed to work harder to get the same result because of women's superior language abilities.

Cahill himself may have found evidence of compensatory circuits at work, involving the amygdalae, a pair of almond-shaped structures deep within the brain thought to be involved in the processing and memory of emotional reactions. Cahill's group showed that even when the brain is at rest, amygdala activity is different in men and women.

That made neuroscientists sit up and take notice, because most imaging studies require resting activity levels to be subtracted from levels seen during experimental tasks in order to reveal changes caused by the task. Given these findings, important results may be going unseen because at the moment men and women's results tend not to be analysed separately.

Cahill thinks the difference in amygdala activity could be a compensatory mechanism to make up for differences in testosterone levels. "There are instances where everyone agrees that there is no sex difference on the behavioural level. But that doesn't mean there isn't a sex difference in the brain," he says. "It remains possible that the equal behaviour was achieved in different ways.

I can't help but think of compensation when I remember the car accident. I don't think my behaviour was any different from that of my male friend. We were both a bit rattled, of course, but more impatient to finish the paperwork and be on our way. But were our brains behaving any differently? Recent work from Jill Goldstein's lab at Harvard Medical School in Boston suggests they may have been. While she did not go looking for a compensation effect, she believes de Vries's theory could explain her results.

Goldstein's team did fMRI scans on 12 women and 12 men as they viewed a variety of photos, some of which were designed to be shocking (think car accidents and dismembered bodies). The women did the test twice: once at the beginning of their menstrual cycle, when oestrogen levels would have been low and then again just before ovulation, when they would have been peaking.

When viewing the gruesome photos the women reported similar subjective feelings of stress as the men, irrespective of the stage in their menstrual cycle. But when their oestrogen was high, the women had less activity than men in several different brain regions involved in the stress response. Goldstein thinks this was to damp down a more sensitive stress response that otherwise would have been triggered by the surging oestrogen. "They had the same subjective feelings of stress but their brains were acting slightly differently to get to that state," she says.

While the compensation theory has not yet gained much traction among neuroscientists, it is getting harder to ignore as the number of possible human examples accumulates. Even where compensatory brain differences have no net effect on behaviour or ability, they could still help explain why certain medical conditions are more common in one sex than the other. Women, for instance, are more vulnerable to mental illnesses like anxiety and depression, while men have a higher incidence of developmental disorders like autism.

Goldstein's work on stress is a case in point. "We need to understand how these circuits develop differently in the healthy male and female brain," she says. "Only then can we understand how these circuits are disrupted in psychiatric disorders."

Funders are also starting to take the issue seriously. In 2014, the US National Institutes of Health issued new policies requiring that sex differences be addressed in future biomedical research programmes funded by the agency.

No one is saying the compensation theory can explain away all the observable brain differences between men and women. Many of them do in fact correspond to differences in performance. But some do not.

That suggests we should be more careful about how we interpret brain data from now on, according to Lise Eliot, a neuroscientist at Rosalind Franklin University in Chicago, who coined a phrase with the title of her 2010 book on sex differences, *Pink Brain, Blue Brain*.

"The more we learn, the more we realise that sex differences don't translate very well into that Mars-Venus pop culture everyone seems to want to project," she says. "Neuroscientists, the media, parents – we all need to be careful about how this data is interpreted and what conclusions we draw from it." ■

Answer to diagram question: yes

CHAPTER SIX

CONSCIOUSNESS

Closing in on consciousness

We are closer than we think to solving one of science's hardest puzzles, says **Christof Koch** – understanding how feelings of love and ennui, the taste of an apple or sight of alpenglow on a distant peak relate to the physical brain. What is the secret?

We know the world by seeing and hearing, lusting and hating, remembering and imagining

A QUICK glance at the thousands of books that purport to explain consciousness makes the real understanding of it look like a Herculean task. There is, after all, a profound explanatory gap between neural activity of any sort and subjective feelings. The first belongs to the realm of physics, to space and time, energy and mass, the second to experience. And while experiences are ephemeral, they are the very stuff of life. The only way we know about the world, about space and time, about energy and mass, about anything in fact is by seeing, hearing and smelling, by lusting and hating, by remembering and imagining.

That these two realms are closely related is revealed by the effects of a stroke, a strong blow to the head, or by a neurosurgeon stimulating electrically some part of a person's brain and evoking a childhood memory. Yet consciousness does not appear in the equations of physics, nor in chemistry's periodic table, nor in the A-T-G-C molecular chatter of our genes. Somehow it emerges from the nervous system.

I have spent 25 years – the first 16 years working with my mentor, colleague and friend Francis Crick – linking specific aspects of consciousness to the mammalian brain. We popularised the idea of the neuronal correlates of consciousness (NCC): the minimal neuronal mechanisms – the synapses, neurons and brain regions – that are jointly sufficient for any one conscious percept.

Since then, much progress has been made. We now know that some sectors of the cerebral cortex making up the bulk of the brain (for its size the most complex organ in the universe) have a privileged relationship to consciousness, that not all of its many regions participate equally in generating the content of a conscious experience. Micro-electrodes and magnetic scanners have also shown us that the neocortex can be active without necessarily giving rise to a conscious experience. This is the domain of the non-conscious.

Yet Crick and I looked deeper. Why did a particular NCC give rise to one specific conscious experience? Why should particular vibrations of highly organised matter trigger conscious feelings? It seems as magical as rubbing a lamp and having a genie emerge.

What is needed is a fundamental account of how activity in any system can give rise to consciousness. We therefore turned to the ideas of Giulio Tononi at the University of Wisconsin-Madison. He advocates a sophisticated information theory account of consciousness, called integrated information. The theory introduces a precise measure, called phi, which captures the extent of consciousness. Expressed in bits, phi quantifies the extent to which any system of interacting parts is both differentiated and integrated when that system enters a particular state.

This is the heart of phenomenal experience: any one conscious experience is both highly differentiated from any other one but also unitary, holistic. The larger the phi, the richer the conscious experience of that system. Furthermore, the theory assigns any state of any network of causally interacting parts (these neurons are firing, those ones are quiet) to a shape in a high-dimensional space. The shape (think of it as a crystal in a fantastically high-dimensional space) accounts for the peculiar feel of any one conscious experience. If the network switches into a different state – you fantasise about sex rather than listen to a droning speaker – the crystalline shape changes as well.

This crystal is the system viewed from within. It is the voice in the head, the light

CHLOE DEWE MATHEWS/PANOS PICTURES

inside the skull. It is everything you will ever know of the world. It is your only reality. It is the quiddity of experience. The dream of the lotus-eater, the mindfulness of the meditating monk, the agony of the cancer patient, all feel as they do because of the shape of the distinct crystals in a space of a trillion dimensions.

Integrated information makes specific predictions about which brain circuits are involved in consciousness and which ones are peripheral players, even though they might contain many more neurons. The theory should let doctors build a consciousness meter to measure the extent to which severely brain-injured patients are in a vegetative state, and which ones are partially conscious but unable to signal their pain and discomfort.

I am now pursuing a different tack at the Allen Institute for Brain Science in Seattle, a few hours north of Pasadena by plane. In 2012, we embarked on an ambitious 10-year project involving hundreds of scientists and technologists. Philanthropist Paul G. Allen, who founded the institute in 2003, has pledged $300 million for the first four years of the project. Our goal is to understand how information is encoded, transformed and represented in the mouse and the human cerebral neocortex and its satellites.

The neocortex is a layered structure: the human neocortex is about twice as thick that of the mouse, and has about 1000 times the surface area. It is a highly versatile, computational tissue that excels at processing sensory information, making and storing associations, and planning and producing complex motor patterns. The neocortex is partitioned into multiple areas, made up of smaller columns with reasonably similar cell types and architectures across species and brain regions.

The institute plans to build a series of brain "observatories" to identify, record and intervene in the cortical networks underlying visually guided behaviours in the mouse, including visual perception, decision-making, and even murine consciousness. The fast-developing technology of optogenetics will allow us to control defined events in defined neurons at defined times in mouse brains. That is, we will move from correlation to causation. Building these observatories is a large-scale

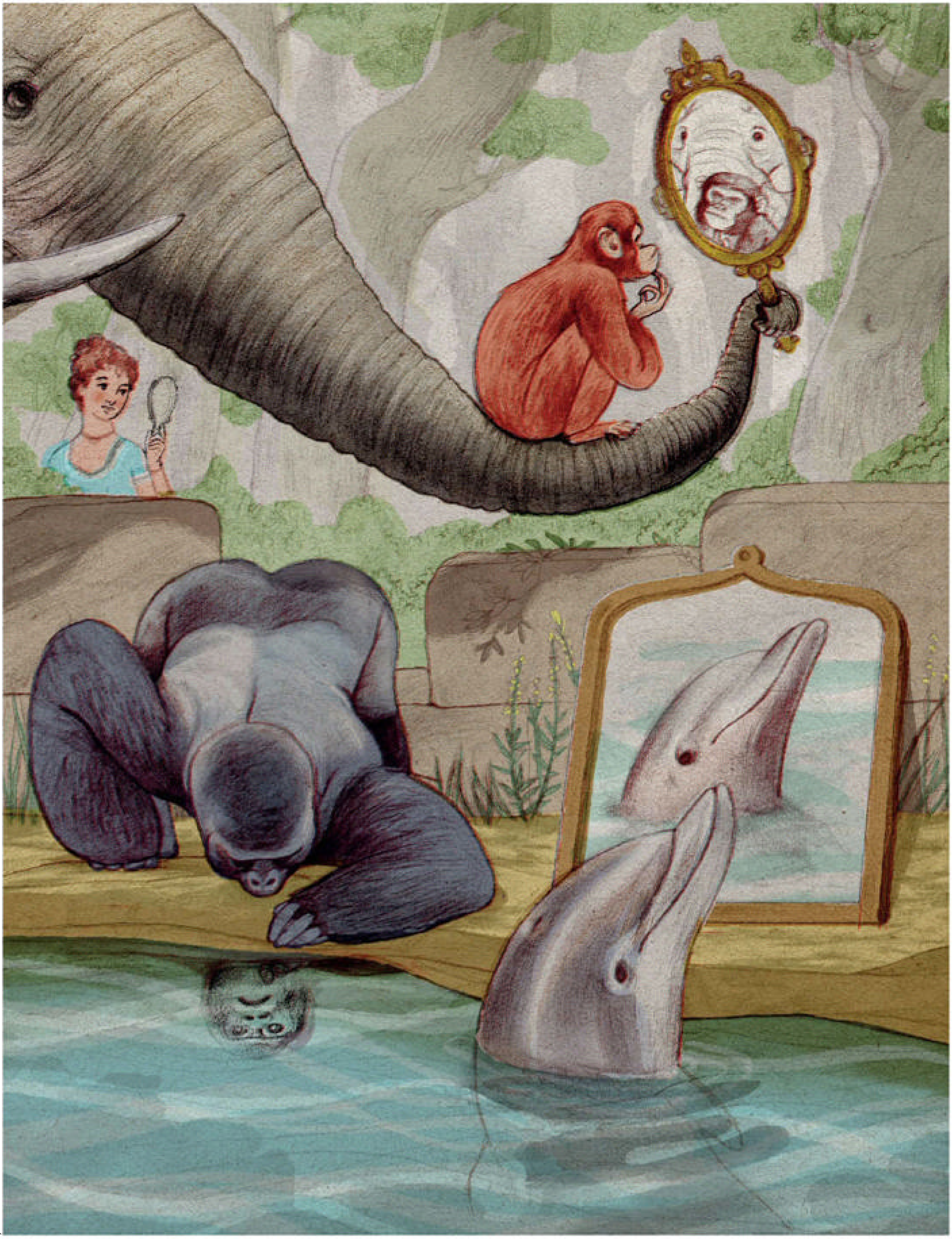
"Why should vibrations of organised matter trigger conscious feelings?"

effort to synthesise anatomical, physiological and theoretical knowledge into a model of the cerebral cortex, which we think has the potential to revolutionise our understanding of the mammalian brain. The fruits of this cerebroscope will be freely available.

Throughout my quest to understand consciousness, I never lost my sense of living in a magical universe. I do believe some deep and elemental organising principle created the universe and set it in motion for a purpose I cannot comprehend. I grew up calling this god – but a god much closer to Baruch de Spinoza's god than the god of Michelangelo's paintings.

A pioneering generation of stars had to die in spectacular supernovae to seed space with the heavier elements needed for the rise of self-replicating bags of chemicals, on a rocky planet orbiting a young star at just the right distance. The competitive pressures of natural selection made possible the accession of creatures with nervous systems. As the complexity of these systems grew to staggering proportions, some of the creatures evolved the ability to reflect on themselves, to contemplate their beautiful but cruel world.

While the rise of sentient life was inevitable, it does not mean Earth had to bear life or that bipedal, big-brained primates had to walk the African grasslands. But I do believe the laws of physics overwhelmingly favoured the emergence of consciousness, and that those laws will lead us to a more or less complete knowledge of it. ■



JONATHAN BURTON

The consciousness connection

Could a special type of brain cell give us and other smart animals our emotions, empathy and sense of self? **Caroline Williams** investigates

THE origin of consciousness has to be one of the biggest mysteries of all time, occupying philosophers and scientists for generations. So it is strange to think that a little-known neuroscientist called Constantin von Economo might have unearthed an important clue nearly 90 years ago.

When he peered down the lens of his microscope in 1926, von Economo saw a handful of brain cells that were long, spindly and much larger than those around them. In fact, they looked so out of place that at first he thought they were a sign of some kind of disease. But the more brains he looked at, the more of these peculiar cells he found – and always in the same two small areas that evolved to process smells and flavours.

Von Economo briefly pondered what these "rod and corkscrew cells", as he called them, might be doing, but without the technology to delve much deeper he soon moved on to more promising lines of enquiry.

Little more was said about these neurons until nearly 80 years later when Esther Nimchinsky and Patrick Hof, then both at Mount Sinai University in New York, also stumbled across clusters of these strange-looking neurons. Now, after more than a decade of functional imaging and post-mortem studies, we are beginning to piece together their story. Certain lines of evidence hint that they may help build the rich inner life we call consciousness, including emotions, our sense of self, empathy and our ability to navigate social relationships.

Many other big-brained, social animals also seem to share these cells, in the same spots as the human brain. A greater understanding of the way these paths converged could therefore tell us much about the evolution of the mind.

Admittedly, to the untrained eye these giant brain cells, now known as von Economo neurons (VENs), don't look particularly exciting. But to a neuroscientist they stand out like a sore thumb. For one thing, VENs are at least 50 per cent, and sometimes up to 200 per cent, larger than typical human neurons. And while most neurons have a pyramid-shaped body with a finely branched tree of connections called dendrites at each end of the cell, VENs have a longer, spindly cell body with a single projection at each end with very few branches (see diagram, page 89). Perhaps they escaped attention for so long because they are so rare, making up just 1 per cent of the neurons in the two small areas of the human brain: the anterior cingulate cortex (ACC) and the fronto-insular (FI) cortex.

Their location in those regions suggests that VENs may be a central part of our mental machinery, since the ACC and FI are heavily involved in many of the more advanced aspects of our inner lives. Both areas kick into action when we see socially relevant cues, be it a frowning face, a grimace of pain or simply the voice of someone we love. When a mother hears a baby crying, both regions respond strongly. They also light up when we experience emotions such as love, lust, anger and grief. For John Allman, a neuroanatomist at the California Institute of Technology in Pasadena, this adds up to a kind of "social monitoring network" that keeps track of social cues and allows us to alter our behaviour accordingly.

The two brain areas also seem to play a key role in the "salience" network, which keeps a subconscious tally of what is going on around us and directs our attention to the most pressing events, as well as monitoring sensations from the body to detect any changes.

What's more, both regions are active when a person recognises their reflection in the mirror, suggesting that these parts of the ›

"Von Economo neurons might be a vital adaptation in large brains for keeping track of social situations"

brain underlie our sense of self – a key component of consciousness. "It is the sense of self at every possible level – so the sense of identity, this is me, and the sense of identity of others and how you understand others. That goes to the concept of empathy and theory of mind," says Hof.

To Bud Craig, a neuroanatomist at Barrow Neurological Institute in Phoenix, Arizona, it all amounts to a continually updated sense of "how I feel now": the ACC and FI take inputs from the body and tie them together with social cues, thoughts and emotions to quickly and efficiently alter our behaviour.

This constantly shifting picture of how we feel may contribute to the way we perceive the passage of time. When something emotionally important is happening, Craig proposes, there is more to process, and because of this time seems to speed up. Conversely, when less is going on we update our view of the world less frequently, so time seems to pass more slowly.

VENs are probably important in all this, though we can only infer their role through circumstantial evidence. That's because locating these cells, and then measuring their activity in a living brain hasn't yet been possible. But their unusual appearance is a signal that they probably aren't just sitting there doing nothing. "They stand out anatomically," says Allman, "And a general proposition is that anything that's so distinctive looking must have a distinct function."

Fast thinking

In the brain, big usually means fast, so Allman suggests that VENs could be acting as a fast relay system – a kind of social superhighway – which allows the gist of the situation to move quickly through the brain, enabling us to react intuitively on the hop, a crucial survival skill in a social species like ours. "That's what all of civilisation is based on: our ability to communicate socially, efficiently," says Craig.

A particularly distressing form of dementia that can strike people as early as their 30s supports this idea. People who develop fronto-temporal dementia lose large numbers of VENs in the ACC and FI early in the disease, when the main symptom is a complete loss of social awareness, empathy and self-control. "They don't have normal empathic responses to situations that would normally make you disgusted or sad," says Hof. "You can show them horrible pictures of an accident and they just don't blink. They will say 'oh, yes, it's an accident'."

Post-mortem examinations of the brains of people with autism also bolster the idea that VENs lie at the heart of our emotions and empathy. According to one recent study, people with autism may fall into two groups: some have too few VENs, perhaps meaning that they don't have the necessary wiring to process social cues, while others have far too many. The latter group would seem to fit with one recent theory of autism, which proposes that the symptoms may arise from an over-wiring of the brain. Perhaps having too many VENs makes emotional systems fire too intensely, causing people with autism to feel overwhelmed, as many say they do.

Another recent study found that people with schizophrenia who committed suicide had significantly more VENs in their ACC than schizophrenics who died of other causes. The researchers suggest that the overabundance of VENs might create an overactive emotional system that leaves them prone to negative self-assessment and feelings of guilt and hopelessness.

VENs in other animals provide some clues, too. When these neurons were first identified, there was the glimmer of hope that we might have found one of the key evolutionary changes, unique to humankind, that could explain our social intelligence. But the earliest studies put paid to that kind of thinking, when VENs turned up in chimpanzees and gorillas. In recent years, they have also been found in elephants and some whales and dolphins.

Like us, many of these species live in big social groups and show signs of the same kind of advanced behaviour associated with VENs in people. Elephants, for instance, display something that looks a lot like empathy: they work together to help injured, lost or trapped elephants, for example. They even seem to show signs of grief at elephant "graveyards".

What's more, many of these species can recognise themselves in the mirror, which is usually taken as a rudimentary measure of consciousness. When researchers daub paint on an elephant's face, for instance, it will notice the mark in the mirror and try to feel the spot with its trunk. This has led Allman and others to speculate that von Economo neurons might be a vital adaptation in large brains for keeping track of social situations – and that the sense of self may be a consequence of this ability.

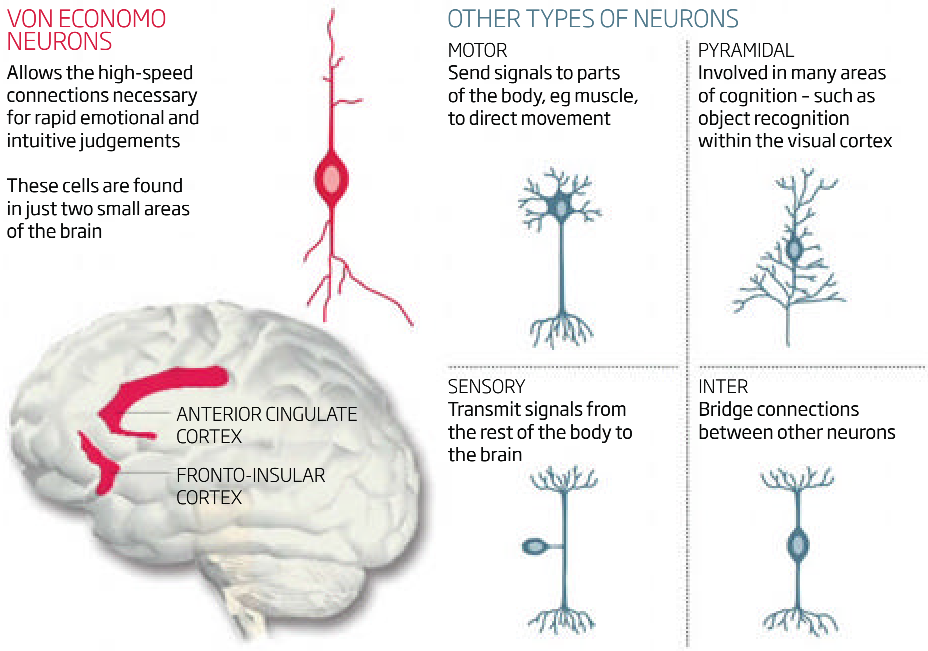
Yet VENs also crop up in other animals including manatees, hippos and giraffes – not renowned for their busy social lives. The cells have also been spotted in macaques, which don't reliably pass the mirror test, although

Nice ice: sharing food was, perhaps, the setting in which empathy evolved


MARTIN PARR/MAGNUM PHOTOS

Judgement cells

Von Economo neurons may play an important role in our sense of self



they are social animals. Although this seems to put a major spanner in the works for those who claim that the cells are crucial for advanced cognition, it could also be that these creatures are showing the precursors of the finely tuned cells found in highly social species. "I think that there are homologues of VENs in all mammals," says Allman. "That's not to say they're shaped the same way but they are located in an analogous bit of cortex and they are expressing the same genes."

It would make sense, after all, that whales and primates might both have recycled, and refined, older machinery present in a common ancestor rather than independently evolving the same mechanism. Much more research is needed, however, to work out the anatomical differences and the functions of these cells in the different animals.

That work might even help us understand how these neurons evolved in the first place. Allman already has some ideas about where they came from. Our VENs reside in a region of the brain that evolved for olfaction, which integrates taste and smell, so he suggests that many of the traits now associated with the FI and the ACC evolved from the simple act of deciding whether food is good to eat or likely to make you ill. When reaching that decision, he says, the quicker the "gut" reaction kicks in the better. And if you can detect this process in others, so much the better.

"One of the important functions that seems to reside in the FI has to do with empathy," he says. "My take on this is that empathy arose in the context of shared food – it's very important to observe if members of your social group are becoming ill as a result of eating something." The basic feeding circuity, including the rudimentary VENs, may then have been co-opted by some species to work in other situations that involve a decision, like working out if a person is trustworthy or to be avoided. "So when we have a feeling, whether it be about a foodstuff or situation or another person, I think that engages the circuitry in the fronto-insular cortex and the VENs are one of the outputs of that circuitry," says Allman.

"Far from being the pinnacle of brain evolution, consciousness might have been a big, happy accident"

Allman's genetics work suggests he may be on to something. His team found that VENs in one part of the FI are expressing the genes for hormones that regulate appetite. There are also a lot of studies showing links between smell and taste and the feelings of strong emotions. Our physical reaction to something we find morally disgusting, for example, is more or less identical to our reaction to a bitter taste, suggesting they may share common brain wiring.

Other work has shown that judging a morally questionable act, such as theft, while smelling something disgusting leads to harsher moral judgements. What's more, Allman points out that our language is loaded with analogies – we might find an experience "delicious", say, or a person "nauseating". This is no accident, he says.

Red herring

However, it is only in highly social animals that VENs live exclusively in the scent and taste regions. In the others, like giraffes and hippos, VENs seem to be sprinkled all over the brain. Allman, however, points out that these findings may be a red herring, because without understanding the genes they express, or their function, we can't even be sure how closely these cells relate to human VENs. They may even be a different kind of cell that just looks similar.

Based on the evidence so far, however, Hof thinks that the ancestral VENs would have been more widespread, as seen in the hippo brain, and that over the course of evolution they then migrated to the ACC and FI in some animals, but not others – though he admits to having no idea why that might be. He suspects the pressures that shaped the primate brain may have been very different to those that drove the evolution of whales and dolphins.

Craig has hit on one possibility that would seem to fit all of these big-brained animals. He points out that the bigger the brain, the more energy it takes to run, so it is crucial that it operates as efficiently as possible. A system that continually monitors the environment and the people or animals in it would therefore be an asset, allowing you to adapt quickly to a situation to save as much energy as possible. "Evolution produced an energy calculation system that incorporated not just the sensory inputs from the body but the sensory inputs from the brain," Craig says. And the fact that we are constantly updating this picture of "how I feel now" has an interesting and very useful by-product: we have a concept that there is an "I" to do the feeling. "Evolution produced a very efficient moment-by-moment calculation of energy utilisation and that had an epiphenomenon, a by-product that provided a subjective representation of my feelings."

If he's right – and there is a long way to go before we can be sure – it raises a very humbling possibility: that far from being the pinnacle of brain evolution, consciousness might have been a big, and very successful accident. ■

GEORGE DOYLE/STOCKBYTE/GETTY

To understand consciousness, we need to work out how anaesthesia makes it fade away. Linda Geddes journeys…

Into the void

I WALK into the operating theatre feeling vulnerable in a draughty gown and surgical stockings. Two anaesthetists in green scrubs tell me to stash my belongings under the trolley and lie down. "Can we get you something to drink from the bar?" they joke, as one deftly slides a needle into my left hand.

I smile weakly and ask for a gin and tonic. None appears, of course, but I begin to feel light-headed, as if I really had just knocked back a stiff drink. I glance at the clock, which reads 10.10 am, and notice my hand is feeling cold. Then, nothing.

I have had two operations under general anaesthetic this year. On both occasions I awoke with no memory of what had passed between the feeling of mild wooziness and waking up in a different room. Both times I was told that the anaesthetic would make me feel drowsy, I would go to sleep, and when I woke up it would all be over.

What they didn't tell me was how the drugs would send me into the realms of oblivion. They couldn't. The truth is, no one knows.

The development of general anaesthesia has transformed surgery from a horrific ordeal into a gentle slumber. It is one of the commonest medical procedures in the world, yet we still don't know how the drugs work. Perhaps this isn't surprising: we still don't understand consciousness, so how can we comprehend its disappearance?

That is starting to change, however, with the development of new techniques for imaging the brain or recording its electrical activity during anaesthesia. "In the past five years there has been an explosion of studies, both in terms of consciousness, but also how anaesthetics might interrupt consciousness and what they teach us about it," says George Mashour, an anaesthetist at the University of Michigan in Ann Arbor. "We're at the dawn of a golden era."

Consciousness has long been one of the great mysteries of life, the universe and everything. It is something experienced by every one of us, yet we cannot even agree on how to define it. How does the small sac of jelly that is our brain take raw data about the world and transform it into the wondrous sensation of being alive? Even our increasingly sophisticated technology for peering inside the brain has, disappointingly, failed to reveal a structure that could be the seat of consciousness.

Altered consciousness doesn't only happen under a general anaesthetic of course – it occurs whenever we drop off to sleep, or if we are unlucky enough to be whacked on the head. But anaesthetics do allow neuroscientists to manipulate our consciousness safely, reversibly and with exquisite precision.

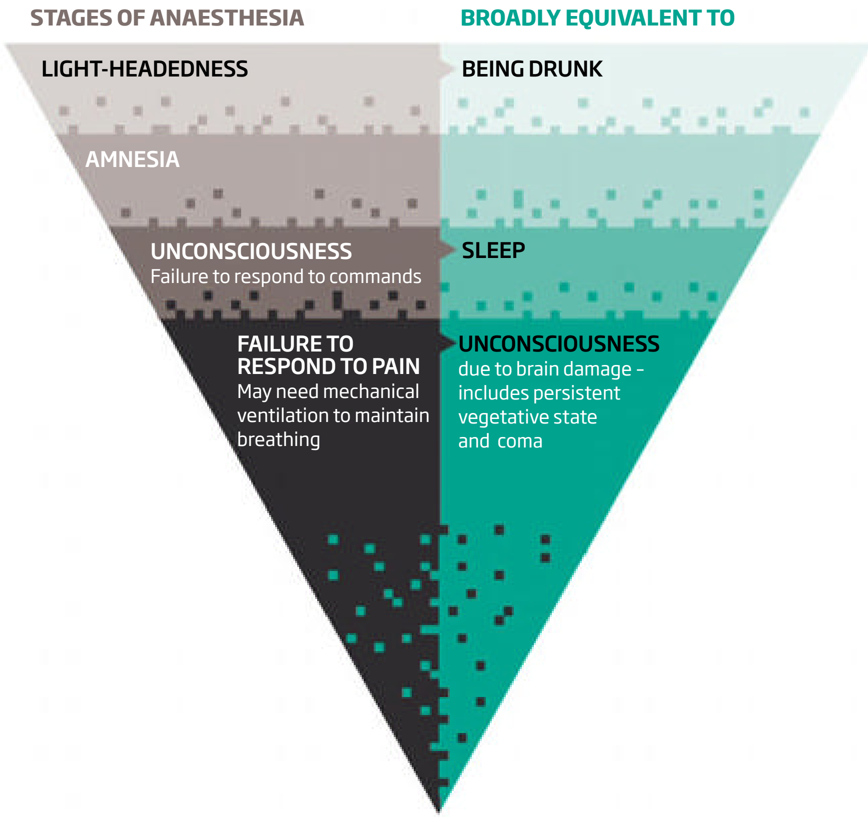
It was a Japanese surgeon who performed the first known surgery under anaesthetic, in 1804, using a mixture of potent herbs. In the West, the first operation under general anaesthetic took place at Massachusetts General Hospital in 1846. A flask of sulphuric ether was held close to the patient's face until he fell unconscious.

Since then a slew of chemicals have been co-opted to serve as anaesthetics, some inhaled, like ether, and some injected. The people who gained expertise in administering these agents developed their own medical speciality. Although long overshadowed by the surgeons who patch you up, the humble "gas man" does just as important a job, holding you in the twilight between life and death.

Consciousness may often be thought of as an all-or-nothing quality – either you're awake or you're not – but as I experienced, there are different levels of anaesthesia (see diagram, page 92). "The process of going into and out of general anaesthesia isn't like flipping a light switch," says Mashour. "It's more akin to a dimmer switch."

You are feeling sleepy

Losing consciousness under anaesthesia is not so much flipping a light switch as turning down a dimmer switch



A typical subject first experiences a state similar to drunkenness, which they may or may not be able to recall later, before falling unconscious, which is usually defined as failing to move in response to commands. As they progress deeper into the twilight zone, they now fail to respond to even the penetration of a scalpel – which is the point of the exercise, after all – and at the deepest levels may need artificial help with breathing.

These days anaesthesia is usually started off with injection of a drug called propofol, which gives a rapid and smooth transition to unconsciousness, as happened with me. (This is also what Michael Jackson was allegedly using as a sleeping aid, with such unfortunate consequences.) Unless the operation is only meant to take a few minutes, an inhaled anaesthetic, such as isoflurane, is then usually added to give better minute-by-minute control of the depth of anaesthesia.

Lock and key

So what do we know about how anaesthetics work? Since they were first discovered, one of the big mysteries has been how the members of such a diverse group of chemicals can all result in the loss of consciousness. Other drugs work by binding to receptor molecules in the body, usually proteins, in a way that relies on the drug and receptor fitting snugly together like a key in a lock. Yet the long list of anaesthetic agents ranges from large complex molecules such as barbiturates or steroids, to the inert gas xenon, which exists as mere atoms. How could they all fit the same lock?

For a long time, there was great interest in the fact that the potency of anaesthetics correlates strikingly with how well they dissolve in olive oil. The popular "lipid theory" said that instead of binding to specific protein receptors, the anaesthetic physically disrupted the fatty membranes of nerve cells, causing them to malfunction.

In the 1980s, though, experiments in test tubes showed that anaesthetics could bind to proteins in the absence of cell membranes. Since then, protein receptors have been found for many anaesthetics. Propofol, for instance, binds to receptors on nerve cells that normally respond to a chemical messenger called GABA. Presumably the solubility of anaesthetics in oil affects how easily they reach the receptors bound in the fatty membrane.

But that solves only a small part of the mystery. We still don't know how this binding affects nerve cells, and which neural networks they feed into. "If you look at the brain under both xenon and propofol anaesthesia, there are striking similarities," says Nick Franks of Imperial College London, who overturned the lipid theory in the 1980s. "They must be triggering some common neuronal change and that's the big mystery."

Many anaesthetics are thought to work by making it harder for neurons to fire, but this can have different effects on brain function, depending on which neurons are being blocked. So brain-imaging techniques such as functional MRI scanning, which tracks changes in blood flow to different areas of the brain, are being used to see which regions of the brain are affected by anaesthetics. Such studies have revealed several areas that are deactivated by most anaesthetics. Unfortunately, so many regions have been implicated it is hard to know which, if any, are the root cause of loss of consciousness.

But is it even realistic to expect to find a discrete site or sites acting as the mind's "light switch"? One intriguing study conducted on a woman who had electrodes implanted in her brain because she had epilepsy found that stimulating just one area – the claustrum – caused the woman to lose consciousness. She regained consciousness as soon as the electrical stimulation stopped. But even if this experiment is repeated in others, such a consciousness-switch is still likely to be one piece in a larger network of brain activity.

A leading theory of consciousness that has gained ground in the past decade states that consciousness is more widely distributed. In this "global workspace" theory, incoming sensory information is first processed locally in separate brain regions without us being aware of it. We only become conscious of the experience if these signals are broadcast to a network of neurons spread through the brain, which then start firing in synchrony.

The idea has recently gained support from recordings of the brain's electrical activity using electroencephalograph (EEG) sensors on the scalp, as people are given anaesthesia. This has shown that as consciousness fades there is a loss of synchrony between different areas of the cortex – the outermost layer of the brain important in attention, awareness, thought and memory.

This process has also been visualised using fMRI scans. Steven Laureys, who leads the Coma Science Group at the University of Liège in Wallonia, Belgium, looked at what happens during propofol anaesthesia when patients descend from wakefulness, through mild sedation, to the point at which they fail to respond to commands. He found that while small "islands" of the cortex lit up in response to external stimuli when people were unconscious, there was no spread of activity to other areas, as there was during wakefulness or mild sedation.

A team led by Andreas Engel at the University Medical Center in Hamburg, Germany, have been investigating this process in still more detail by watching the transition to unconsciousness in slow motion. Normally it takes about 10 seconds to fall asleep after a propofol injection. Engel has slowed it down to many minutes by starting with just a small dose, then increasing it in seven stages. At each stage he gives a mild electric shock to the volunteer's wrist and takes EEG readings.

We know that upon entering the brain, sensory stimuli first activate a region called the primary sensory cortex, which runs like a headband from ear to ear. Then further networks are activated, including frontal regions involved in controlling behaviour, and temporal regions towards the base of the brain that are important for memory storage.

Engel found that at the deepest levels of anaesthesia, the primary sensory cortex was the only region to respond to the electric shock. "Long-distance communication seems to be blocked, so the brain cannot build the global workspace," says Engel. "It's like the message is reaching the mailbox, but no one is picking it up."

Other recent research also suggests that sensory signals reach the cortex but fail to be sent out to the rest of the brain more widely.

What could be causing the blockage? Engel has EEG data suggesting that propofol interferes with communication between the primary sensory cortex and other brain regions by causing abnormally strong synchrony between them. "It's not just shutting things down. The communication has changed," he says. "If too many neurons fire in a strongly synchronised rhythm, there is no room for exchange of specific messages."

The communication between the different regions of the cortex is not just one way; there is both forward and backward signalling between the different areas. EEG studies on anaesthetised animals suggest it is the backwards signal between these areas that is lost when they are knocked out.

Mashour's group recently published EEG work showing that this is important in people too. Both propofol and the inhaled anaesthetic sevoflurane inhibited the transmission of feedback signals from the frontal cortex in anaesthetised surgical patients. The backwards signals recovered at the same time as consciousness returned.

Similar findings are coming in from studies of people in a coma or persistent vegetative state (PVS), who may open their eyes in a sleep-wake cycle, although remain unresponsive. Laureys, for example, has seen a similar breakdown in communication between different cortical areas in people in a coma. "Anaesthesia is a pharmacologically induced coma," he says. "That same breakdown in global neuronal workspace is occurring."

Many believe that studying anaesthesia will shed light on disorders of consciousness such as coma. "Anaesthesia studies are probably the best tools we have for understanding consciousness in health and disease," says Adrian Owen of the University of Western Ontario in London, Canada.

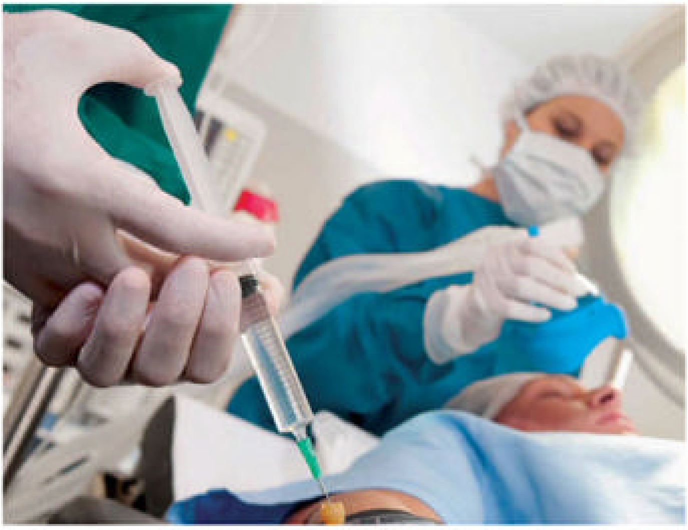
> "Is it realistic to expect to find a discrete site in the brain acting as the mind's light switch? Not according to the leading theory of consciousness"

Owen and others have previously shown that people in a PVS respond to speech with electrical activity in their brain. More recently he did the same experiment in people progressively anaesthetised with propofol. Even when heavily sedated, their brains responded to speech. But closer inspection revealed that those parts of the brain that decode the meaning of speech had indeed switched off, prompting a rethink of what was happening in people with PVS. "For years we had been looking at vegetative and coma patients whose brains were responding to speech and getting terribly seduced by these images, thinking that they were conscious," says Owen. "This told us that they are not conscious."

As for my own journey back from the void, the first I remember is a different clock telling me that it is 10.45 am. Thirty-five minutes have elapsed since my last memory – time that I can't remember, and probably never will.

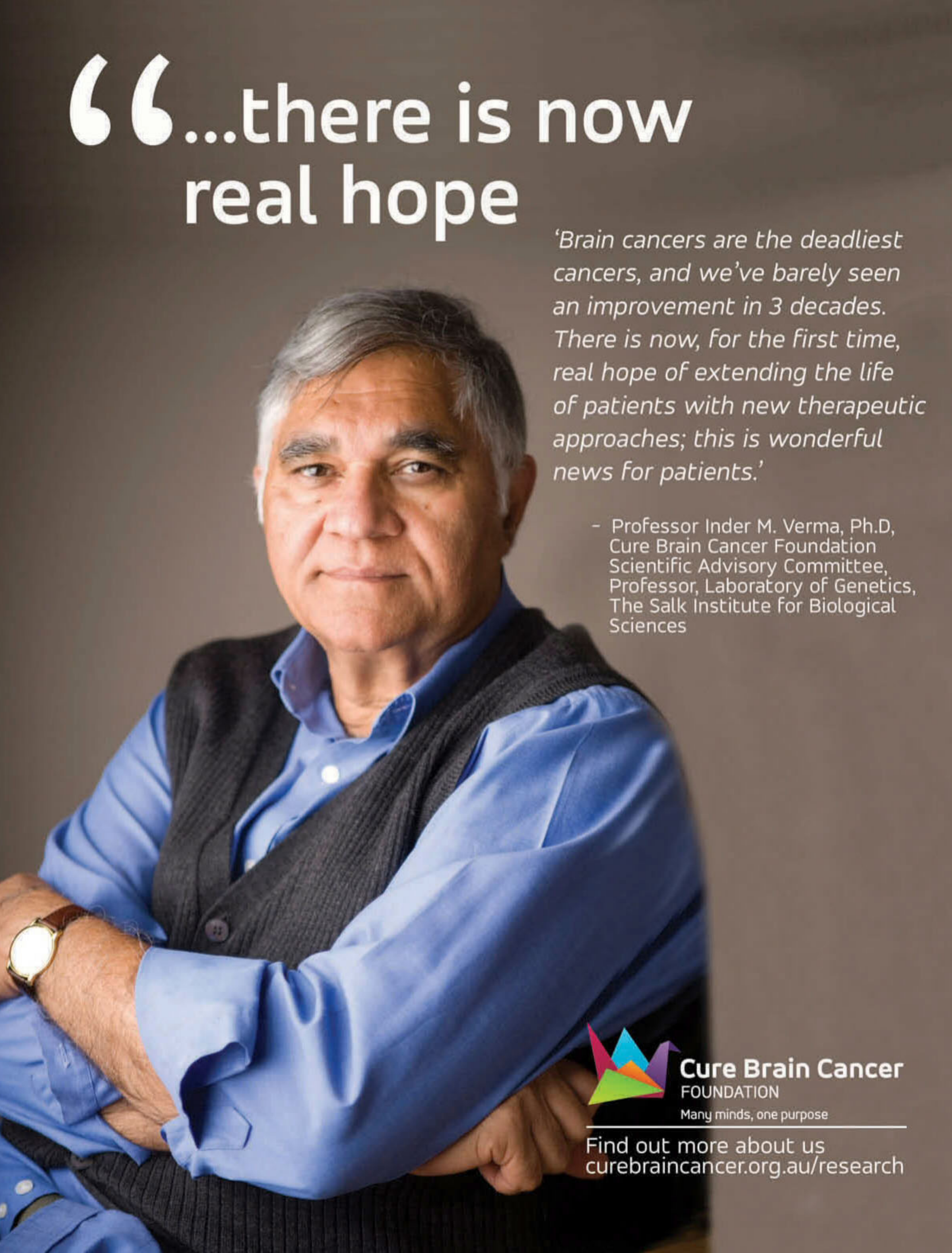
"Welcome back," says a nurse sitting by my bed. I drift in and out of awareness for a further undefined period, then another nurse wheels me back to the ward, and offers me a cup of tea. As the shroud of darkness begins to lift, I contemplate what has just happened. While I have been asleep, a team of people have rolled me over, cut me open, and rummaged about inside my body – and I don't remember any of it. For a brief period of time "I" had simply ceased to be.

My experience leaves me with a renewed sense of awe for what anaesthetists do as a matter of routine. Without truly knowing how, they guide hundreds of millions of people a year as close to the brink of nothingness as it is possible to go without dying. Then they bring them safely back home again. ■



GLOW/GETTY IMAGES

Studying anaesthesia might shed light on conditions such as coma



“...there is now real hope
‘Brain cancers are the deadliest cancers, and we’ve barely seen an improvement in 3 decades. There is now, for the first time, real hope of extending the life of patients with new therapeutic approaches; this is wonderful news for patients.’
- Professor Inder M. Verma, Ph.D, Cure Brain Cancer Foundation Scientific Advisory Committee, Professor, Laboratory of Genetics, The Salk Institute for Biological Sciences
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Solid. Liquid. Consciousness

Consciousness is just another state of matter, like a solid, liquid or gas, says physicist **Max Tegmark**

WHY are you conscious right now? Specifically, why are you having a subjective experience of reading these words, seeing colours and hearing sounds, while the inanimate objects around you presumably aren't having any subjective experience at all?

Different people mean different things by "consciousness", including awareness of environment or self. I am asking the more basic question of why you experience anything at all, which is the essence of what philosopher David Chalmers has coined "the hard problem" of consciousness.

A traditional answer to this problem is dualism – that living entities differ from inanimate ones because they contain some non-physical element such as an "anima" or "soul". Support for dualism among scientists has gradually dwindled. To understand why, consider that your body is made up of about 10^{29} quarks and electrons, which as far as we can tell move according to simple physical laws. Imagine a future technology able to track all of your particles: if they were found to obey the laws of physics exactly, then your purported soul is having no effect on your particles, so your conscious mind and its ability to control your movements would have nothing to do with a soul.

If your particles were instead found not to obey the known laws of physics because they were being pushed around by your soul, then we could treat the soul as just another physical entity able to exert forces on particles, and study what physical laws it obeys.

Let us therefore explore the other option, known as physicalism: that consciousness is a process that can occur in certain physical systems. This begs a fascinating question: why are some physical entities conscious, while others are not? If we consider the most general state of matter that experiences consciousness – let's call it "perceptronium" – then what special properties does it have that we could in principle measure in a lab? What are these physical correlates of consciousness? Parts of your brain clearly have these properties right now, as well as while you were dreaming last night, but not while you were in deep sleep.

Imagine all the food you have eaten in your life and consider that you are simply some of that food, rearranged. This shows that your consciousness isn't simply due to the atoms you ate, but depends on the complex patterns into which these atoms are arranged. If you can also imagine conscious entities, say aliens or future superintelligent robots, made out of different types of atoms then this suggests that consciousness is an "emergent phenomenon" whose complex behaviour emerges from many simple interactions. In a similar spirit, generations of physicists and chemists have studied what happens when you group together vast numbers of atoms, finding that their collective behaviour depends on the patterns in which they are arranged. For instance, the key difference between a solid, a liquid and a gas lies not in the types of atoms, but in their arrangement. Boiling or freezing a liquid simply rearranges its atoms.

> **"Just as there are many types of liquid, there are many types of consciousness"**

My hope is that we will ultimately be able to understand perceptronium as yet another state of matter. Just as there are many types of liquids, there are many types of consciousness. However, this should not preclude us from identifying, quantifying, modelling and understanding the characteristic properties shared by all liquid forms of matter, or all conscious forms of matter. Take waves, for example, which are substrate-independent in the sense that they can occur in all liquids, regardless of their atomic composition. Like consciousness, waves are emergent phenomena in the sense that they take on a life of their own: a wave can traverse a lake while the individual water molecules merely bob up and down, and the motion of the wave can be described by a mathematical equation that doesn't care what the wave is made of.

Something analogous happens in computing. Alan Turing famously proved that all sufficiently advanced computers can simulate one another, so a video-game character in her virtual world would have no way of knowing whether her computational substrate ("computronium") was a Mac or a PC, or what types of atoms the hardware was made of. All that would matter is abstract information processing. If this created character were complex enough to be conscious, like in the film *The Matrix*, then what properties would this information processing need to have?

I have long contended that consciousness is the way information feels when processed in certain complex ways. The neuroscientist Giulio Tononi has made this idea more specific and useful, making the compelling argument that for an information processing system to be conscious, its information must be integrated into a unified whole. In other words, it must be impossible to decompose the system into nearly independent parts – otherwise these parts would feel like two separate conscious entities. Tononi and his collaborators have incorporated this idea into an elaborate mathematical formalism known as integrated information theory (IIT).

IIT has generated significant interest in the neuroscience community, because it offers answers to many intriguing questions. For example, why do some information processing systems in our brains appear › to be unconscious? Based on extensive research correlating brain measurements with subjectively reported experience, neuroscientist Christof Koch and others have concluded that the cerebellum – a brain area whose roles include motor control – is not conscious, but is an unconscious information processor that helps other parts of the brain with certain computational tasks.

The IIT explanation for this is that the cerebellum is mainly a collection of "feed-forward" neural networks in which information flows like water down a river, and each neuron affects mostly those downstream. If there is no feedback, there is no integration and hence no consciousness. The same would apply to Google's recent feed-forward artificial neural network that processed millions of YouTube video frames to determine whether they contained cats. In contrast, the brain systems linked to consciousness are strongly integrated, with all parts able to affect one another.

IIT thus offers an answer to the question of whether a superintelligent computer would be conscious: it depends. A part of its information processing system that is highly integrated will indeed be conscious. However, IIT research has shown that for many integrated systems, one can design a functionally equivalent feed-forward system that will be unconscious. This means that

"Consciousness is the way information feels when processed in certain ways"

so-called "p-zombies" can, in principle, exist: systems that behave like a human and pass the Turing test for machine intelligence, yet lack any conscious experience whatsoever. Many current "deep learning" AI systems are of this p-zombie type. Fortunately, integrated systems such as those in our brains typically require far fewer computational resources than their feed-forward "zombie" equivalents, which may explain why evolution has favoured them and made us conscious.

Another question answered by IIT is why we are unconscious during seizures, sedation and deep sleep, but not REM sleep. Although our neurons remain alive and well during sedation and deep sleep, their interactions are weakened in a way that reduces integration and hence consciousness. During a seizure, the interactions instead get so strong that vast numbers of neurons start imitating one another, losing their ability to contribute independent information, which is another key requirement for consciousness according to IIT. This is analogous to a computer hard drive where the bits that encode information are forced to be either all zeros or all ones, resulting in the drive storing only a single bit of information. Tononi, together with Adenauer Casali, Marcello Massimini and other collaborators, recently validated these ideas with lab experiments. They defined a "consciousness index" that they could measure by using an EEG to monitor the electrical activity in people's brains after magnetic stimulation, and used it to successfully predict whether they were conscious.

Detection devices

Awake and dreaming people had comparably high consciousness indices, whereas those anaesthetised or in deep sleep had much lower values. The index even successfully identified as conscious two patients with locked-in syndrome, who were aware and awake but prevented by paralysis from speaking or moving. This illustrates the promise of this technique for helping doctors determine whether unresponsive patients are conscious.

Despite these successes, IIT leaves many questions unanswered. If it is to extend our consciousness-detection ability to animals, computers and arbitrary physical systems, then we need to ground its principles in fundamental physics. IIT takes information measured in bits as a starting point. But when I view a brain or computer through my physicist's eyes, as myriad moving particles, then what physical properties of the system should be interpreted as logical bits of information? I interpret as a "bit" both the position of certain electrons in my computer's RAM memory (determining whether the micro-capacitor is charged) and the position of certain sodium ions in your brain (determining whether a neuron is firing), but on the basis of what principle? Surely there should be some way of identifying consciousness from the particle motions alone, even without this information interpretation? If so, what aspects of the behaviour of particles correspond to conscious integrated information?

The problem of identifying consciousness in an arbitrary collection of moving particles is similar to the simpler problem of identifying objects in such a system. For instance, when you drink iced water, you perceive an ice cube in your glass as a separate object because its

PLAINPICTURE

parts are more strongly connected to one another than to their environment. In other words, the ice cube is both fairly *integrated* and fairly *independent* of the liquid in the glass. The same can be said about the ice cube's constituents, from water molecules all the way down to atoms, protons, neutrons, electrons and quarks. Zooming out, you similarly perceive the macroscopic world as a dynamic hierarchy of objects that are strongly integrated and relatively independent, all the way up to planets, solar systems and galaxies.

This grouping of particles into objects reflects how they are stuck together, which can be quantified by the amount of energy needed to pull them apart. But we can also reinterpret

Why do we experience things in the ways that we do?

this in terms of information: if you know the position of one of the atoms in the piston of an engine, then this gives you information about the whereabouts of all the other atoms in the piston, because they all move together as a single object. A key difference between inanimate and conscious objects is that for the latter, too much integration is a bad thing: the piston atoms act much like neurons during a seizure, slavishly tracking one another so that very few bits of independent information exist in this system. A conscious system must thus strike a balance between too little integration (such as a liquid with atoms moving fairly independently) and too much integration (such as a solid). This suggests that consciousness is maximised near a phase transition between less- and more-ordered states; indeed, humans lose consciousness unless key physical parameters of our brain are kept within a narrow range of values.

An elegant balance between information and integration can be achieved using error-correcting codes: methods for storing bits of information that know about each other, so that all information can be recovered from a fraction of the bits. These are widely used in telecommunications, as well as in the ubiquitous QR codes from whose characteristic pattern of black and white squares your smartphone can read a web address. As error correction has proven so useful in our technology, it would be interesting to search for error-correcting codes in the brain, in case evolution has independently discovered their utility – and perhaps made us conscious as a side effect.

We know that our brains have some ability to correct errors, because you can recall the correct lyrics for a song you know from a slightly incorrect fragment of it. John Hopfield, a biophysicist renowned for his eponymous neural network model of the brain, proved that his model has precisely this error-correcting property. However, if the hundred billion neurons in our brain do form a Hopfield network, calculations show that it could only support about 37 bits of integrated information – the equivalent of a few words of text. This raises the question of why the information content of our conscious experience seems to be significantly larger than 37 bits. The plot thickens when we view our brain's moving particles as a quantum-mechanical system. As I showed in a recent paper, the maximum amount of integrated information then drops from 37 bits to about 0.25 bits, and making the system larger doesn't help.

This problem can be circumvented by adding another principle to the list that a physical system must obey in order to be conscious. So far I have outlined three: the *information principle* (it must have substantial information storage capacity), the *independence principle* (it must have substantial independence from the rest of the world) and the *integration principle* (it cannot consist of nearly independent parts). The aforementioned 0.25 bit problem can be bypassed if we also add the *dynamics principle* – that a conscious system must have substantial information-processing capacity,

"Glaring problems in physics come from our confusion about consciousness"

and it is this processing rather than the static information that must be integrated. For example, two separate computers or brains can't form a single consciousness.

These principles are intended as necessary but not sufficient conditions for consciousness, much like low compressibility is a necessary but not sufficient condition for being a liquid. As I explore in my book *Our Mathematical Universe*, this leads to promising prospects for grounding consciousness and IIT in fundamental physics, although much work remains and the jury is still out on whether it will succeed.

If it does succeed, this will be important not only for neuroscience and psychology, but also for fundamental physics, where many of our most glaring problems reflect our confusion about how to treat consciousness. In Einstein's theory of general relativity, we model the "observer" as a fictitious disembodied massless entity having no effect whatsoever on that which is observed. In contrast, the textbook interpretation of quantum mechanics states that the observer does affect the observed. Yet after a century of spirited debate, there is still no consensus on how exactly to think of the quantum observer. Some recent papers have argued that the observer is the key to understanding other fundamental physics mysteries, such as why our universe appears so orderly, why time seems to have a preferred forward direction, and even why time appears to flow at all.

If we can figure out how to identify conscious observers in any physical system and calculate how they will perceive their world, then this might answer these vexing questions. ■

Mind into matter

Our minds extend way out into the material world around us, argues cognitive archaeologist **Lambros Malafouris**

WHERE should we look for the mind? This might sound like an odd question: surely, thinking takes place inside people's heads. Nowadays, we even have sophisticated neuroimaging techniques to prove it. As deeply intuitive as this assumption about the boundaries of the mind may be, I think it is quite mistaken.

I see no compelling reason why the study of the mind should stop at the skin or the skull. Quite the contrary. There is an abundance of evidence, ranging from earliest prehistory to the present, to testify that things, as well as neurons, participate in human cognitive life. From the viewpoint of archaeology, it is clear that stone objects, body ornaments, engravings, clay tokens and writing systems play an active role in human evolution and the making of the human mind. Consequently, I suggest that what is outside the head may not necessarily be outside the mind. In fact, I doubt if notions like "inside" and "outside" make any useful sense in the study of human cognition.

It is easy to see how the mind and the brain became equated. Most of what we know about the human mind has been uncovered through isolating people from the material culture they are usually surrounded by in order to study them. This makes good sense if you are a neuroscientist, because of the constraints imposed by using a brain-scanning machine. But as a result, it often goes unnoticed that much of our thinking takes place outside our heads. Naturally, I do not mean to question the neural basis of cognition, but to point out that mind is more than a brain.

Instead, it would be more productive to explore the hypothesis that human intelligence "spreads out" beyond the skin into culture and the material world. I am a cognitive archaeologist, trying to understand the way ancient people thought by studying the archaeological evidence they left behind. And this is exactly where the challenge for this field lies: at the realm of engagement with the material world. Meeting this challenge demands reconnecting the brain with the body and beyond, breaking with reductionistic "internalist" explanations that separate the mental realm from the realm of the material world. This is where a theory I've developed – material engagement theory (MET) – comes in.

At its heart, MET aims to explore the different ways in which things become cognitive extensions or are incorporated by the human body, such as when one makes numbers and symbols out of clay, or uses a stone to strike another, forming a tool. It also investigates how those ways might have changed since earliest prehistory, and what those changes mean for the ways we think. This approach gives a new understanding of what minds are, and what they are made of, by changing what we know about what things do for the mind.

Think of a blind person with a stick. Where does this person's self begin? This famous example is one of my favourites. The unity of the blind man and the stick offers a way to conceptualise minds and things as continuous, but it also provides an analogy for the profound plasticity of the human mind: using a stick, the blind man turns touch into sight, but the stick has its own interesting active role. Tactile sensation is somehow projected onto the point of contact between the tip of the stick and the outside environment. As a result, the brain treats the stick as part of the body. This is not simply a matter of expanding "peripersonal space" – that is, the space surrounding the body. Neither is it simply a matter of substituting vision for touch. The stick does more than that. It becomes an interface of a peculiarly transformative sort – what might be called a brain-artefact interface, or a "cognitive prosthesis".

A blind person's walking stick is an extension of their mind – a "cognitive prosthesis"

It is especially in the latter sense that the example of the blind man's stick encapsulates the spirit of MET. It reminds us of something that many people forget; namely, that it is in the nature of human intelligence to remain amenable to drastic, deep reorganisation by incorporating new technological innovations.

Let me explain. My approach sees the human mind as an unfinished project, in a permanent state of ongoing evolution and neural reuse. It is important to keep in mind that, whatever actual form the "stick" might have taken in the history of our species – from

SOE ZEYA TUN/REUTERS/CORBIS

the earliest Palaeolithic stone tools to the internet – its primary function was that of a pathway instead of a boundary. Through the "stick", the human species, much like the blind man in our example, feels, discovers, and makes sense of the environment, but also enacts the way forward.

Let's not forget that from an evolutionary point of view, the main reason we have a brain is to move, not to contemplate. And it seems fair to say that the reason we came to have our sophisticated capacities for thought and language is that, unlike any other animal, we gave our movement purpose, direction and meaning. We had to use a "stick" to accomplish that; something concrete, a material scaffold to think through, with and about. We came to have a sapient mind because we are *Homo faber* – a concept developed by the French philosopher Henri Bergson in his 1907 book *Creative Evolution*, which holds that human intelligence was originally a facility to create artificial objects. Tool-making and tool use was just the beginning in a series of prostheses and material signs. Indeed, things do much of our thinking.

"It often goes unnoticed that much of our thinking takes place outside our heads"

That is also why a stick used by a monkey in captivity to retrieve food is of a different kind. For humans, "sticks" are also used for sight – in the Aristotelian sense in which "seeing" is intimately associated with our desire to know. In contrast, for non-human animals, sticks are basically for eating. That's a difference that makes a difference.

This unique human predisposition for engagement with material culture explains why we humans, more than any other species, make things, and how those things, in return, make our minds what they are. I call that metaplasticity – we have plastic minds that develop and change as they interact with the material world.

I want to put materiality back into the cognitive equation. MET offers a new way of understanding how different forms of material culture, from the stone hand-axe to the iPhone, may have provided a powerful mechanism of defining, but also transforming, what we are and how we think. Mind-changing technology has a futuristic, sci-fi ring to it, but what most people don't realise is that humans have used it since they first evolved. ■

Your clever body

It's not just your mind that does the thinking, David Robson discovers

TAKE a minute out of the hustle and bustle of your busy life and sit very still. Now, place your hands on the arms of the chair or the desk in front of you, and try to focus your attention on counting your heartbeats. Can you feel a throbbing drum roll, a slight murmur or nothing at all? How does your bladder feel – is it empty or will you need to dash for the bathroom within the next half hour? You may be surprised to learn that these bodily sensations are helping you think.

We tend to view the mind as an aloof, disembodied entity, but it is becoming increasingly clear that the whole body is involved in the thinking process. Without input from your body, your mind would be unable to generate a sense of self or process emotions properly. Your body even plays a role in thinking about language and mathematics. And physiological sensations, such as those from your heart and bladder, influence such diverse personal attributes as the strength of your tendency to conform, your willpower and whether you are swayed by your intuitions or governed by rational thought.

In the past few years, discoveries about mind-body connections have overturned the long-held view of the body as a passive vehicle driven by the brain. Instead there is more of a partnership, with bodily experiences playing an active role in your mental life. "The brain cannot act independently of the body," says Arthur Glenberg at the University of Wisconsin-Madison. Tune in to the body's signals, and you can exploit this to improve your creativity, memory and self-control.

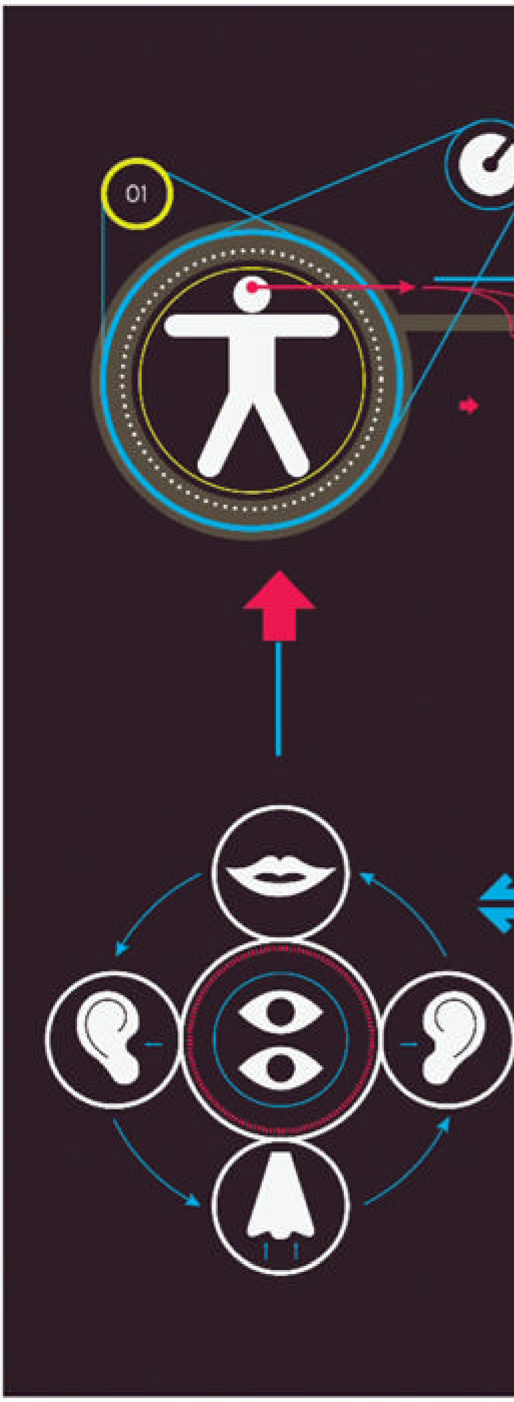
René Descartes must be turning in his grave at these findings. In his *Meditations on First Philosophy*, published in 1641, he famously argued that the mind and body are, in essence, two separate entities that could theoretically exist entirely independently of one another. The book sparked a fierce debate into the exact nature of the mind-body connection – a debate that continues to this day. At the centre of the modern discussion is the puzzling sensation of embodiment. The feeling that we own the flesh and blood that stretches from the tips of our toes to the crown of our head is the essence of our sense of self. As such, embodiment is central to consciousness, yet, until recently, we knew little about it.

The first hint of the answer came from an eerie illusion discovered in the late 1990s by Matthew Botvinick, then a doctoral student at Carnegie Mellon University in Pittsburgh, Pennsylvania. He had the idea that embodiment emerges from the brain's need to integrate the information it is receiving from various senses. A Halloween party gave him the perfect opportunity to test this, when he discovered that someone had brought a rubber arm along as part of their costume. Placing the fake arm where he could see it on a table, while hiding his real arm from view, Botvinick asked an accomplice to stroke both rubber and real arms at equivalent places and in time with one another. As he suspected, in an attempt to reconcile the tactile and visual stimuli, he began to feel as if the stroking sensation was coming from the arm he could see. It was as if his brain had forgotten about the real arm and now felt it owned the fake one. He was suitably spooked by the sensation: "I was so unsettled I threw the arm across the room."

Subsequent lab experiments confirmed the result wasn't just the product of a hard night's partying. Importantly, Botvinick also found that the illusion did not occur when brush strokes on the real and fake arm were out of sync, because then the brain was not receiving confused messages that it had to resolve.

Soon, other groups saw the potential of the rubber-hand illusion for unlocking the secrets of embodiment. Brain scans taken as people fell for the trick showed that we have a crude body map in the brain's right temporoparietal junction. When our senses provide information about our bodies, this is compared and integrated with the map in the premotor and parietal cortices (see diagram, page 103). Any mismatch must be resolved at this stage, leading to illusions such as the rubber hand. However, it is only when the integrated information reaches another area called the insular cortex that the feeling of embodiment pops into conscious awareness.

That's not all. The insular cortex also processes our internal bodily signals,



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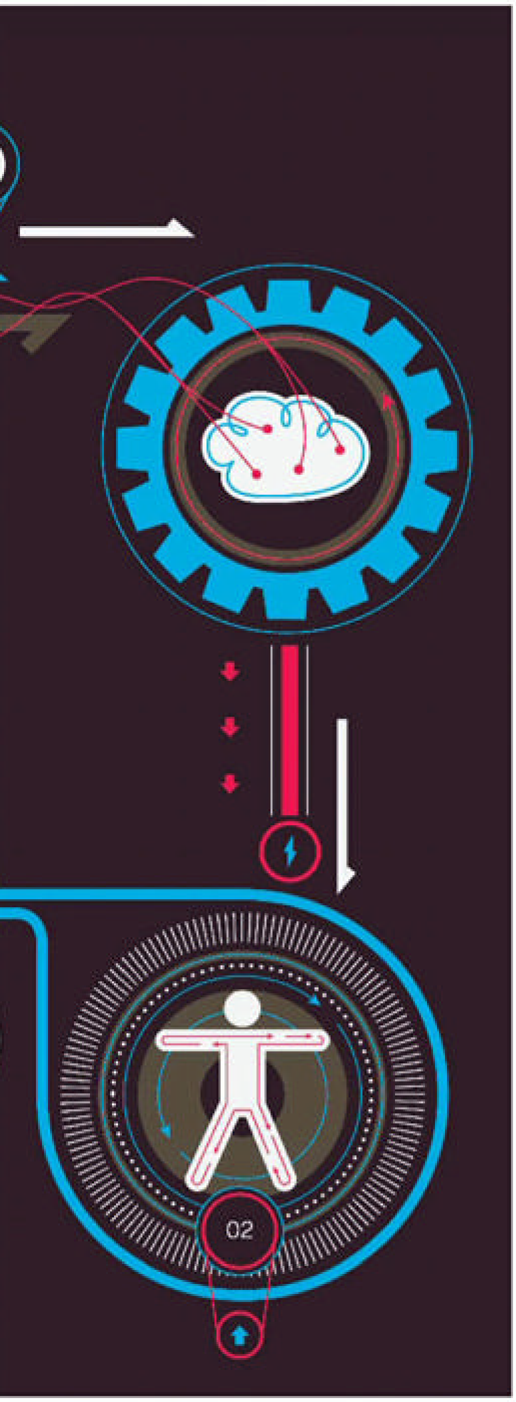


CREATIVE POSTURING

Truman Capote once described himself as a "horizontal author", saying: "I can't think unless I'm lying down, either in bed or stretched on a couch and with a cigarette and coffee handy." Vladimir Nabokov was a similarly supine writer.

They might have had a point. In 2005, Darren Lipnicki and Don Byrne, both then at the Australian National University in Canberra, found that people solved anagrams in about 10 per cent less time when lying down compared with standing. The mechanism is fairly simple. Stress is well known to be the enemy of creativity, and we feel more relaxed on our backs than on our feet.

If you can't persuade your boss to buy you a chaise longue for the office, there are some more discreet ways to get those creative juices flowing. For instance, Joël Cretenet and Vincent Dru from Paris West University Nanterre La Défense suggest that you extend your left arm out in front of you or bend your right arm at the elbow, so you resemble Auguste Rodin's iconic statue *The Thinker*. Volunteers who made these moves performed much better on a creative thinking task, in which they had to find innovative uses for an everyday object, such as a brick. The explanation is complicated, but it seems the movements are tied to our instincts to approach or distance ourselves from a situation. This helps broaden our outlook on the problem, which is known to be crucial for flexible thinking.

Even simple eye movements left and right across your field of vision can help you to think more laterally. It is thought that this temporarily encourages communication between the right and left hemispheres of the brain, which boosts creativity.

"Mathematical thinking seems to piggyback on our experience of movement and space"

including the throb of our pulse and rumble of our gut. And it turns out that people vary greatly in how good they are at detecting these, an ability known as interoception. A team led by Manos Tsakiris at Royal Holloway, University of London, found that around a quarter of volunteers were able to count their own heartbeats with an accuracy of at least 80 per cent without taking their pulse, while another quarter had little conscious awareness of it, missing the actual number by 50 per cent or more. Intriguingly, the team also found that those who were particularly good at interoception were less susceptible to embodiment illusions, perhaps because these internal sensations override the contradictory information from their eyes. "If you have a strong sense of self from the inside, you don't rely so much on external information like vision and touch," says Tsakiris.

Since those pioneering experiments, all kinds of related illusions have surfaced, each unveiling more about the mind-body connection and the way it moulds our thinking. Henrik Ehrsson and his colleagues at the Karolinska Institute in Stockholm, Sweden, for example, recently used a set-up similar to Botvinick's to persuade volunteers to embody plastic bodies of various sizes, including the diminutive figure of a Barbie doll. Ehrsson noticed that the subjects perceived things as being much bigger when they were under the illusion that they were just 30 centimetres tall. "When we sat next to them, they had the sense that a giant body was nearby," he says. This suggests that our body awareness affects how we interpret the raw information hitting our eyes.

Tsakiris, meanwhile, has found that if he strokes someone's face in sync with a random face being stroked on a screen, he can persuade them to feel as if the image is their own reflection. This illusion is particularly intriguing, since it indicates that the body's influence might reach beyond sensory perception to determine how we relate to other people. Tsakiris believes it could explain why we warm to people who subtly copy our facial expressions and body language. He thinks that seeing a reflection of our ›

MARTIN POOLE/IMAGEBANK/GETTY

FLEXING YOUR WILLPOWER

Before you make your next important decision, try to hold off from visiting the bathroom for a few hours, says Mirjam Tuk at Imperial College London. "It could give you a little more self-control." She's not joking.

Tuk's discovery came after she read that just one neural circuit determines our self-control in lots of different areas. She wondered whether flexing willpower in one domain might therefore bolster resolve in another. Just then, nature started to call, suggesting the perfect way to test her idea. In her subsequent experiment, Tuk, who was at the time working at the University of Twente in the Netherlands, asked half of her volunteers to drink a few glasses of flavoured water, under the ruse that they were taking a taste test; the rest just took a sip of each sample. They waited a while before trying numerous tasks, including a classic test of self-control – considering whether they would prefer to receive a small amount of money now, or a larger sum at a later date. The subjects who had downed the drinks were more likely to choose to wait.

Fortunately, a bursting bladder is not the only way your body can help to increase your willpower. Walking backwards, or tensing your muscles, can strengthen your resolve, too. Folding your arms, meanwhile, seems to make you more persistent at a task in hand.

movements in someone else may evoke a faint version of the face-swap illusion, prompting us to act towards them rather as if we are admiring ourselves in the mirror.

An experiment by Maria-Paola Paladino at the University of Trento in Italy lends some support to this idea. She asked volunteers experiencing the face-swap illusion to rate their own personality, and to guess at the personality of the person on the screen in front of them. They considered themselves to be strikingly similar to the person on the screen. In a subsequent perceptual test, they were asked to estimate the number of letters flashed on a screen, while being told how the virtual person had answered. They were more likely to chose a figure around that answer than were people who had not been subjected to the illusion. Since people who are naturally sensitive to their internal signals are not as easily hoodwinked by body illusions, they may be less affected by this kind of social manipulation, and less empathic as a result.

If the simple feeling of the heart beating in our chest is somehow connected to our subconscious reactions to a person, how might the body's myriad other processes be shaping our thinking? That is exactly what researchers studying "embodied cognition" would like to know. Running against Descartes's philosophy, this school of thought maintains that many, if not all, aspects of our mental lives are inextricably linked to the experiences of our flesh and blood.

> **"Before you make your next important decision, try to hold off from visiting the bathroom"**

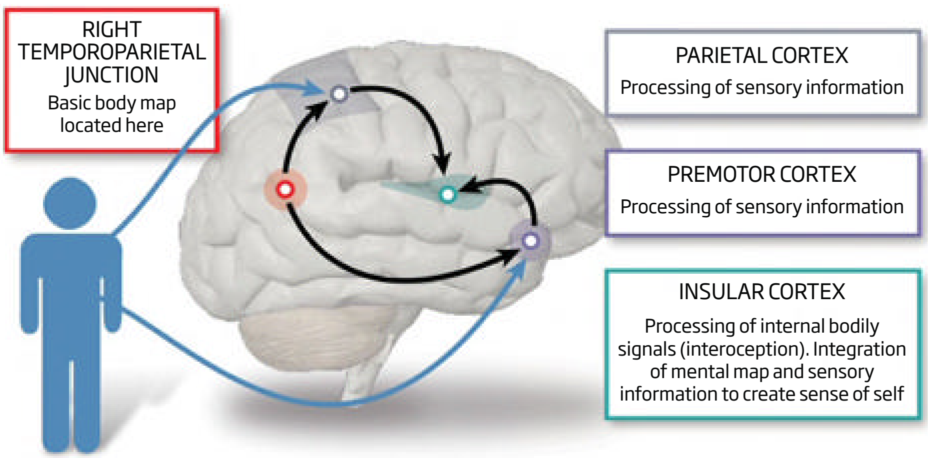
Emotional experience is perhaps the best-studied area of embodied cognition. As a simple example, you may think that you smile because you are happy, but in fact happy feelings arise in a large part from the physical sensation of smiling. Even very subtle facial expressions appear to be essential for us to process emotions. In one particularly elegant example, Glenberg's team showed that people whose frown muscles had been frozen with botox took longer to read sad or angry sentences than they did before receiving the treatment. Emotions are also linked to physical sensations. We tend to feel colder when we feel lonely, for example, and we associate warmth with friendliness and inclusion.

Such findings suggest that people who are in tune with their bodies are more sensitive to their own feelings. The jury is out on this one, though the fact that the same brain region – the insular cortex – handles both interoception and emotional processing supports the idea. There is also evidence that you can tap into this connection to improve your intuitive decision-making (see "How to follow your heart", right).

Touchy-feely emotions are one thing, but embodied cognition might stretch even further to abstract thought processes. Mathematical thinking, for example, seems somehow to piggyback on our experience of movement and space. When people are asked

The feeling of being you

Your sense of self, a key aspect of consciousness, is created by both your body and your brain



to think of random numbers, they are more likely to come up with smaller ones if they look down and to the left, and bigger ones if they look up and to the right. Other studies show that language is also deeply embodied. Every time we hear a word, the brain seems to simulate the actions associated with its meaning. When someone says the word "climb", for example, it activates the same neural regions that trigger our muscles to pull our weight up a tree. What's more, appropriate hand gestures can help our understanding of these words.

The field of embodied cognition is only just beginning to blossom, although it has had a relatively long history. Many questions remain, including where these mind-body associations come from. Are they innate or learned in infancy? "When we're cuddled up with mum, we might learn to associate warmth with feelings of social closeness," says Glenberg. But the link could be hardwired. It also remains to be seen exactly how much our mental and physical lives intertwine. "My personal belief is that all cognition is embodied," says Glenberg, "and the evidence is slowly inching towards this view."

None of this detracts from the many exciting applications of mind-body research. Tsakiris is looking at the clinical uses of illusions. A version of the rubber-hand illusion might help the brain to accept a prosthetic limb, while something akin to the face illusion could ease the rehabilitation of anyone receiving a face transplant. Face-swap illusions could also be used to help us better understand empathy and prejudice.

Experiments in which white and black faces are interchanged using a virtual environment, for example, have been shown to help people deal with implicit biases, while other experiments have shown that giving people superhero powers in a virtual reality can make them behave in a more helpful manner in real life. On a more frivolous note, body illusion techniques could help players embody virtual avatars in immersive video games.

Education should benefit, too. Glenberg has found that young children learn much more quickly, and understand more, if they are encouraged to play-act what they are reading. Their memory of the words seems to attach itself to the sensory experiences involved, he thinks. Susan Goldin-Meadow at the University of Chicago noticed something very similar in children learning simple equations. Those encouraged to gesture tended to understand the material more quickly and remember what they had learned for longer. The mechanism remains murky, although it is clear that the movements somehow activate an implicit understanding of the material.

You might be able to make use of these discoveries in your own life. Whether you want to increase your willpower, creativity or memory, there are numerous ways to exploit the mind-body connection for your own benefit (see "Creative posturing", page 101, and "Flexing your willpower", page 102). The effects may be moderate, but sometimes that's all you need. With your body helping you to think more effectively, you never know what you might achieve. ■

HOW TO FOLLOW YOUR HEART

We often use metaphors involving the body to describe the process of intuition – we talk about going with our "gut instincts" or "following our hearts". Perhaps we should take these phrases more literally. Barnaby Dunn, then at the Medical Research Council Cognition and Brain Sciences Unit in Cambridge, UK, and his colleagues have found that people who take notice of subtle physiological changes tend to be more intuitive.

The team first asked volunteers to sit quietly and try to count out their heartbeats without feeling for their pulse. All the while, an ECG machine took an accurate measurement. Comparing these two results gives a good indication of a person's "interoception", their ability to read their body's internal signals. Then, to test their intuition, the participants played a simple computer game. The computer offered them four decks of cards and on each round they had to guess which deck would present a card of a certain colour. Unbeknownst to the players, the set-up was rigged – two of the decks were always slightly more likely to have the winning cards than the other two. The results were surprising. Those with the best interoception tended to be either the best, or the worst, at this card game. Those who were bad at reading their body's signals came right in the middle.

Why could this be? Dunn suspects it is down to the way we process our emotions. In another experiment, he asked the same subjects to rate their emotional reactions as they looked at a series of emotive pictures. The better they were at interoception, the more these ratings correlated with physiological change, such as a shift in heart rate. Dunn suggests that having a hunch might create a flicker of excitement or interest that is reflected in subtle changes in physiology. Because people with good interoception are more sensitive to these signals, their perception of the hunch is stronger, making it more likely that they will act on it. "Their bodies are driving what they decide," he says. That doesn't mean the hunch is right, though – which would explain why these people did the best, and worst, of the group.

If you would like to tap into the signals that your subconscious mind is sending your body, you might want to take up meditation. Jocelyn Sze and colleagues at the University of California, Berkeley, have found that meditating improves bodily awareness and results in the same kind of link between physiological and emotional reactions that Dunn found to be crucial for intuition.

VAN WANTEN ETCETERA/SOUVEREIN PAGE DETAIL: ANNE FRANK FONDS/ANNE FRANK HOUSE VIA GETTY IMAGES

We are all collections of memories. They dictate how we think, act and make decisions, and even define our identity.

Yet memory, with its many virtues and flaws, has puzzled us for centuries. How are memories made and stored in the brain? Why do we remember some events but not others? What do other animals remember? And how can we improve the flawed instrument handed to us by evolution?

Over the following pages we answer these questions and many more, starting with a revolutionary new understanding of memory's purpose.

Memory
The ultimate guide

WHEN thinking about the workings of the mind, it is easy to imagine memory as a kind of mental autobiography – the private book of you. To relive the trepidation of your first day at school, say, you simply dust off the cover and turn to the relevant pages. But there is a problem with this idea. Why are the contents of that book so unreliable? It is not simply our tendency to forget key details. We are also prone to "remember" events that never actually took place, almost as if a chapter from another book has somehow slipped into our autobiography. Such flaws are puzzling if you believe that the purpose of memory is to record your past – but they begin to make sense if it is for something else entirely.

That is exactly what memory researchers are now starting to realise. They believe that human memory didn't evolve so that we could remember but to allow us to imagine what might be. This idea began with the work of Endel Tulving, now at the Rotman Research Institute in Toronto, Canada, who discovered a person with amnesia who could remember facts but not episodic memories relating to past events in his life. Crucially, whenever Tulving asked him about his plans for that evening, the next day or the summer, his mind went blank – leading Tulving to suspect that foresight was the flipside of episodic memory.

Subsequent brain scans supported the idea, suggesting that every time we think about a possible future, we tear up the pages of our autobiographies and stitch together the fragments into a montage that represents the new scenario. This process is the key to foresight and ingenuity, but it comes at the cost of accuracy, as our recollections become frayed and shuffled along the way. "It's not surprising that we confuse memories and imagination, considering that they share so many processes," says Daniel Schacter, a psychologist at Harvard University.

Over the next 10 pages, we will show how this theory has brought about a revolution in our understanding of memory. Given the many survival benefits of being able to imagine the future, for instance, it is not surprising that other creatures show a rudimentary ability to think in this way (page 106). Memory's role in planning and problem solving, meanwhile, suggests that problems accessing the past may lie behind mental illnesses like depression and post-traumatic stress disorder, offering a new approach to treating these conditions (page 110). Equally, a growing understanding of our sense of self can explain why we are so selective in the events that we weave into our life story – again showing definite parallels with the way we imagine the future (page 108). The work might even suggest some dieting tips (page 112).

It is still early days, but what's clear is that we are at the beginning of a long and exciting journey. "The one thing that we really have learned is that memory is extraordinarily more complicated than anyone would have thought 10 or 20 years ago," says Tulving. **David Robson** ■

When I was a chick...

Memory in its simplest form is as ancient as life itself. But do other creatures remember like we do, asks **Emma Young**

EVERY morning, you take a walk in the park, bringing some bread to feed the pigeons. As the days wear on, you begin to see the birds as individuals; you even start to name them. But what do the pigeons remember of you? Do they think kindly of you as they drop off to sleep at night, or is your face a blank, indistinguishable from the others strolling through the park?

These questions may seem whimsical, but knowing what other creatures recall is crucial if we are to understand their inner lives. It turns out that the range of mnemonic feats in the wild is nearly as varied as life itself.

If you take memory to mean any ability to store and respond to past events, even the simplest organisms meet the grade. Blobs of slime mould, for instance, which can slowly crawl across a surface, seem to note the timing of changes to their climate, slowing their movement in anticipation of an expected dry spell – even when it never actually arrives.

With the emergence of the first neurons about half a billion years ago, memories became more intricate as information could be stored in the patterns of electrical connections within the nervous system (see "The making of a memory", right). This type of learning may have been behind the Cambrian explosion – the sudden appearance and rapid evolution of more complex species about 530 million years ago – because it enabled animals to exploit new niches, say Eva Jablonka at Tel Aviv University and Simona Ginsburg at the Open University of Israel.

Over the following few hundred million years, increasingly advanced skills could emerge with different forces driving the evolution of each creature's mind. The result is a surprising range of mnemonic feats throughout the animal kingdom. Migratory cardinal fish, for instance, can remember where they laid their eggs during the breeding

Hey, it's that guy with the bread again

THE MAKING OF A MEMORY

When we talk about memory, we can mean many things. In the short term, we use our working memory to juggle small lists of information, such as a round of drinks. These are held in fleeting changes in the brain's electrical or chemical activity that quickly fade as the mind wanders.

Long-term memories, in contrast, can last a lifetime. They can be classed as semantic memories of facts, or episodic memories of events. Psychologists also refer to autobiographical memories, which include the episodic and semantic memories that relate to our life story.

All these different kinds of long-term memories are woven into the webs of connections between brain cells. By the creation of new receptors at the end of a neuron, by a surge in the production of a neurotransmitter, or by the forging of new ion channels that allows a brain cell to boost the voltage of its signals, the brain alters the communication between networks of cells. As a result, the same pattern of neurons will fire when we recall the memory, bringing the thought back into our consciousness. Many brain regions are involved in this process, but the hippocampus, near the base of the brain, is considered to be especially important in consolidating our memories.

Ultimately, these changes to the neural network are probably stored semi-permanently through epigenetic changes, which involve small alterations to the structure of a gene and determine its activity within the cell. Certain genes linked to the formation of memories have been shown to have fewer methyl groups attached to their DNA after learning, for instance – a clear example of an epigenetic change.

But the brain is not like a video camera. Every time we recall a memory, new proteins are made and the epigenetic markers will alter – changing it in subtle ways.

MATT JACOB/TENDANCE FLOUE

season and, after over-wintering in deep water, return to within half a metre of the same spot. Animals as diverse as lizards, bees and octopuses can learn the way out of a maze, and pigeons have an excellent visual recognition, learning to recognise more than a thousand different images. They can even recognise individual humans and aren't fooled by a change of clothes.

Such skills, although impressive, don't match our experiences of episodic memory, in which we immerse ourselves in specific events. A pigeon might learn to associate your face with food, but it probably can't remember your last meeting in the way you might be able to recall details of your last trip to the park.

"Santino the chimp collects and hides rocks to later throw at visitors"

It is an important distinction, because episodic memory is thought to allow us to imagine and plan for the future. This skill, known as mental time travel, was long thought to be unique to humans, but there are now some signs that a handful of other species might also be able to escape the present.

Some of the most convincing evidence comes from Nicola Clayton and Sergio Correia at the University of Cambridge, who have shown that western scrub jays can learn from their experiences to anticipate the actions of other birds. If one bird knows that another is watching it bury its food, for instance, it will later move the stash, presumably to prevent it from being stolen. But they will only do this if they have previously stolen food themselves – suggesting that they were drawing on their memories while forming the plan. Similar studies have suggested that bonobos and orang-utans are also capable of mental time travel.

Initially, the work attracted a lot of scepticism from researchers like Michael Corballis at the University of Auckland in New Zealand, who believed that the results could be explained by a complex kind of classical conditioning, for instance. But some recent work has begun to change his mind. He points to a study of activity in the hippocampi of rats, which suggests that they replay their movements through a maze, and may even imagine future paths that they could take. He is also impressed by Santino, a chimp at Furuvik Zoo in Sweden that collects and hides rocks to throw at visitors, using premeditation that would rely on episodic memory.

Unfortunately, so few animals have been studied that it is difficult to pinpoint exactly when this skill emerged, although the researchers suspect that it evolved separately in the different lineages, rather than emerging in one of our common ancestors.

Thomas Suddendorf at the University of Queensland in Australia is less willing to accept that animal memories rival our own. He proposes that episodic memory depends on a host of different components, and although some animals may be able to use limited foresight when it comes to food, for instance, only humans demonstrate the kind of capacity and flexibility that can allow us to imagine all kinds of futures.

"These simulations allow us to plan, prepare for and deliberately shape the future, like no other animal appears to do," Suddendorf says. Santino might be able to plan a rock attack – but he could not plan anything so conniving as a bid for freedom. ■

Us vs the machines

Just how do our memories compare to today's PCs?

SHORT-TERM MEMORY

We can remember about **7** pieces of information at any one time, be it shapes, names, colours or numbers

LONG-TERM MEMORY

If the brain processed binary information like a computer, with each synapse holding a single bit of information, we could store roughly **12,000GB**

You could hold a 700-page book like *Moby Dick* nearly 10 million times, or 2.5 million songs

10m or **2.5m**

Speed and motivation are probably our biggest limits. Memorising a substantial work of literature word for word can take years or even decades

SHORT-TERM MEMORY

A mid-range computer may hold **6GB** in its random access memory (RAM), many million times more than human short-term memory

LONG-TERM MEMORY

A computer hard drive stores data by magnetising sections of a ferromagnetic disk. On a computer with a **500GB** hard drive, you could store *Moby Dick* 400,000 times

400,000

A computer can lay down memories astonishingly quickly – absorbing *Moby Dick* in about

0.5 seconds

A likely story

How do we piece together an autobiography from the many events in our lives, wonders **Kirsten Weir**

JULIE BOURGES/PICTURETANK

GRADUATION day. The first concert you attended. Your first kiss. These personal recollections stand apart from memories of shopping lists or the world's capital cities. Autobiographical memories define us; they are who we are.

Yet they are far from complete, with some periods of our lives producing heaps of recollections while others receive relatively patchy coverage. What forces lead us to remember one event but forget another? Until recently, the subject had largely been a black box to researchers, but they have now begun to make huge strides towards an understanding of the way our minds write our life story.

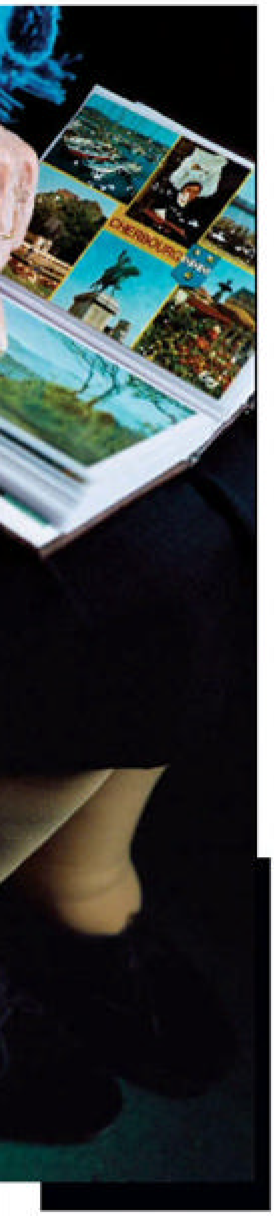
Our brains certainly start remembering at a young age, learning simple associations before we are born. One small study even found that newborns tend to stop crying when they hear the theme tune of a TV show their mother often watched while pregnant, perhaps because it reminds them of the comfort of the womb. But we cannot consciously remember specific events from before the age of 2 or 3, when our autobiographical memory begins to develop. Even then, we are hard-pressed to remember much from before our sixth birthday (for more on this, see "Our forgotten years", page 70).

So far, three different factors have emerged that might explain this hazy recall. One possibility is that the neural pathways are not mature enough between the hippocampus – where memories are consolidated – and the rest of the brain, so our experiences from this period may never be cemented into long-term storage. Our burgeoning language skills also play a key role, says Martin Conway at City University London, because words provide a kind of scaffold on which we hang our memories for future retrieval. His experiments have shown that children don't tend to remember an event until they have learned the words to describe it.

"Your personality determines the events that you remember"

A sense of our own identity is also crucial for our memory of particular experiences. Experiments show that children who can recognise themselves in a mirror – a sign that they have developed a sense of self – are able to recall certain events when tested a week later, while toddlers who fail the mirror test draw a blank.

As we get older, our identities and recollections develop together in an intimate dance. While the events in your life shape your opinion of yourself, your personality also determines what you remember; someone who thinks they are courageous might fail to remember a time when they acted in a cowardly manner, for example. "Your sense of who you are and how you enact your personality traits is very tied up in autobiographical memory,"



Your memory is made from the scraps of your life

says Robyn Fivush at Emory University in Atlanta, Georgia.

Guiding all of this are our parents, who form our identities and cement our memories with their storytelling. When families discuss personal events in an elaborate way, children develop more detailed narratives of their own by the time they reach school age than those whose parents weave less intricate stories. Psychologist Qi Wang at Cornell University in Ithaca, New York, believes this may explain the influence of culture on the way we reminisce. Chinese parents tend to focus less on individual experiences and emotions when discussing the past, with fewer details, than Americans, for instance. As a result, Wang has found that Chinese people's memories, even during adulthood, tend to be less personal, focusing instead on events of social or historical significance.

NILU IZADI/MILLENNIUM

Events like family holidays are moulded to fit the flowing narrative of our life story

As we venture further from the safety of our parents' embrace, our autobiographical memories continue to mature. The difference is quite noticeable, says Conway; a 10-year-old cannot relay a coherent life story, but a 20-year-old can go on for hours. "Something happens over that adolescent period." But what? So far, studies to tackle that question are lacking. "There's a big lacuna between about age 7 to late adolescence where we don't really know what's going on," he says.

The cultural script

We do know, however, that we are more likely to remember events from the end of this period, in young adulthood, than from any other period in our lives. This "reminiscence bump" may be the result of anatomical changes to the still developing brain. Alternatively, it may be that our brains feel emotions more keenly during adolescence and early adulthood – and memories linked to intense feelings stick in the mind for longer.

Or perhaps it is simply down to the fact that many important landmarks in our lives – learning to drive, graduating and falling in love for the first time – tend to fall within this period. "Those distinct events are more likely to be remembered, because they're culturally marked," Fivush says.

This idea is supported by work conducted by Annette Bohn and Dorthe Berntsen at Aarhus University in Denmark. They found that when young children were asked to write their future life stories, most of the events they imagined took place in young adulthood, mirroring the reminiscence bump. So it seems that we are aware of the "cultural life script" from a young age, which may mould our recollections of events as they occur.

The finding dovetails with the idea that memory and foresight share the same machinery in the brain. A child's ability to imagine the future seems to develop in tandem with his or her autobiographical memory, for instance. Wang, meanwhile, has found that the cultural differences that shape our personal narratives can also influence our planning abilities, showing that Chinese people are less likely to give specific, personal details than Americans when they talk about events to come.

Our autobiographical memories aren't perfect, to be sure. But whether we are looking forward or gazing back into the past, our personal narratives are central to understanding our place in the world. That's a point worth remembering. ■

SHARED RECALL

Autobiographical memories are, by definition, personal. But that doesn't mean they are all our own, says Amanda Barnier, a cognitive scientist at Macquarie University in Sydney, Australia. She and her colleagues interviewed couples that had been married for decades. Not surprisingly, couples who remembered together, rather than independently, were able to recall significantly more than those who took a solo approach.

Much research focuses on the downsides of this process, including the risk of false memories: it is not uncommon for people to absorb their siblings' or spouse's recollections into their own life stories, for example.

But Barnier argues that collaborative recall's benefits have long been overlooked. Understanding the cues that couples use to prompt one another could offer new ways to shore up memory in elderly people facing dementia, for instance.

"We often hear about this idea of someone losing their long-term partner, and all of a sudden they experience a rapid decline," she says. "It must be like they've lost a part of their mind."

TANSY SPINKS/MILLENNIUM

Fade to black

Subtle memory losses may lead us to an unexpectedly dark place. **David Robson** investigates

WHAT pushes someone to try to take their own life? That's what psychologist Mark Williams was trying to find out as he visited people recovering from attempted suicide in the UK's Addenbrookes Hospital in the 1980s. Williams knew he had to tread carefully: the patients had been hospitalised for an attempted overdose in the past 48 hours. "These people had done dangerous things to themselves," he recalls. "You can't ask them to do complicated tests."

Williams was there because he suspected there was something different about the long-term memories of people who are depressed or suicidal, and had devised a simple exercise to test his theory on the patients at Addenbrookes. Sitting at their bedside, he would read out a cue word, such as "happy" or "clumsy", before asking them to describe a past event it brought to mind. Perhaps not surprisingly, they were quicker to tell him about negative experiences than positive ones, but Williams was struck by something more subtle.

While his comparison group – other hospital patients who weren't depressed – tended to focus on specific events, the overdose patients were noticeably vaguer. One responded to the word "happy" with "the first years of my marriage", for instance; another person given the word "safe" said: "when I'm in bed". Even when Williams encouraged them to be more specific, they were less likely to dig out a single incident – such as a particular film, or an insult that had upset them.

It was as if the depressed patients were merely skimming the chapter headings of their autobiographies, without reading the text that followed. It might seem a minor detail compared with the desperation that leads to a suicide attempt. But Williams's findings, which are now supported by a host of studies from other groups, have emphasised just how important our memories are in shaping our well-being, offering a new perspective on depression and perhaps other mental illnesses too.

Holding on

According to this theory, our memories act as a kind of ballast that holds us steady during times of stress; they can suggest ways to solve problems and offer comfort when we are feeling wounded. When people find it hard to recall specific events from their past, however, they feel overwhelmed by life's challenges, which slowly pushes them into depression.

"In the right circumstances, the effect can be striking," says Williams, who is now at the University of Oxford. If the theory is right, there may be new ways of treating depression that directly target the underlying memory problems.

A new approach would certainly be welcome. Depression is the commonest form of mental illness, affecting somewhere between 10 and 20 per cent of us at some point in our lives. Antidepressants help some people, particularly the most severely affected, but these drugs can bring side effects, including weight gain and loss of libido. Meanwhile, talking therapies such as cognitive behavioural therapy can be costly and often take weeks or months to make an impact.

Williams is by no means the first to suggest that memory plays a part in mental illness; Sigmund Freud once suggested that the repression of unpleasant memories from childhood could lead to hysteria. In the case of Williams's suicidal patients, however, theirs was a more general difficulty. When questioned, they painted their past in broad brush strokes – "I always enjoyed a good party" that missed the details of specific events – "my brother's 30th birthday".

Williams's paper, published in 1986 in the *Journal of Abnormal Psychology*, triggered a trickle, then a torrent, of similar studies. They revealed that "over-general memory", as the phenomenon came to be known, was not limited to people who had tried to commit suicide, but was linked to depression in general.

Further studies found it to be present before the low mood developed, lending weight to the idea that the memory problems led to depression and not the other way around. For instance, one team examined the memories and well-being of 74 women who had undergone IVF and failed to get pregnant. Those who had the least specific recall before the treatment were most likely to develop symptoms of depression after the disappointment. Another study, published in April, found that teenagers judged to have over-general memory were more likely to develop depression in the 12 months after they first met the researchers. And a recent small study has also linked this kind of poor recall to bipolar disorder.

As the body of evidence supporting this idea has grown, various theories have emerged about just how memory problems could send our mood into a downward spiral. One idea is that remembering the good times is important for chasing the blues away. "Thinking of better times gives you more hope for the future," says Jennifer Sumner of Northwestern University in Evanston, Illinois.

Given the role of memory in imagination and foresight (see page 105), poor access to our past may also impair our problem-solving skills, which are known to be weaker in people with depression. When asked how you might make friends after moving to a new neighbourhood, for example, most people can come up with good ideas, like inviting the neighbours round for drinks. Those with depression, in contrast, tend to be stumped by these questions. Importantly, people with over-general memory also seem to fare poorly at this kind of task. "When you face problems in your life, you don't have an analogy to help you solve the current situation," says Rachel Anderson at the University of Hull, UK. It is easy to imagine how, with your difficulties mounting, you may then begin to feel desperate and helpless, trapped by your circumstances with no obvious escape.

"Memories act as a kind of ballast that holds us steady during times of stress"

Flashbacks

That might explain her finding that people with less specific recall only develop depression when they face long-term stresses, such as ongoing quarrels with their partner; those with fewer hassles show few ill-effects.

As well as depression, over-general memories could make people more vulnerable to post-traumatic stress disorder. It may seem counter-intuitive, because PTSD involves vivid memories of a traumatic incident. But these flashbacks appear to be the exception rather than the rule because people with PTSD tend to have trouble recalling other events from their past. Once again, these difficulties seem to be present long before the onset of the disorder – firefighters with hazy recall are often the first to develop the symptoms of PTSD, for instance. Perhaps a poor memory just weakens our mental fortress – and when the defences are down, it's easier for anxiety, fear and painful flashbacks to intrude into our thoughts.

Why do people lose access to their recollections in the first place? Given the complexity of the human mind, it's probably the outcome of many interlinked processes. Williams thinks we may learn the over-general style of thinking from our parents, if they tend to talk in broad terms about the past. It could also begin as a coping mechanism, helping people to retreat from the pain of a difficult experience.

Tim Brennen at the University of Oslo in Norway probed the memories of Bosnian teenagers who had been young children during the Bosnian war in the 1990s. "They had seen people being killed, villages burnt down. They were kept in a state of terror for years," says Brennen. The teens found it harder to remember specific events in their past than their Norwegian peers.

PATRICK CHAUVEL/SYGMA/CORBIS

Growing up in a war zone has been linked with later memory problems

"Poor memory weakens our mental fortress, allowing fear to intrude into our thoughts"

By the time Brennen met the Bosnians in the late 2000s, many were living a relatively peaceful life and hadn't yet developed signs of mental illness as a result of their experiences, over-general memories or otherwise. That doesn't necessarily contradict the theory. As Anderson has found, the weaknesses in our defences only show during times of stress. Brennen suspects that the consequences might kick in once they face the challenges of adult life.

Although this theory of depression is gaining converts among researchers, it still has plenty of critics. Mark Howe at City University London points to a contradictory study showing that people with depression simply take longer to access their recollections. If you give them enough time, they can usually summon specific incidences for a cue word, he says. Perhaps they are just less keen than other people on sharing personal recollections with a stranger. "I don't think their memory has fundamentally changed," he says.

While the theory's merits are still being debated, its proponents are already exploring whether a kind of memory training can be used to improve people's recall and so reduce their symptoms of depression. Tim Dalgleish at the MRC Cognition and Brain Sciences Unit in Cambridge, UK, for instance, has investigated a technique called Memory Specificity Training (MeST), which encourages people to practise delving into their memories. In effect, they are asked to repeat a similar version of Williams's memory test over and over again, recalling detailed specific incidents for different cue words. Crucially, the events need not have anything to do with the person's current anxieties. People can be taught MeST in groups and may only need five weekly sessions to see improvement if early results are anything to go by.

One of the first trials took place in Iran, carried out by Hamid Neshat-Doost at the University of Isfahan, who worked with Dalgleish in Cambridge before returning to his home country. It involved 23 Afghani refugees with depression, living in a community with little access to cognitive behavioural therapists. The 11 people who received five group sessions of MeST improved significantly, unlike the others, who went untreated. Importantly, those with the most improvements in their ability to recall specifics reported the greatest improvements in their mood.

Admittedly that was a small, unblinded trial and memory training would have to be compared with traditional talking therapies in a head-to-head trial before any conclusions could even begin to be drawn about their relative merits. After all, cognitive behavioural therapy is also becoming more widely and cheaply available through online programmes and group therapy. But Williams, who has worked on a similar form of memory training, says MeST could be another useful option for those who don't respond well to cognitive behavioural therapy or antidepressants. "What's nice is that it brings the patient on board in a collaborative way," he says. "It isn't stigmatising."

Sumner agrees that memory training looks promising, having tried to encourage her own patients to reminisce more specifically, with positive results. "They don't see their past and future as [uniformly] negative," she says. "It gives them something to latch on to, motivating them to make changes." ■


PAULINE DANIEL/PICTURETANK

Stuck in the present

People who are lost in the here and now reveal a strange interplay between memory and body, says **Catherine de Lange**

Second helpings are easy when you can't remember your first

TO THE casual observer, there would have been nothing unusual about Henry Molaison as he tucked into dinner at his usual slow-and-steady pace. But to the group of psychologists at the Massachusetts Institute of Technology who were observing him, his behaviour was astonishing: just 60 seconds earlier, he had polished off an identical three-course meal. Yet Molaison was no glutton. Instead, part of his brain had been removed in an attempt to cure his epilepsy. From then on, he was unable to form new memories and became stuck in the present for perpetuity.

Scientists usually consider feelings of hunger to arise from hormonal signals in the gut, but Molaison's behaviour suggested that our memories of what we have just eaten may be more important in curbing our appetite. The idea found further support a decade later, in 1998, when Morris Moscovitch at the University of Toronto, Canada, replicated this experiment using two people with a similar memory condition. Not only did these people eat a second meal, just 15 minutes after finishing the first, but in some trials they unquestioningly ate a third.

There is always the possibility that the brain damage may have brought on complications besides the memory loss that interfered with the gut's signals to the brain, but a recent experiment by Suzanne Higgs at the University of Birmingham in the UK suggests otherwise. She tapped into "sensory specific satiety" – the familiar sensation that our liking for a given food decreases the more we eat of it, whereas a different dish will feel more appetising; it is the reason that we can find extra space for pudding. Higgs found that people with amnesia retain such preferences. After a hearty lunch of sandwiches they will prefer crisps or cookies to further sandwiches, even though they couldn't tell you what they had just eaten. She concludes that the digestive signals are reaching the brain, and that the amnesiacs' lack of memory lies behind their seemingly insatiable appetite.

"Just 60 seconds earlier, Henry Molaison had polished off an identical three-course meal"

Incredible endurance

The unexpected effects of memory on our feelings and behaviour might not stop with food. Diane Van Deren is one of the world's elite ultra runners. In one recent race she ran more than 1500 kilometres over 22 days. On some of those days, she ran for as long as 20 hours. Van Deren had always been good at sport, but her incredible endurance seems to be down in part to her poor short-term memory, again the result of brain surgery for epilepsy.

Often, she just cannot remember how long she has been running for, underestimating the time by as much as 8 hours. "Most people with amnesia suffer a tyranny of the present," says Adam Zeman, a neurologist studying memory and epilepsy at the University of Exeter, UK, but Van Deren's inability to remember how long she has been running seems to free her from the feelings of fatigue that plague other runners. Perhaps, while others get caught up in the details of where they have been and where they are going, Van Deren gets into a more zen-like state that lets her run for longer without feeling so much strain. Of course, it could also be that after the challenges in her life Van Deren has a higher threshold for discomfort than most people.

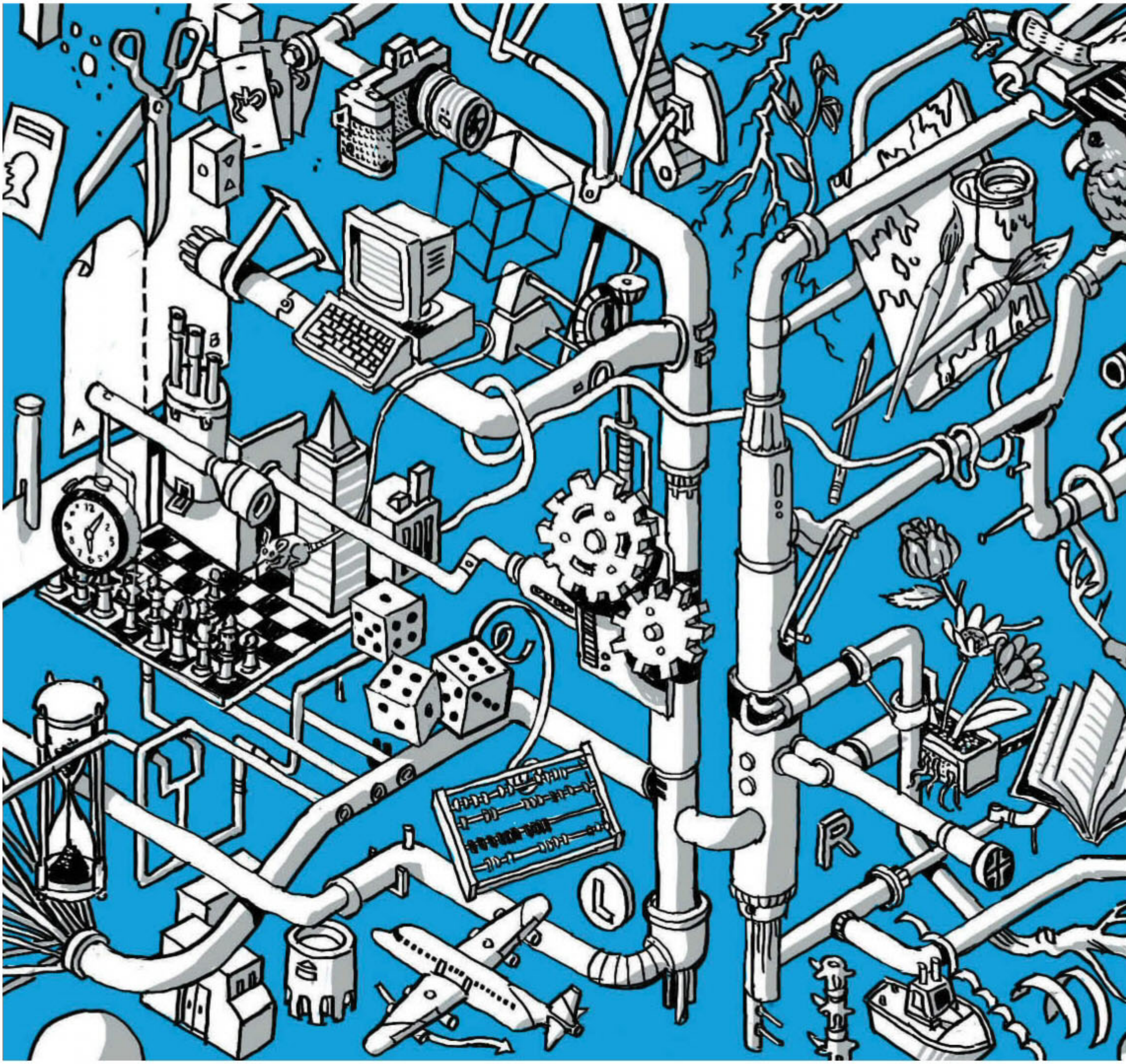
For the rest of us, losing track of time on a long run is difficult, but there are certainly ways in which these findings affect us all. Higgs has found that simple distractions such as watching TV can stop people from forming good memories of what they are eating. As a result, they tend to snack more after the meal than control groups who were not distracted.

Imagination can play a powerful role too. Thanks perhaps to its close link to memory, simply imagining the process of eating something can lead people to feel more satiated, causing them to eat less. Which all goes to show that in the fight against overeating, memory could be your biggest ally, even if at times it would be more palatable to forget. ■

A USER'S GUIDE TO THE MIND

The human mind is the most complex information processing system we know. It has all sorts of useful design features but also many glitches and weaknesses. The problem is, it doesn't come with a user's manual. You just have to plug and play.

But if anyone knows how to get the best out of our brains, it's neuroscientists. So we asked some of the best to explain how the human brain performs many of its most useful functions and how to use them to the max. By **Caroline Williams**



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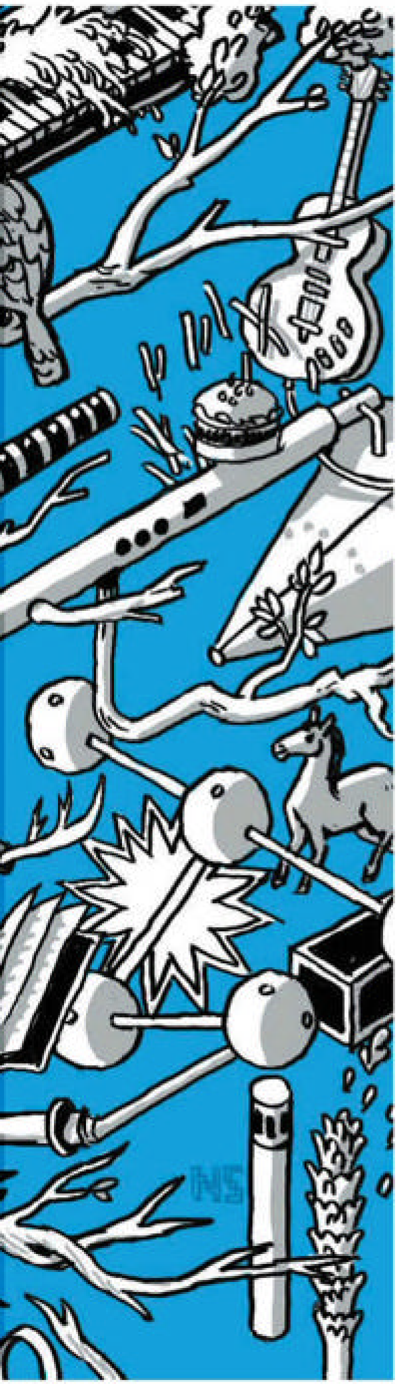


1 ATTENTION
2 WORKING MEMORY
3 LOGICAL & RATIONAL THOUGHT
4 LEARNING
5 KNOWLEDGE
6 CREATIVITY
7 INTELLIGENCE

1 ATTENTION

Almost every useful feature of your brain begins with attention. Attention determines what you are conscious of at any given moment, and so controlling it is just about the most important thing that the brain can do.

To make any sense of the world around us we need to filter out almost everything and focus solely on what is relevant. Not only that, but focused attention is essential for learning or memorising. So it follows that if you can boost your ability to pay attention, you can improve at almost anything.

In simple terms, the brain has two attention systems. One, the "bottom-up" system, automatically snaps awareness to potentially important new information, such as moving objects, sudden noises or sensations of touch. This system is fast, unconscious and always on (at least when you are awake).

The other, the "top down" system, is deliberate, focused attention, which zooms in on whatever we need to think about and, hopefully, stays there long enough to get the job done. This is the form of attention that is useful for doing tasks that require concentration.

Unfortunately distractibility comes as both a bug and a design feature. Top-down attention requires effort and so is prone to losing focus, or being rudely interrupted by the bottom-up system.

The good news is that we can tweak our attention settings to stay focused more easily. As well as cutting down on bottom-up distractions by turning off email notifications, putting your phone on silent and so on, Nilli Lavie, a cognitive neuroscientist at University College London, suggests actually giving your brain more to do.

"Top-down attention is prone to losing focus, or being rudely interrupted"

Lavie's work has shown that better control of top-down attention comes not by reducing the number of inputs, but by increasing them. Her load theory says that once the brain reaches its limit of sensory processing, it can't take anything else in, including distractions.

This seems to work for both distractions and mind wandering, says Lavie. In real life, she suggests thinking about adding visual aspects to a task that make it more attention-grabbing without making it more difficult – putting a colourful border around a blank document and making the bit you are working on purple, perhaps. It works with all the senses, she says, so choosing somewhere with a bit of background noise might also help.

There are also signs that cognitive training might help. Researchers working with people with attention-deficit hyperactivity disorder (ADHD) and brain injuries have found that cognitive training, combined with non-invasive magnetic brain stimulation, can improve focus on a task that needs sustained attention.

Wider studies are under way, and initial results seem to suggest that the right kind of brain training could help more or less anyone.

While we wait, the next best option is learning to chill out in exactly the right way. Long-term meditators have been shown to have thicker parts of the brain associated with attention, while other studies have found that attention test scores improved after a short course of meditation. So learning to focus better may be as simple as making time to sit still and focus on not very much. ›

2 WORKING MEMORY

Like attention, working memory is one of the brain's most crucial front-line functions. Everything you know and remember, whether it's an event, a skill or a fascinating fact, started its journey into storage by going through your working memory.

But working memory is much more than just a clearing house for long-term memories. It has been described as the brain's scratch pad: the place where information is held and manipulated. If you are doing anything that requires effortful, focused thought, you are using your working memory.

In the 1970s, Alan Baddeley and Graham Hitch of the University of York, UK, came up with an influential model to explain how the system works. The main component is the executive controller, which runs the show by focusing your attention on the relevant information.

It also kicks "slave" systems into action. One of these holds up to four pieces of visual information at a time; another can memorise about 2 seconds of sound, especially spoken words, which it loops over and over again (think of mentally repeating a phone number while you search for a pen). The third is the episodic buffer, which adds relevant information from long-term memory.

A weakness of this model is that working memory doesn't occupy a discrete brain area that can be watched in action in a brain scanner. Because of this, some cognitive neuroscientists have suggested that it might not be a separate system at all, but just the part of long-term memory that we are currently paying attention to.

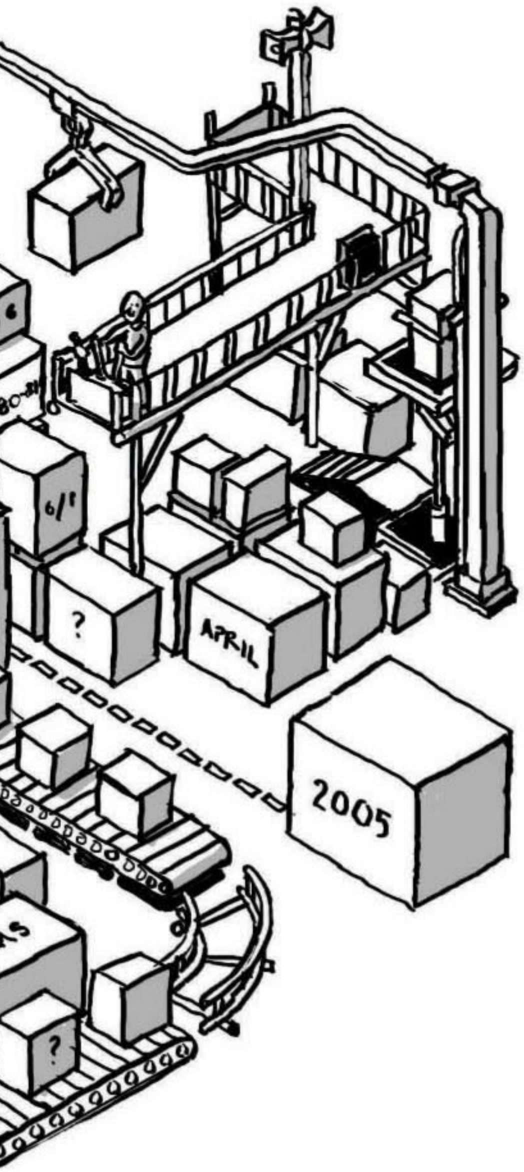
Whatever it is, working memory comes as standard in the human brain, but some people have better working memories than others. Working memory capacity is a better predictor of academic success than IQ, so getting the most out of it is useful.

The good news is that the system can probably be upgraded. Some studies have shown that brain training programmes aimed specifically at working memory can produce improvements, and there are even a handful of training packages on the market. But it's not clear whether they make you better at anything other than working memory tests.

Cognitive neuroscientist Jason Chein of Temple University in Philadelphia, Pennsylvania, who studies working memory, says there seems to be evidence of improvements in other cognitive skills, although any changes are quite small. "A small effect may still be important in the sense that even modest gains can have a meaningful impact on everyday cognition," he says.

> *"Even modest gains in working memory can improve general cognition"*

3 LOGICAL AND RATIONAL THOUGHT



We like to think of ourselves as rational and logical creatures. And so we can be – but not without some effort.

Logical thought requires us to behave like a microprocessor, executing stepwise operations on information using the rules of logic. This doesn't come naturally to most people, requiring outside instruction to learn and lengthy training to master. Even then, we struggle to maintain a purely rational perspective.

It turns out that there is a kernel of truth in the popular wisdom that "left brain equals logic". Imaging studies have shown that the left prefrontal cortex is needed to make logical trains of thought happen and, a lot of the time, no input is needed from the right.

But when there is conflict between what seems logical and beliefs we already hold, the right side of the prefrontal cortex kicks in to help sort out the confusion. Unfortunately, the right hemisphere usually wins. Study after study has shown that where new information conflicts with existing beliefs, our brains bend over backwards to keep beliefs intact rather than revise them.

Another surprise is that, contrary to popular wisdom, emotions aren't necessarily the enemy of rationality. People who have damage to the part of the prefrontal cortex that processes emotions struggle to make decisions at all, especially when there is no logical advantage to either option (for more on the mind-body connection, see "Your clever body", page 100).

So embracing our not-particularly logical gut feelings about decisions might actually help us make more rational choices. But not always: other studies have shown that strong emotions can interfere with making rational decisions, particularly when they concern people we love.

Other than hard graft – and an appreciation of the role of belief and emotion – is there anything we can do to become more logical?

Vinod Goel, a cognitive psychologist at York University in Toronto, Canada, says that a zap to the head might one day help. "Brain stimulation techniques may eventually offer a route to improving reasoning," he says. His team recently used a similar approach to enhance creative thought and, he says, "one can imagine the same techniques being used to enhance our ability for logical reasoning". As yet, though, there is no shortcut. For now, he says, practice is your best option. Recent studies have shown that a few months' training in rational thought, as part of law degree training, increased the number of connections between frontal and parietal lobes and between the two hemispheres. The catch is, without regular practice this effect would almost certainly fade a few months after the course ended. ›

"There is a kernel of truth in the popular wisdom that left brain equals logic"

4 LEARNING

Learning is what your brain does naturally. In fact, it has been doing it every waking minute since about a month before you were born. It is the process by which you acquire and store useful (and useless) information and skills. Can you make it more efficient?

The answer lies in what happens physically as we learn. As it processes information, the brain makes and breaks connections, growing and strengthening the synapses that connect neurons to their neighbours, or shrinking them back. When we are actively learning, the making of new connections outweighs the breaking of old ones. Studies in rats have shown that this rewiring process can happen very quickly – within hours of learning a skill such as reaching through a hole to get a food reward. And in some parts of the brain, notably the hippocampus, the brain grows new brain cells as it learns.

But once a circuit is in place, it needs to be used if it is going to stick. This largely comes down to myelination – the process whereby a circuit that is stimulated enough times grows a coat of fatty membrane. This membrane increases conduction speed, making the circuit work more efficiently.

What, then, is the best way to learn things and retain them? The answer won't come as a huge surprise to anyone who has been to school: focus attention, engage working memory and then, a bit later, actively try to recall it.

Alan Baddeley of the University of York, UK, says it is a good idea to test yourself in this way as it causes your brain to strengthen the new connection. He also suggests consciously trying to link new bits of information to what you already know. That makes the connection more stable in the brain and less likely to waste away through underuse.

The learning process carries on for life, so why is it so much harder to learn when we reach adulthood? The good news is that there seems to be no physiological reason for the slowdown. Instead, it seems to be a lot to do with the fact that we simply spend less time learning new stuff, and when we do, we don't do it with the same potent mix of enthusiasm and attention as the average child.

Part of the problem seems to be that adults know too much. Research by Gabriele Wulf at the University of Nevada, Las Vegas, has shown that adults tend to learn a physical skill, like hitting a golf ball, by focusing on the details of the movement. Children, however, don't sweat the details, but experiment in getting the ball to go where they want. When Wulf taught adults to learn more like kids, they picked up skills much faster.

This also seems to be true for learning information. As adults we have a vast store of mental shortcuts that allow us to skip over details. But we still have the capacity to learn new things in the same way as children, which suggests that if we could resist the temptation to cut corners, we would probably learn a lot more.

A more tried-and-tested method is to keep active. Ageing leads to the loss of brain tissue, but this may have a lot to do with how little we hare about compared with youngsters. With a little exercise, the brain can spring back to life. In one study, 40 minutes of exercise three times a week for a year increased the size of the hippocampus – which is crucial for learning and memory. It also improved connectivity across the brain, making it easier for new things to stick.

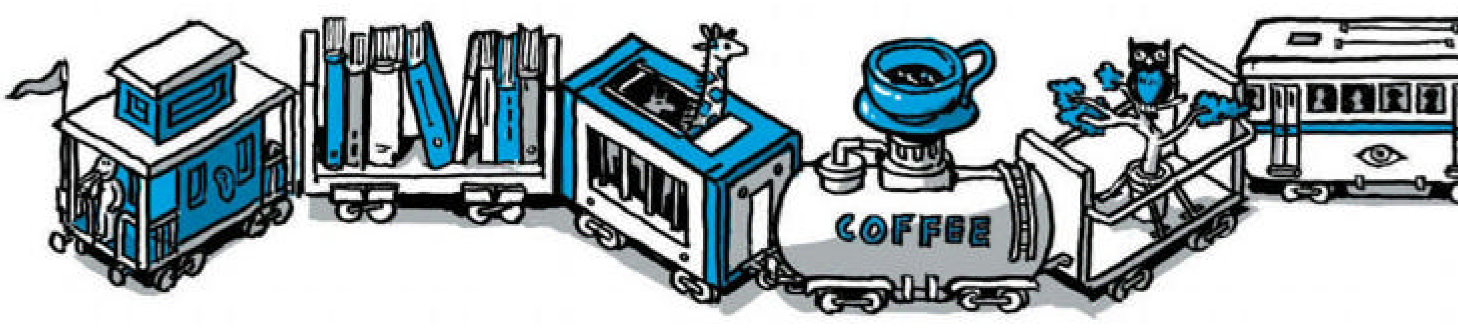
KNOWLEDGE 5

One of the brain's most useful features is the ability to absorb pieces of information and make connections between them. Knowledge really is power: a little can be a dangerous thing and the more you know the better equipped you are to deal with life.

But what exactly is knowledge? How are facts stored, organised and recalled when needed?

Knowledge obviously relies on memory – in particular the type of memory that stores general information about objects, places, facts and people, known as semantic memory. This is the part of memory which knows that Paris is the capital of France, a constitutional republic in western Europe – but not the part which stores memories of a weekend break there.

> *"There seems to be no limit to the knowledge that can fit into a brain"*



Knowledge isn't so much about what information you store as how you organise it to create a rich and detailed understanding of the world that connects everything you know.

The sight of a dog, for example, automatically activates other bits of information about dogs: how they look, smell, sound and move, the fact that they are domesticated wolves, the names of similar dogs you know, and your feelings about dogs.

How the brain achieves this gargantuan feat is far from clear. A recent proposal is that it has a "hub" that tags categories to everything we know and encounter, allowing us to connect related things.

In 2003, Tim Rogers, a cognitive psychologist now at the University of Wisconsin-Madison, proposed the anterior temporal lobe (ATL) as the hub. The ATL is badly affected in people with semantic dementia, who progressively lose their knowledge of the meanings of words and objects but retain their skills and autobiographical memories. Experiments since then have backed this up – when the ATL is temporarily knocked out by a small electromagnetic pulse, people lose the ability to name objects and understand the meanings of words.

Rogers says that without this system we would spend a lot of time being confused about how things fit together. "How would you infer, for instance, that when making a collage with your kids, if you run out of sticky tape you can use the glue stick instead?" he says. "The tape is not similar to the glue stick in its shape, colour or how you use it. You need a representation that specifies similarity of kind."

The good news is that there seems to be no limit to the knowledge that can fit into a brain. As far as we know no one has ever run out of storage space.

But it seems you can know too much. Michael Ramscar at Tübingen University in Germany reckons that anyone who lives long enough eventually hits that point just by virtue of a lifetime's knowledge. He suggests that cognitive skills slow down with age not because the brain withers but because it is so full. And that – like an overused hard drive – takes longer to sift through.

6 CREATIVITY

J. K. Rowling has said that the idea for Harry Potter popped into her head while she was stuck on a very delayed train. We have all had similar – although probably less lucrative – "aha" moments, where a flash of inspiration comes along out of the blue. Where do they come from? And is there any way to order them on demand?

Experiments led by John Kounios, a neuroscientist at Drexel University in Philadelphia, suggest that the reason we aren't all millionaire authors is that some brains come better set up for creativity than others. EEG measurements taken while people were thinking about nothing in particular revealed naturally higher levels of right hemisphere activity in the temporal lobes of people who solved problems using insight rather than logic. Kounios says recent work hints that this brain feature might be inherited, but even if you happen to have a more focused, less creative brain, there are plenty of general tips on how to get it into creative mode.

Boringly, the first is to put in the groundwork to build up a good store of information so that the unconscious has something to work with. Studies on subliminal learning have poured cold water on the idea that knowledge can drift into the brain without any conscious effort, so it pays to focus intently on the details of the problem until all the facts are safely stored. At this stage, anything that helps with focus, such as caffeine, should help.

Once that's taken care of, it's time to cultivate a more relaxed, positive mood by taking a break to do something completely different – like watching a few entertaining cat videos. Studies where people have either watched a comedy film or a thriller before coming up with new ideas have shown that a relaxed and happy mood is far more conducive to ideas than a tense and anxious one. Not only that, but it pays to turn down the focus knob a little, and the easiest way to do that is to look for ideas when your brain is too tired to focus properly. A 2011 study showed that morning people had their most creative ideas late at night, while night owls had theirs early in the morning.

Mental exhaustion might be a more realistic state of mind than relaxation when an important deadline is looming, but if the ideas are still refusing to come there may one day be an easier solution. Brain stimulation studies, in which activity was boosted in the right temporal lobe and suppressed in the left, increased the rate of problem-solving by 40 per cent. So the stressed creative of the future might be able to pop on a "thinking cap" to help those juices flow. ›

7 INTELLIGENCE

Intelligence has always been tricky to quantify, not least because it seems to involve most of the brain and so is almost certainly not one "thing". Even so, scores across different kinds of IQ tests have long shown that people who do particularly well – or badly – on one seem to do similarly on all. This can be crunched into a single general intelligence factor, or "g", which correlates pretty well with academic success, income, health and lifespan.

So more intelligence is clearly a good thing, but where does it come from? A large part of the answer seems to be genetics. In 1990, the first twin studies showed that the IQ scores of identical twins raised apart are more similar to each other those of non-identical twins raised together. Since then, a few genes have been linked to IQ, but all of them seem to have a tiny effect and there are probably thousands involved (for more on this, see Chapter 3, page 42).

That doesn't mean the environment plays no part, at least in childhood. While the brain is developing, everything from diet to education and stimulation plays a huge part in developing the brain structures needed for intelligent thought. Children with a bad diet and poor education may never fulfil their genetic potential.

But even for educated and well-fed children, the effects of environment wear off over time. By adulthood, genes account for 60 to 80 per cent of the variance in intelligence scores, compared with less than 30 per cent in young children. Like it or not, we get more like our close family members the older we get.

"Like it or not, we get more like our close family members as we get older"

So if genes play such a big part, is there anything adults can do to improve IQ? The good news is that one type of intelligence keeps on improving throughout life. Most researchers distinguish between fluid intelligence, which measures the ability to reason, learn and spot patterns, and crystallised intelligence, the sum of all our knowledge so far. Fluid intelligence slows down with age, but crystallised intelligence doesn't. So while we all get a little slower to the party as we get older, we can rest assured that we are still getting cleverer.

AND FINALLY: THE RIGHT TIME?

The brain is a fickle beast – at some times as sharp as a tack, at others like a fuzzy ball of wool. At least some of that variation can be explained by fluctuations in circadian rhythms, which means that, in theory, if you do the right kind of task at the right time of day, life should run a little more smoothly.

The exact timing of these fluctuations varies by about 2 hours between morning and evening types, so it is difficult to give any one-size-fits-all advice. Nevertheless there are a few rules that it's worth bearing in mind whatever your natural waking time.

It's an idea not to do too much that involves razor-sharp focus in the first couple of hours after waking up. Depending on how much sleep you have had it can take anything from 30 minutes to 4 hours to shake off sleep inertia – also known as morning grogginess. If you want to think creatively, though, groggy can be good (see "Creativity", page 119).

If hard work can't wait, though, the good news is that researchers have backed up what most of us already know – a dose of caffeine helps you shake off sleep inertia and get on with some work.

Another tip is to time your mental gymnastics to coincide with fluctuations in body temperature. Studies measuring variation in everything from attention and verbal reasoning to reaction times have shown that when our core temperature dips below 37 °C the brain isn't at its best.

By this measure, the worst time to do anything involving thinking is, unsurprisingly, between midnight and 6am. It is almost as bad in the afternoon slump between 2pm and 4pm, which has more to do with body temperature than lunch – studies of people who have no lunch or just a small one have the same problem. All in all, the best time to get stuck in is between mid-morning and noon and then again between 4pm and 10pm.

There may be a way to hack the system, though. Studies have shown that body temperature changes and alertness also work independently of the internal clock, so a well-timed bit of exercise or hot shower can work wonders.

Competitive sports, though, are worth leaving until the end of the day. Studies have shown that reaction times and hand-eye coordination get progressively better throughout the day, reaching a peak at around 8pm.

After that, there's time for a little more focused energy before the body cools down, the brain slows and there's nothing more to do with it but dream. ■

"If you want to think creatively, morning grogginess can be good"

CHAPTER TEN

SLEEP

The origins and purpose of sleep

Sleep has fascinated philosophers, writers and scientists for centuries, but research into it only began in earnest in the 1950s. Our slumbers are now much less mysterious to us, say **Derk-Jan Dijk** and **Raphaëlle Winsky-Sommerer**

WHAT IS SLEEP?

Strictly speaking, the term "sleep" only applies to animals with complex nervous systems. Nevertheless it is possible to identify sleep-like states in invertebrates, which allows us define sleep more broadly. These include cycles of rest and activity, a stereotypical body position, lack of responsiveness and compensatory rest after sleep deprivation. Insects in particular have a state very similar to sleep, as do scorpions and some crustaceans.

Even microorganisms, which lack a nervous system, have daily cycles of activity and inactivity driven by internal body clocks known as circadian clocks. The origins of sleep might therefore date back to the dawn of life about 4 billion years ago, when microorganisms changed their behaviour in response to night and day.

Some researchers consider sleep to be part of a continuum of inactive states found throughout the animal kingdom. Once we understand exactly what aspects of an organism benefit from these states, we may be able to provide a meaningful answer to the question of whether simple organisms sleep.

HALF AWAKE

Sleep feels like an on-or-off condition, but brains can be awake and asleep at the same time. This phenomenon is well known in dolphins and seals – animals that can sleep "uni-hemispherically": one half of their brain is asleep while the other half shows electrical activity characteristic of wakefulness.

A study in rats found that after prolonged wakefulness, some neurons go offline and display sleep-like activity. Tellingly, this mosaic brain state is accompanied by occasional lapses in attention.

Sleep researchers are investigating if human and other animal sleep is a "global" state or whether the process of sleep can, to some extent, be regulated locally. There is mounting evidence for the latter. For example, the most active brain regions during wakefulness subsequently undergo deeper sleep for longer.

This localised view of sleep could lead to a better understanding of cases when wakefulness intrudes into sleep, such as in sleep-talking, sleepwalking and episodes of insomnia in which people report being awake all night even though recording brainwaves (see "Slumber cycles", below) from a single location suggests they have been asleep.

It also promises to explain how sleep can intrude into wakefulness, such as during lapses of attention when we are sleep-deprived. These "micro sleeps" can be particularly dangerous when driving and various ways to detect them have been developed, for instance by monitoring how a car moves relative to white lines on roads or analysing the movements of the eyes for signs of sleepiness.

SLUMBER CYCLES

During sleep, complex changes occur in the brain. These can be observed with an electroencephalogram (EEG), which measures the brain's electrical activity and associated brainwaves.

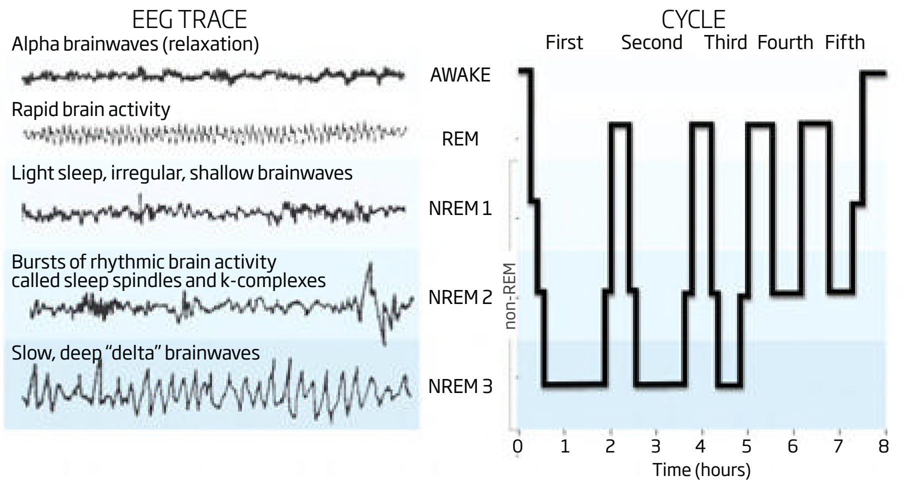
After lying awake for 10 minutes or so we enter non-rapid eye movement sleep or NREM sleep. NREM sleep is divided into three stages, NREM1, NREM2 and NREM3, based on subtle differences in EEG patterns. Each stage is considered progressively "deeper".

After cycling through the NREM stages we enter rapid-eye-movement or REM sleep. The EEG during REM sleep is similar to wakefulness or drowsiness. It is during this stage that many of our dreams occur.

Each cycle lasts for about 1.5 hours and a night's sleep usually consists of five or six cycles.

In addition to changes in brain activity, sleep is also characterised by a reduction in heart rate of about 10 beats per minute, a fall in core body temperature of 1 °C to 1.5 °C as well as a reduction in movement and sensation.

Sleep scientists break sleep into four distinct stages.
A typical night's sleep involves several cycles, which includes both REM and non-REM (NREM) sleep



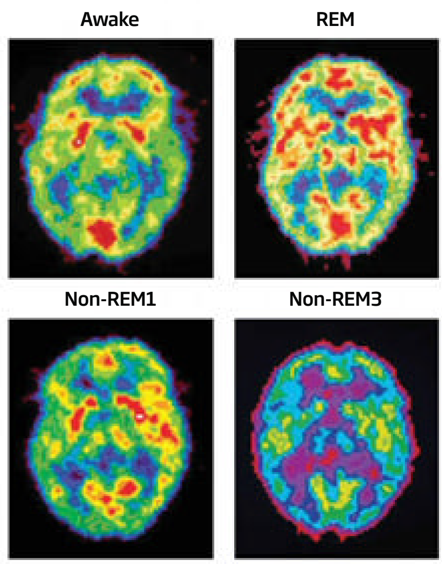
REASONS FOR REST

There are many explanations for sleep, ranging from keeping us out of harm's way to saving energy, regulating emotions, processing information and consolidating memory. Each has strengths – and weaknesses too. Rather than seek a single, universal function of sleep we might do better to study its influence at each level of biological organisation.

At the level of the whole organism, a primary function of sleep may be the regulation of autonomic nervous activity such as heart rate – sleep disorders are often associated with dysfunction of the autonomic nervous system, such as an abnormal heartbeat. At the level of the brain, it may support memory consolidation by reducing the amount of information travelling through the central nervous system. Studies in mice have found that sleep promotes the formation of new connections between brain cells, which might be how sleep helps to consolidate memory. However, memory consolidation occurs when we are awake too.

At the level of nerve cells, sleep alters firing rates of neurons and also changes the temporal distribution and synchronisation of firing across networks of cells, which may alter their connectivity. The regulation of nerve-cell connectivity, called synaptic homeostasis, can help prevent the nervous system from becoming overloaded. Support for this idea has come from studies of fruit flies.

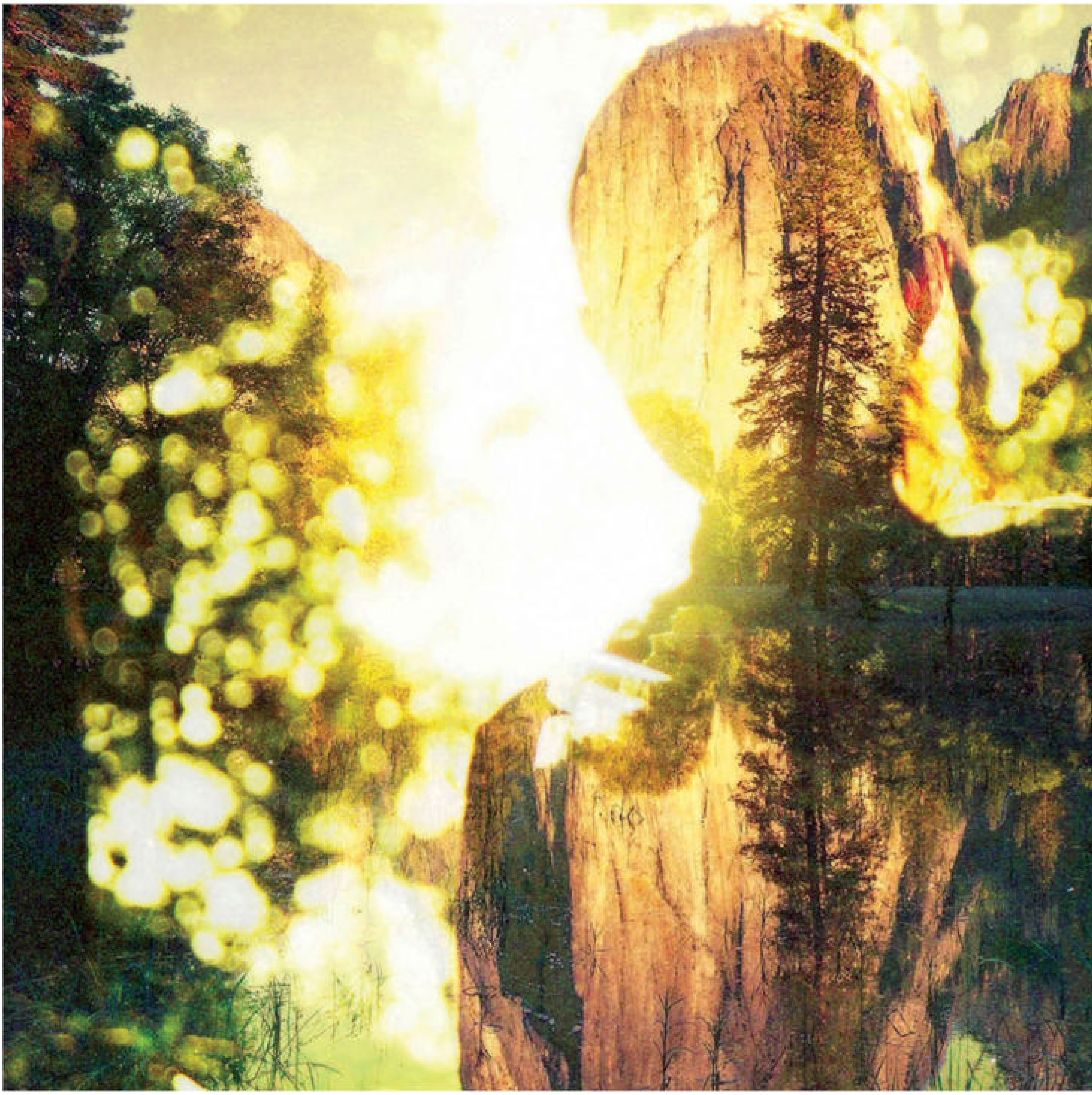
One neglected role of sleep in humans is social isolation. As social animals, we may need sleep to consolidate the rules and insights of our complex social lives.



PET scans show differences in brain activity between wakefulness and various sleep states. Activity is in red, inactivity in blue (also see "Slumber cycles", above)

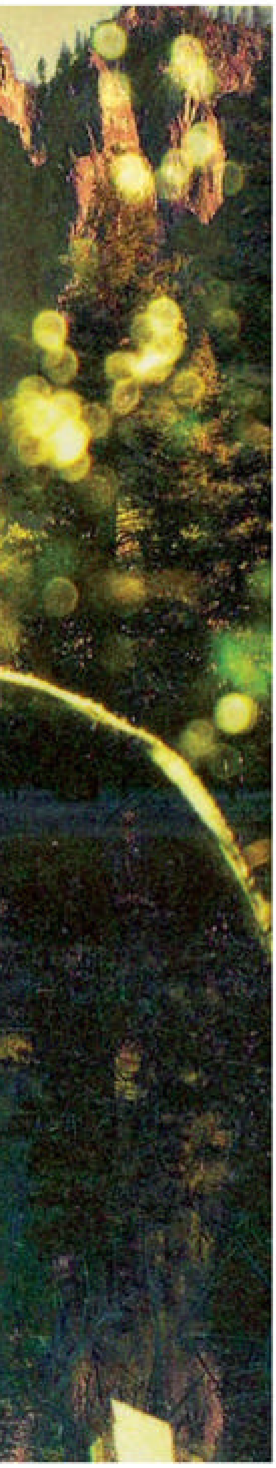
PASCAL AIMAR/TENDANCE FLOUET

FENK/FLICKR/GETTY



Dreams don't reveal your secrets and desires… they are far more important than that. **Emma Young** reports

The I in dreaming



Memory traces from our waking experiences are replayed in our dreams

"THE interpretation of dreams is the royal road to a knowledge of the unconscious activities of the mind." So wrote Sigmund Freud in his 1900 classic *The Interpretation of Dreams*. He saw this idea as a "once in a lifetime" insight, and for much of the 20th century the world agreed. Across the globe, and upon countless psychoanalysts' couches, people recounted their dreams in the belief that they contained coded messages about repressed desires. Dreams were no longer supernatural communications or divine interventions – they were windows into the hidden self.

Today we interpret dreams quite differently, and use far more advanced techniques than simply writing down people's recollections. In sleep laboratories, dream researchers hook up volunteers to EEGs and fMRI scanners and awaken them mid-dream to record what they were dreaming. Still tainted by association with psychoanalysis, it is not a field for the faint-hearted. "To say you're going to study dreams is almost academic suicide," says Matt Walker at the University of California, Berkeley. Nevertheless, what researchers are finding will make you see your dreams in a whole new light.

Modern neuroscience has pushed Freud's ideas to the sidelines and has taught us something far more profound about dreaming. We now know that this peculiar form of consciousness is crucial to making us who we are. Dreams help us to consolidate our memories, make sense of our myriad experiences and keep our emotions in check.

Changing patterns of electrical activity tell us that the sleeping brain follows 90-minute cycles, each consisting of five stages – two of light sleep at the start, then two of deep sleep, followed by a stage of REM, or rapid eye movement sleep (see diagram, page 127). There is no characteristic pattern of brain activity corresponding to dreaming, but as far as we know all healthy people do it. And while dreaming is commonly associated with REM sleep, during which it occurs almost all of the time, researchers have known since the late 1960s that it can also occur in non-REM sleep – though these dreams are different. Non-REM dreams tend to be sparse and more thought-like, often without the complexity, length and vivid hallucinatory quality of REM dreams.

Despite their differences, both types of dreams seem to hold a mirror to our waking lives. Dreams often reflect recent learning experiences and this is particularly true at the start of a night's sleep, when non-REM dreaming is very common. Someone who has just been playing a skiing arcade game may dream of skiing, for example. The link between waking experience and non-REM sleep has also been observed in brain scanning studies. Pierre Maquet at the University of Liège, Belgium, looked at the later stages of non-REM sleep and found that the brains of volunteers replayed the same patterns of neural activity that had earlier been elicited by waking experiences. Many REM-sleep dreams also reflect elements of experiences from the preceding day, but the connection is often more tenuous – so someone who has been playing a skiing game might dream of rushing through a forest or falling down a hill.

Sleep on it

But we do not simply replay events while we dream, we also process them, consolidating memories and integrating information for future use. Robert Stickgold of Harvard Medical School in Boston recently found that people who had non-REM dreams about a problem he had asked them to tackle subsequently performed better on it. Likewise, REM sleep has been linked with improved abilities on video games and visual perception tasks, and in extracting meaning from a mass of information.

"It's clear that the brain does an immense amount of memory processing while we sleep – and it certainly isn't mere coincidence that while our brain is sorting out these memories and how they fit together, we're dreaming," says Stickgold. He suspects that the two types of dream states have different functions for memory, although what these functions are is a matter of debate. Non-REM dreaming might be more important for stabilising and strengthening memories, Stickgold suggests, while REM dreaming reorganises the way a memory is stored in the brain, allowing you to compare and integrate a new experience with older ones.

Jan Born and Susanne Diekelmann, now both at the University of Tübingen in Germany, however, have looked at the same evidence and come to the opposite conclusion – that REM sleep supports the strengthening of a new memory, while non-REM sleep is for higher-level consolidation of memories. "I think this means that we're still lost when it comes to understanding the role of different sleep stages in memory," says Stickgold.

Also unclear is how central is the role of dreams in memory formation. During ›

"While you are dreaming, your brain is literally reshaping itself, so dreams play a key role in making you who you are"

dreaming is certainly not the only time our brains consolidate memories. For example, when we daydream certain areas of the brain, called the default network, become active. We now know this network is involved in memory processing and many of the same brain regions are active during REM sleep. What's more, daydreaming, like REM dreaming, can improve our ability to extract meaning from information and have creative insights.

Does this mean we don't actually need dream sleep to process memories? Not necessarily, says Walker, who points out that the way new memories are replayed in the brain is different in daydreaming and dreaming. Rat studies show that the reruns happen in reverse when the animals are awake and forwards when they are sleeping. No one is quite sure what this difference means for memory processing, but Walker believes it shows that daydreaming is not simply a diluted version of sleep dreaming. Maquet agrees. "Different brain states may all have somewhat different functions for memory. Memory consolidation is probably organised in a cascade of cellular events that have to occur serially," he says – some while you are awake, and then some while you are asleep.

Even if dreaming is crucial for memory, Walker for one does not see this as its main function. "I think the evidence is mounting in favour of dream sleep acting as an emotional homeostasis: basically, rebalancing the emotional compass in a good way at the biological level," he says. Everyone knows how a short nap can transform a cantankerous 2-year-old and Walker has shown something similar in adults. He found that a nap that includes REM dreaming mitigates a normal tendency in adults to become more sensitive to angry or fearful faces over the course of a day, and makes people more receptive to happy faces.

Walker has also found that sleep, and REM sleep in particular, strengthens negative emotional memories. This might sound like a bad thing – but if you don't remember bad experiences you cannot learn from them. In addition, both he and Stickgold think that reliving the upsetting experience in the absence of the hormonal rush that accompanied the actual event helps to strip the emotion from the memory, making it feel less raw as time goes on. So although dreams can be highly emotional, Walker believes they gradually erode the emotional edges of memories. In this way, REM dreams act as a kind of balm for the brain, he says. In people with post-traumatic stress disorder, this emotion-stripping process seems to fail for some reason, so that traumatic memories are recalled in all their emotional detail – with crippling psychological results.

As with memory processing, REM and non-REM dreaming may play different psychological roles. Patrick McNamara of Boston University has found that people woken at different sleep stages give different reports of their dreams. REM dreams contain more emotion, more aggression and more unknown characters, he says, while non-REM dreams are more likely to involve friendly encounters. This has led him to speculate that non-REM dreams help us practise friendly encounters while REM dreams help us to rehearse threats (see "The interpretation of nightmares", left).

So what do they mean?

All this suggests that we couldn't function properly without dreaming, but it doesn't answer the perennially intriguing question: what do dreams actually mean?

For some sleep researchers, the answer is simple – and disappointing. Born argues that dreams themselves have no meaning, they are just an epiphenomenon, or side effect, of brain activity going on during sleep, and it is this underlying neuronal activity, rather than the actual dreams, that is important. Walker finds it hard to disagree. "I don't want to believe it. But I don't see large amounts of evidence to support the idea [that dreams themselves are significant]," he says.

Those researchers who refuse to accept the notion that the content of dreams is unimportant point to work by Rosalind Cartwright of Rush University, Chicago. In a long series of studies starting in the 1960s, she followed people who had gone through

The interpretation of nightmares

Antii Revonsuo enjoys his nightmares. "At least in hindsight," he qualifies, "as though they were good horror movies where you don't know it's a movie until it's over." But then Revonsuo, at the University of Turku in Finland, thinks that nightmares are the main biological reason for why we dream – they allow us to simulate scary encounters, and so be better prepared for them in our waking life.

"The theory predicts correctly several features of our dream content," says Revonsuo. For example, he and his colleagues have found that about two-thirds of the dreams of healthy adults involve at least one threat. About 40 per cent of these take the form of aggressive encounters – running away from an attacker or getting into a fight. Such encounters are higher among children, accounting for over half of threat dreams in Finnish kids and three-quarters among traumatised Palestinian children.

Revonsuo argues that children's dreams are closer to our evolutionarily original form of dreaming because children haven't yet had a chance to adjust to the modern environment. He has found that between 40 and 50 per cent of children's dreams contain animal characters, often as enemies, which is similar to the instance among adult hunter-gatherers. The figure is just 5 per cent in Western adults. "I don't think any other dream theory has made such specific predictions and shown that they hold," he says.

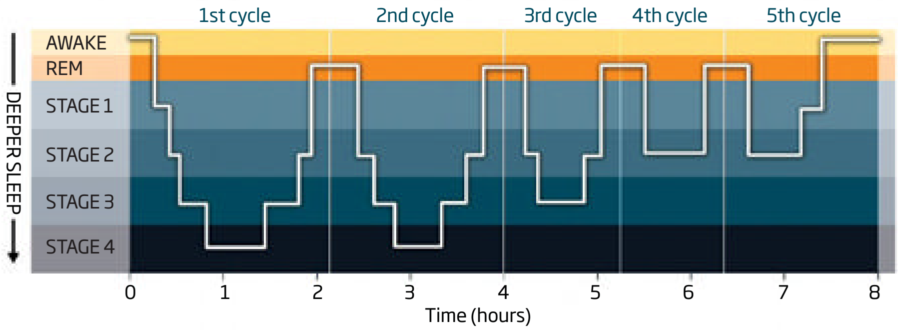
It is a neat idea, but Robert Stickgold at Harvard Medical School in Boston cannot believe that's all there is to dreaming. "I think Revonsuo has made the same mistake as Freud – which is to limit dreaming's functionality. I think dreaming is absolutely about threat rehearsal some of the time. But it's absolutely about other things, too."

NICOLAS GIRAUD/MILLENNIUM IMAGES

A strange form of consciousness we cannot live without

Dream on

A typical night's sleep involves five cycles and during each one we pass through several stages of varying sleep depth. Almost all REM sleep is filled with dreams but dreaming can also occur in the other stages



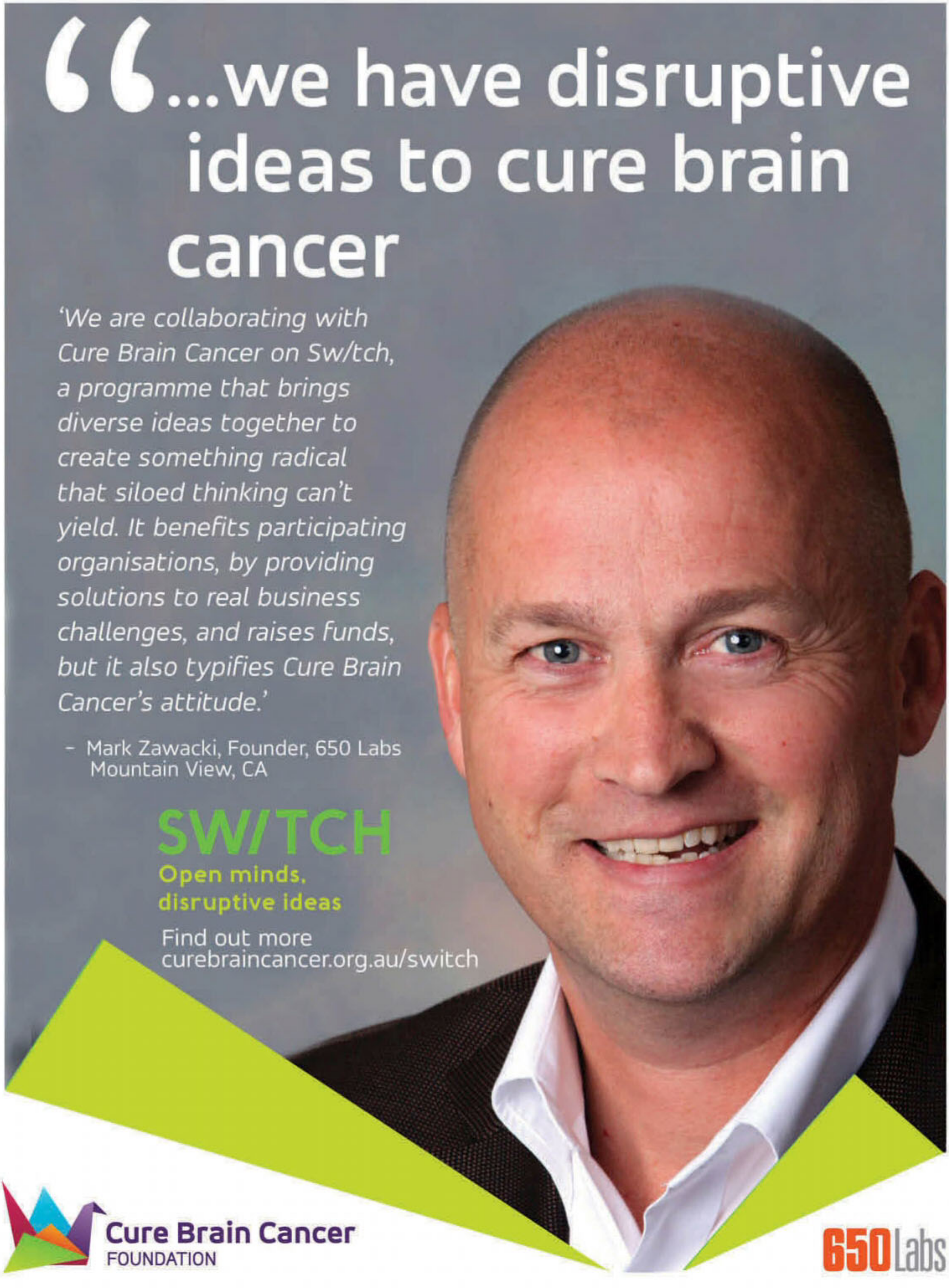
divorces, separations and bereavements. Those who dreamed most about these events later coped better, suggesting that their dreams had helped. "Cartwright's work provides some of the most solid evidence that dreaming serves a function," says Erin Wamsley at Furman University in Greenville, South Carolina. There is no hard data showing that dreaming is not an epiphenomenon, she admits, but the same could be said about waking consciousness.

In fact, Wamsley's own research hints that the form and function of a dream are connected. She worked with Stickgold on the study which found that non-REM dreams boost people's performance on a problem. Their volunteers were given an hour's training on a complex maze then either allowed a 90-minute nap or kept awake. The dreamers subsequently showed bigger improvements, but the biggest gains of all were in people who dreamed about the maze. It didn't seem to matter that the content of these dreams was obtuse. One volunteer, for example, reported dreaming about the maze with people at checkpoints – although there were no people or checkpoints in the real task – and then about bat caves that he had visited a few years earlier. Stickgold didn't expect this to improve the volunteer's ability to navigate the maze, "and yet this person got phenomenally better".

He points out that the dream content is consistent with the idea that during dreaming memories are filed with other past experiences for future reference. "Dreams have to be connected in a meaningful, functional way to improvements in memory – not just be an epiphenomenon," he says. "I say this with fervent emotion, which is what I use when I don't have hard data."

Such evidence may one day be forthcoming, though. In the past, there has been no objective way to record what someone is dreaming, but that is changing. In 2008, Yukiyasu Kamitani at the ATR Brain Information Communication Research Laboratory in Kyoto, Japan, and colleagues used fMRI scans to decode and then recreate scenes that volunteers were picturing in their mind while awake. To see if they could do the same thing with people's dreams, in a later study the team repeatedly woke volunteers as they slept in a scanner and asked them to describe their dreams. Using that information, they were able to categorise what certain patterns on fMRI scans meant and tell with 60 per cent accuracy what kinds of things people were dreaming about – for instance whether they were dreaming about a man or woman, or certain types of objects, such as a car.

Some may think all this peering and prodding at our dream world is taking away its magic, but the researchers don't see it that way. While you are dreaming, your brain literally reshapes itself by rewiring and strengthening connections between neurons. So although dreams do not reveal the secret you, they do play a key role in making you who you are. "The mystery and the wonder of dreams is untouched by the science," says Stickgold. "It just helps us appreciate better how amazing they really are." ■



“...we have disruptive ideas to cure brain cancer
'We are collaborating with Cure Brain Cancer on Sw/tch, a programme that brings diverse ideas together to create something radical that siloed thinking can't yield. It benefits participating organisations, by providing solutions to real business challenges, and raises funds, but it also typifies Cure Brain Cancer's attitude.'
- Mark Zawacki, Founder, 650 Labs Mountain View, CA
SW/TCH
Open minds, disruptive ideas
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