INSIDE THE BRAIN

Big Picture

ISSUE 17 | SPRING 2013

BRINGING CUTTING-EDGE SCIENCE INTO THE CLASSROOM

A free resource for teachers and learners

MIND-BLOWING BRAINS

How research helps us look inside the brain

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BigPicture

The brain is one of our most fascinating organs. Developments in technology and medicine mean that doctors and scientists can examine our brains in more ways and more detail than ever before, all without having to open up the body. Join us as we find out more about how imaging research has changed the way we can look inside the human brain.

INSIDE

ONLINE

Go to **www.wellcome.ac.uk/bigpicture/brain** *for more teaching resources, including extra articles, videos, image galleries, curriculum links, lesson ideas, a poster and an animation of the action potential. You can also download the PDF of this magazine or subscribe to the* Big Picture *series.*

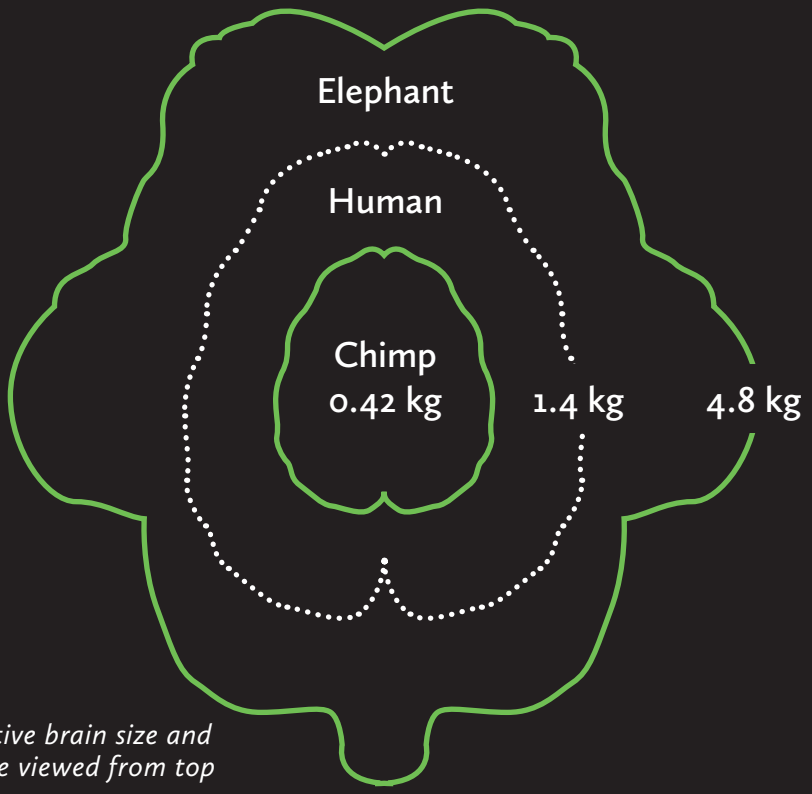
Neurons by numbers

The vital stats of brains and brain imaging

AVERAGE HUMAN BRAIN VOLUME

Source: www.ncbi.nlm.nih.gov/pmc/articles/PMC2711771/

BRAIN SIZE AND MASS



Relative brain size and shape viewed from top

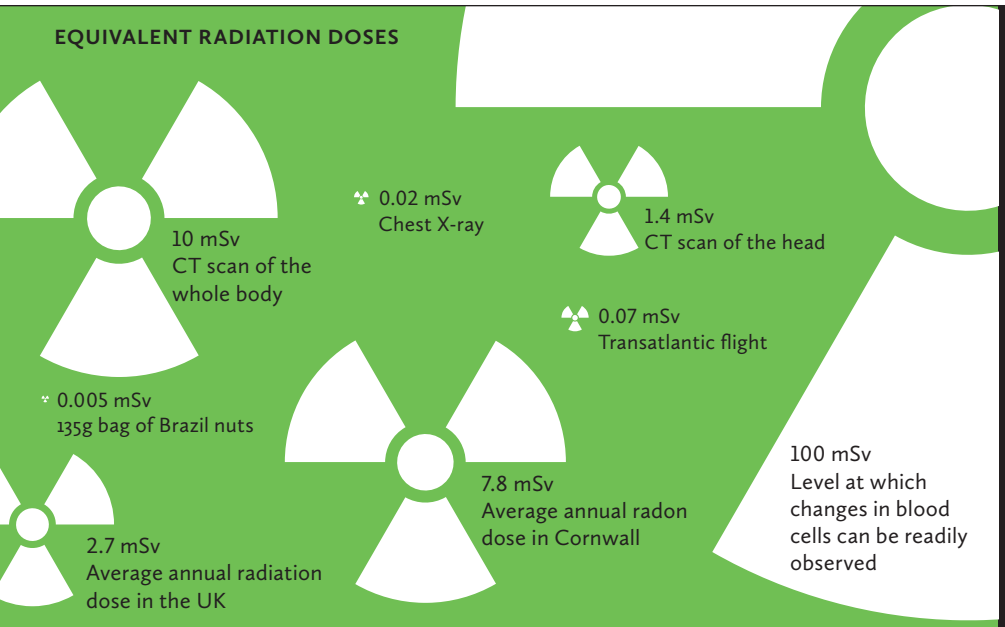
Sources: faculty.washington.edu/chudler/facts.html, www.frontiersin.org/neuroanatomy/10.3389/fnana.2011.00029/full

TOTAL NUMBER OF SYNAPSES IN HUMAN NEOCORTEX

150 000 0

The neocortex is a six-layered part of the cerebral cortex found in mammals.
Source: postcog.ucd.ie/files/Pakkenberg%202003.pdf

EQUIVALENT RADIATION DOSES



Area relates to dose in millisieverts.

Source: www.hpa.org.uk/Topics/Radiation/UnderstandingRadiation/UnderstandingRadiationTopics/DoseComparisonsForIonisingRadiation

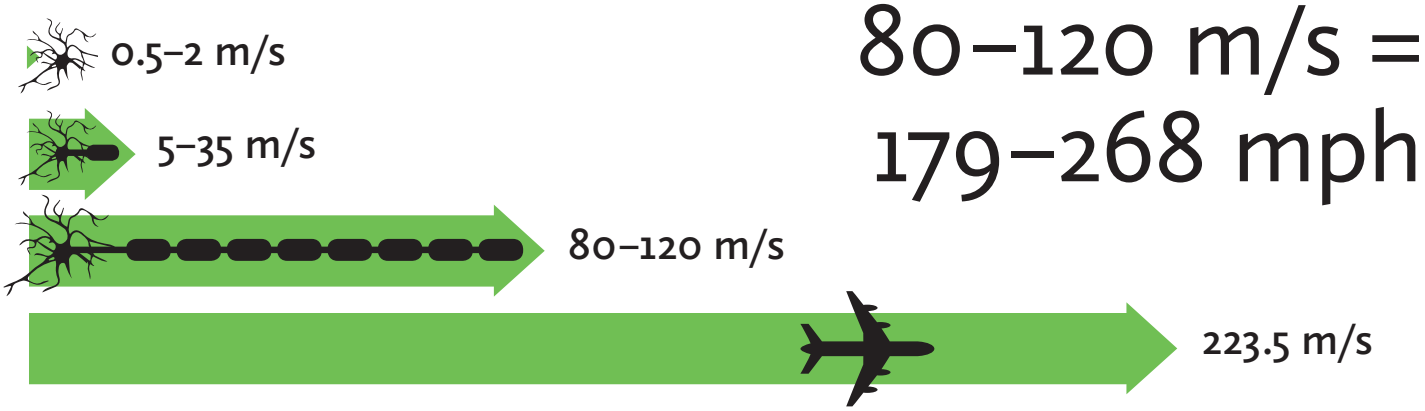
NUMBER OF NEURONS IN THE HUMAN BRAIN

86bn

There is roughly the same number of glia (supporting cells).

Source: www.ncbi.nlm.nih.gov/pmc/articles/PMC3386878/?tool=pubmed

SPEED OF NERVE TRANSMISSION

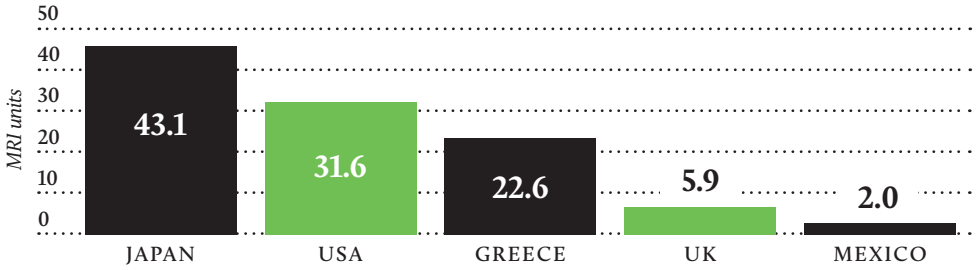


80–120 m/s = 179–268 mph

From top: unmyelinated fibre, thin myelinated fibre, thick myelinated fibre, cruising commercial airliner.

Sources: faculty.washington.edu/chudler/cv.html, forums.x-plane.org

MRI UNITS (SCANNERS) PER MILLION PEOPLE



Source: www.oecd.org (2010 data)

(0.15 quadrillion)

00 000 000

FINDING DATA

Putting this diagram together, we found that different sources gave different numbers for the same thing. Why don't they match?

Well, data can be interpreted in different ways, and estimates can be made using different methods and/or baseline data. Definitions matter, too – different sources might define 'volume' or 'mass' differently.

Which should you choose? The source itself is important – is it reliable? Are the figures recent? How might an organisation's 'agenda' affect how it calculates and presents data?

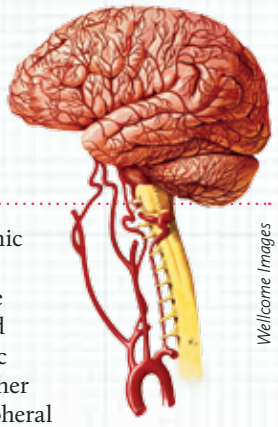
Cover image: The surface of the human brain during an operation. *Robert Ludlow/Wellcome Images*. Top and bottom row: Neuron illustration. *VLADGRIN/iStockphoto*.

Why the brain?

The brain has mystified and inspired philosophers, doctors and scientists for centuries, and our fascination with it today only seems to be growing. So what exactly does this 1.4 kg of tissue do for us?

YOU AND YOUR BRAIN

Your brain is your body's control centre



Wellcome Images

Your brain underpins who you are. It stores your knowledge and memories, gives you the capacity for thought and emotion, and enables you to control your body. The brain is just one part of the nervous system. Together with the spinal cord, it makes up the central nervous system.

The brain is the control centre, which sends and receives information to and from the body via the spinal cord. This involves the peripheral nervous system, which contains mixed nerves made up of sensory and motor nerve fibres. Sensory fibres carry information about what the body is sensing into the spinal cord, and motor fibres transmit signals from the central nervous system to the muscles and glands.

The autonomic nervous system (divided into the sympathetic and parasympathetic systems) is another part of the peripheral nervous system. It controls involuntary (autonomic) functions such as heart rate, breathing and digestion.

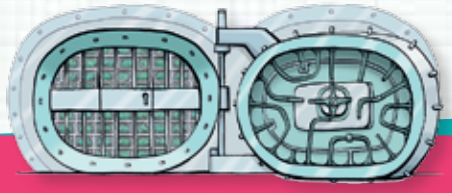
The brain is incredibly complex and can be affected by many diseases, but we still know only a fraction of what there is to know about how it works. A better comprehension of how the brain works will enable scientists to understand mental processes and behaviour better and, eventually, to prevent or treat any problems that occur.

WHITE AND GREY

Inside the brain, only white and grey matter

The brain is made of grey and white matter. Grey matter contains the cell bodies of neurons (nerve cells) and their local connections to each other. White matter contains bundles of nerve fibres that connect distant brain regions to one another; it gets its name from the fatty myelin that insulates the axons, which makes the tissue look white to the naked eye.

The brain contains 86 billion neurons. They are specialised to produce electrical signals called action potentials. When resting, neurons produce a few action potentials (or 'fire') every second, but this increases when they become active. Neurons form intricate networks and communicate with each other across junctions called synapses. Action potentials cause the neuron on one side of the synapse to release a neurotransmitter that travels across the synapse to the neuron on the other side. Receptor proteins detect the neurotransmitter and generate new action potentials in response.



FAST FACT

The world's largest brain bank is at Harvard, where there are over 7000 brains.
Source: **www.youtube.com/watch?v=cVWb5OCgOr8**

IN THE SYSTEM

Exploring the nervous system

Ludovic Collin/Wellcome Images

A cluster of neurons in culture.

Like other systems in the body, the nervous system consists of tissue that is made of collections of cells, each of which contains thousands of different molecules. The cells of the nervous system can be broadly divided into two types – neurons and glia.

Neurons are specialised to produce electrical signals called action potentials. They form networks and communicate with each other by transmitting chemical signals across tiny gaps called synapses.

Different projections from the cell body connect one neuron with others. An axon carries the action potential away from the cell body, while many dendrites carry impulses from other neurons towards the cell body.

Neurons have distinctive shapes that are closely related to their function. Primary sensory neurons, for example, carry information from the body into the spinal cord. They have a single fibre that splits into two. One branch goes out towards the body and the other goes into the spinal cord. Motor neurons in the spinal cord have dendrites that receive signals from other cells, and a long axon that extends to the muscles through peripheral nerves. Interneurons connect sensory and motor neurons to each other and have short dendrites and a branched axon.

The other cells of the nervous system are called glia. They include Schwann cells, which form the myelin sheaths that wrap around the axons of sensory and motor neurons, principally in the peripheral nervous system (the nerves and nerve cells outside of the brain and spinal cord). The myelin sheath is not continuous but is interrupted by gaps called nodes of Ranvier. Although the myelin sheath is an electrical insulator, the gaps actually speed up nerve conduction because they permit saltatory conduction, where action potentials 'jump' from one node to the next, and this increases their conduction speed.

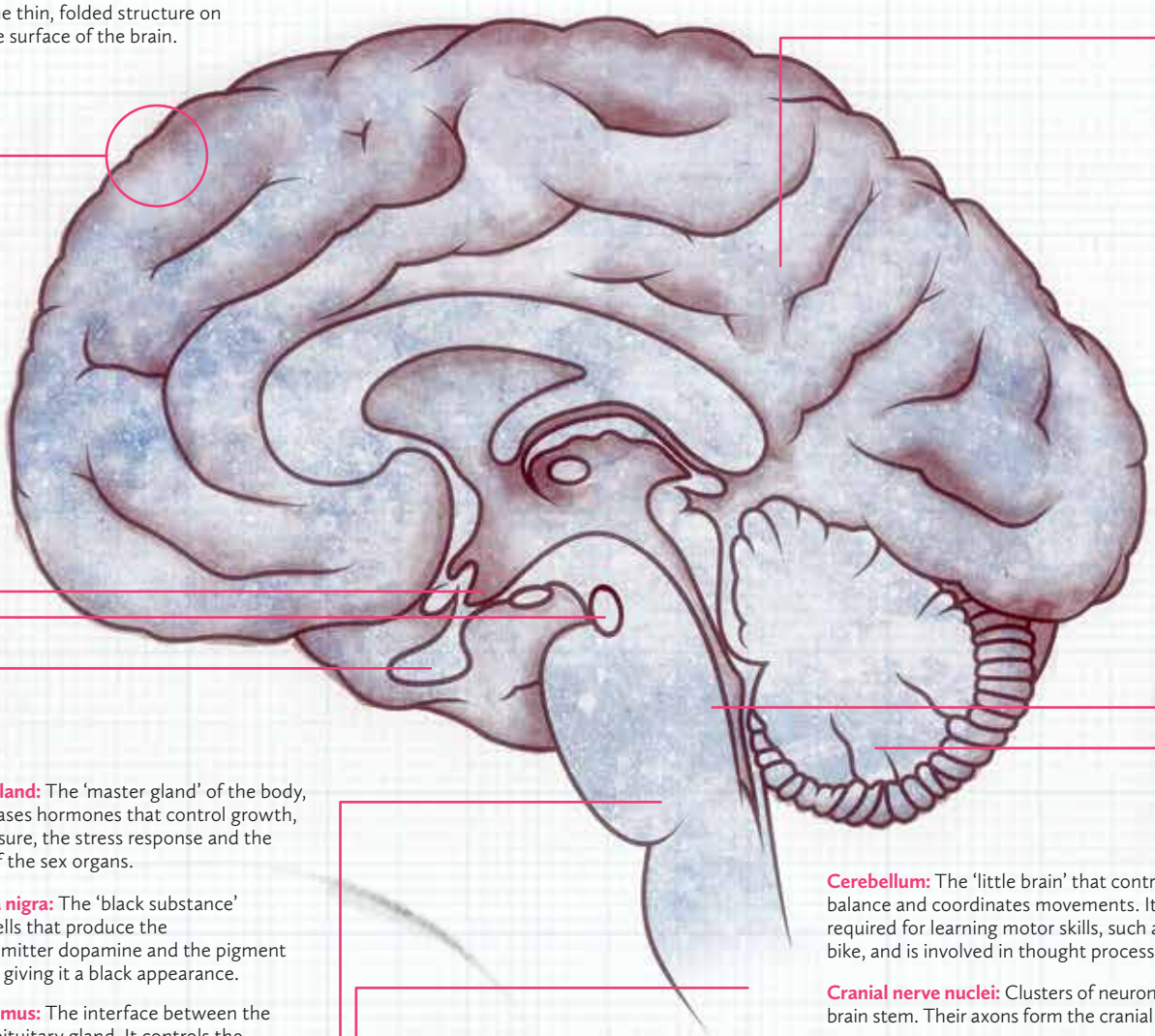
MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain

FINDING YOUR WAY AROUND

Below is an annotated guide to the brain. Remember, many simple and complex psychological functions are mediated by multiple brain regions and – at the same time – a single brain area may control many psychological functions.

Cerebral hemispheres: The two halves of the brain, each of which controls and receives information from the opposite side of the body.

Cortex: The thin, folded structure on the outside surface of the brain.



Pituitary gland: The 'master gland' of the body, which releases hormones that control growth, blood pressure, the stress response and the function of the sex organs.

Substantia nigra: The 'black substance' contains cells that produce the neurotransmitter dopamine and the pigment melatonin, giving it a black appearance.

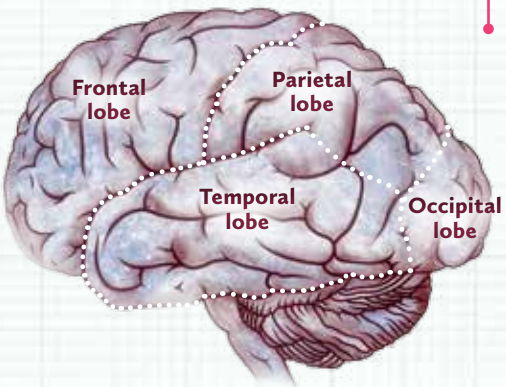
Hypothalamus: The interface between the brain and pituitary gland. It controls the production and release of hormones.

Cerebellum: The 'little brain' that controls balance and coordinates movements. It's normally required for learning motor skills, such as riding a bike, and is involved in thought processes.

Cranial nerve nuclei: Clusters of neurons in the brain stem. Their axons form the cranial nerves.

Spinal cord: A large bundle of millions of nerve fibres, which carries information back and forth between the brain and the body.

Medulla oblongata: Controls vital involuntary functions such as breathing and heart rate.



For even more on the brain (including the limbic system) and neurons, synapses and neurotransmitters, order or download our poster at **www.wellcome.ac.uk/bigpicture/brain**

Structural imaging

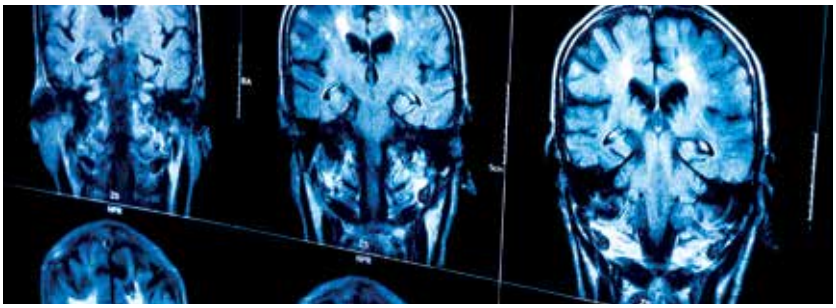
It used to be the case that to see the brain, you would need to open up the skull to expose it. Now, many non-invasive scanning technologies mean we can see inside the head without touching a scalpel.

IN YOUR HEAD

Imaging the living brain is a valuable thing to do

We can image, or 'scan', the brain to examine its structure and function in living people and other animals. This can be done using various methods, such as computerised tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET), alone or in combination. Researchers use these methods to try to understand how the healthy brain develops, performs its functions and changes as we get older, as well as to study the changes that occur in neurological conditions such as Alzheimer's disease and stroke.

In the earliest stages of Alzheimer's disease, for example, the hippocampus begins to shrink, eventually leading to problems with memory. In stroke, damage to the grey matter and the white matter connecting different parts of the brain often affects a person's ability to speak and move. Doctors can image the brain to observe these changes to diagnose diseases more accurately. Brain imaging can also be used to monitor the progression of a disease, as well as the effects of therapy.



Sved Attila Oliver/Shutterstock

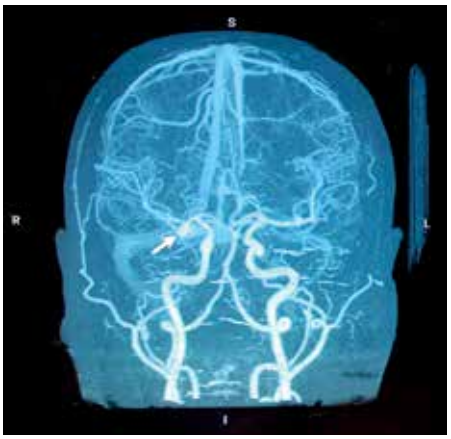
CT scans of the human brain.

SPOT THE DIFFERENCE

	MRI	CT
ADVANTAGES	- It is non-invasive - It is very useful for producing images of soft tissues, such as the brain, eyes, ligaments and cartilage - It can produce images in any plane (e.g. horizontal or vertical)	- It is non-invasive - It is very useful for imaging hard tissues such as bone - It is quick – a scan can take as little as five minutes - It produces highly detailed images - It can be used on patients with metallic implants
DISADVANTAGES	- It is expensive - It cannot be used on patients with artificial pacemakers or metallic implants - It is not portable	- It is not portable - Some patients are allergic to the contrast dyes that are injected for some CT scans - It exposes the patient to radiation

COMPUTERISED TOMOGRAPHY

A technique that slices you up?



hasa/Shutterstock

CT angiography of an aneurysm.

Computerised tomography (CT), or computerised axial tomography (CAT), uses X-rays and a computer to produce detailed images of horizontal slices through the body and brain. It is not used for research purposes very often but is widely used in hospitals to diagnose and monitor a variety of medical conditions, including arthritis and pneumonia. CT can also be used to look for brain tumours, haemorrhages and the damage caused by strokes, and to examine injuries to the bones and internal organs. It is often used to examine abnormalities seen in normal X-rays in more detail.

Some companies are offering people 'health MOTs': paid-for CT and MRI scans and other body imaging. The Nuffield Council on Bioethics has published a report on the potential risks and benefits of this 'direct-to-consumer body imaging' and has called for private whole-body CT imaging to be banned (**www.nuffieldbioethics.org/personalised-healthcare/personalised-healthcare-body-imaging**).

FAST FACT

All mammals have a wrinkled cortex, but the human cortex is much larger in area (in proportion to the overall brain) than any other animal's. Source: **www.dana.org/news/brainhealth/detail.aspx?id=10060**

MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain

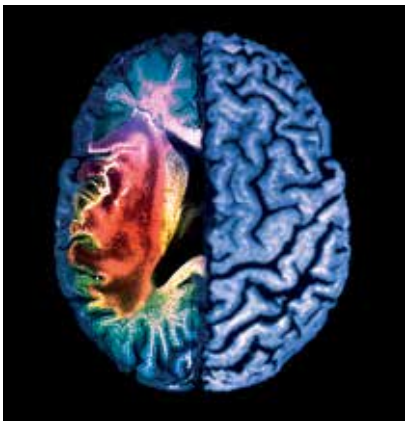
MAGNETIC RESONANCE IMAGING

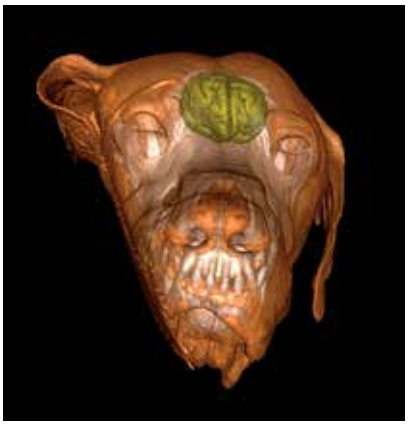
An imaging technique where protons get in a spin

Magnetic resonance imaging (MRI) is well suited to visualising soft tissues such as the brain. It relies on the magnetic properties of atoms to produce images. An MRI scanner is a large cylinder containing an extremely powerful magnet. When a patient lies inside the scanner, the magnetic field it produces causes the protons in atomic nuclei to align themselves with it. The scanner then transmits radio waves through the body, making the protons alter their alignment. This causes the nuclei to produce tiny rotating magnetic fields that can be detected and recorded by the scanner to construct the image.

Researchers use MRI to look at the structure of the brains (both living and dead) of humans and animals. In 2007, neuroscientists used it to scan the brains of two stroke patients who died about 150 years ago. More recently, researchers transplanted human cells into the brains of rats to help them recover from stroke and used MRI to detect the structural changes caused by the transplanted cells.

Doctors use MRI to visualise the changes that occur in a wide variety of neurological diseases, including Alzheimer's disease, epilepsy and multiple sclerosis. In Alzheimer's disease, certain parts of the brain begin to shrink many years before symptoms appear. MRI scans can detect this shrinkage, which is important because early detection can lead to earlier treatment. In addition, the method is used to diagnose brain tumours and to determine exactly where they are so they can be surgically removed.





MRI scan of a human brain after a stroke (dead tissue in red) and 3D MRI of a dog's head.

(L) Zephyr/Science Photo Library. (R) Thierry Berrod, Mona Lisa Production/Science Photo Library

CHECK THE VOLUME

Volume changes in the brain can tell us about disease and ageing

Voxel-based morphometry (VBM) is a type of analysis applied to MRI images that is used to measure the volume of specific brain structures. By comparing healthy and diseased brains, researchers can detect the subtle structural changes that occur in neurological and psychiatric conditions. It can detect the reduction of hippocampus volume that occurs in Alzheimer's disease and depression, as well as the thinning of the cerebral cortex that occurs as a normal part of ageing.

Memory researchers in London have been investigating the changes that occur in taxi drivers' brains as a result of learning. To qualify for the job, London's taxi drivers have to learn 'the Knowledge' (every street name, landmark and direction of traffic flow in a six-mile radius of Charing Cross) so they can navigate the city effectively. Using VBM, the researchers found that those who qualified had an increased volume of grey matter in the hippocampus, a part of the brain known to be involved in generating maps and forming spatial memories. They have also found that the longer a person has been driving a taxi, the larger their hippocampus.

WELL CONNECTED

Neuroscientists want to understand how our brain pathways link up

Neuroscientists see the brain as consisting of hundreds of specialised areas organised into multiple interconnected networks. They use imaging to visualise the white matter tracts that form connections within and between networks and examine how the connections break in diseases such as stroke. One method that is increasingly being used for this is diffusion tensor imaging (DTI) tractography, a form of MRI that detects the diffusion of water molecules along axons.

DTI tractography reveals the brain's largest pathways. Last year, Harvard researchers used it to image large fibres throughout the entire brain for the first time. Researchers at Cardiff University are developing a more advanced method, called DTI tractometry, to image the microscopic structure of the pathways and provide details such as the density and diameter of the axons in the tracts.

Some of this work is part of a larger project called the Human Connectome Project, which some researchers say is too ambitious. If it is eventually possible to produce a complete map of the connections in the brain, even that will not tell us everything about how the brain works.

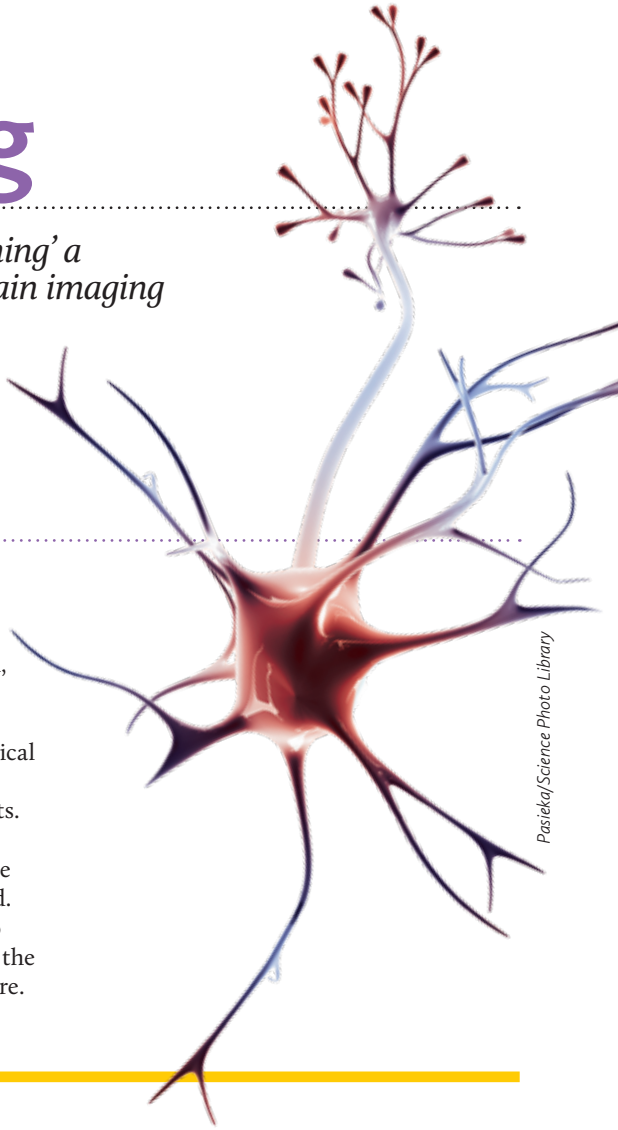
LOOKING AT THE PAST

How did people explore the brain without imaging it?

Before brain imaging was invented, doctors would observe the behaviour of people with brain damage and then examine their brains after they died. This enabled them to link the changes in behaviour to specific parts of the brain. One early example is Phineas Gage, who had a metre-long iron rod propelled by an explosion through his skull. His experience led doctors to link the frontal lobes to social behaviour. Read about Gage and other historical case studies at **www.wellcome.ac.uk/bigpicture/brain**.

Functional imaging

From reconstructing YouTube clips from brain scans to 'watching' a person's brain as they slip under an anaesthetic, functional brain imaging is producing fascinating insights into how our brains work.



Pasieka/Science Photo Library

EEG AND MEG

Imaging techniques that detect electrical activity

Electro-encephalography (EEG) and magneto-encephalography (MEG) are functional imaging methods used to measure brain activity directly and non-invasively (from outside the head). EEG detects synchronised electrical activity of large groups of neurons, whereas MEG detects the tiny changes in magnetic fields that this electrical activity is associated with. The images produced by EEG and MEG are not very localised, but they can monitor how electrical activity changes with time very precisely.

EEG requires electrodes to be attached to the scalp. It can be used to detect general patterns of electrical activity, such as the brain waves that occur during sleep. Researchers used EEG to compare the visual cortex activity of people who are born blind with those who are not blind, and they found that the visual cortex of blind people was active.

EEG can also be used to detect electrical signals associated with specific sensory stimuli, thought processes or movements. Detecting and measuring these 'event-related potentials' can be done at a single electrode, but in practice, many are used. They are spread across the scalp, to help researchers pinpoint where in the brain the neurons responsible for the potentials are.

BOLD THINKING

What does fMRI really measure?

The most common form of fMRI is blood oxygenation level dependent (BOLD) fMRI. It is based on the idea that neurons require more energy when they fire and that increased blood flow to active parts of the brain supplies the oxygen required. This form of MRI measures changes in the concentration of oxygen in red blood cells.

The main limitation of fMRI is that it measures brain activity indirectly, using blood flow as an indication that neurons are active. In 2009, researchers in the USA published important work showing that parts of the brain that receive more oxygenated blood do not necessarily become more active. The researchers used fMRI to scan the brains of monkeys while they looked at pictures, and they found that the brain anticipates which of its parts will be activated over the next few seconds and pre-empts itself by sending more blood to them. Most areas that receive more blood are more active, but some areas that receive more blood do not become more active.

FUNCTIONAL MRI

An imaging technique to show brain activation during tasks

Functional magnetic resonance imaging (fMRI) is used to image the parts of the brain that become active during different mental processes. In medicine, fMRI can be used to map brain functions in patients who are about to undergo neurosurgery to remove a brain tumour or abnormal tissue that causes epileptic seizures. This helps neurosurgeons to minimise the risk of accidentally removing or damaging the parts of the brain involved in functions such as language and memory.

fMRI studies show that different brain areas are specialised for certain functions, often supporting data from previous neurological and psychological studies. For example, the frontal lobe contains areas that plan and control voluntary movements. The frontal lobe also contains areas specialised for complex functions such as making decisions and judgements, which are important for social interactions. fMRI studies show that activity in these areas and their detailed structure is altered in people with autism, but further research is needed to confirm this.

fMRI can also be used to 'decode' brain activity. In 2011, researchers in California scanned participants' brains while they watched different YouTube clips; they then recorded activity in the primary visual cortex, which contains cells that detect contrast and the orientation of moving edges. Researchers then showed the participants different film clips while scanning their brains again and were able to construct low-quality copies of what the participants saw by decoding primary visual cortex activity. Our thoughts are much more complex than this simple mapping of visual images, so we are a long way from decoding the content of minds.

YouTube

MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain

KNOW YOUR NEUROTRANSMITTERS

Imaging can be used to study neurotransmitters too

Imaging can be used to measure the levels of a neurotransmitter, its receptors and its transporters (which remove neurotransmitters from the synapse after release). This is very useful because many neurological conditions involve the death of neurons that produce a specific neurotransmitter, or alterations in the activity or distribution of receptors or transporters within certain parts of the brain. The relationship between diseases and neurotransmitters is complex. For example, other neurotransmitters than those discussed below could also be involved in the conditions presented.

In Parkinson's disease, dopamine-producing neurons in the midbrain die. Alzheimer's disease, depression and schizophrenia involve alterations in the transporter for the neurotransmitter serotonin. Attention deficit hyperactivity disorder (ADHD) has been associated with malfunctions of dopamine receptors and dopa decarboxylase, one of the enzymes needed for making dopamine, in the frontal cortex. ADHD, depression and schizophrenia can all involve disturbances in the function of receptors and transporters for the neurotransmitter noradrenaline.

The imaging methods used most often to measure neurotransmitter levels are positron emission tomography (PET) and single-photon emission computed tomography (SPECT). Both involve injecting a radioactive 'tracer' substance that binds to the molecule being studied. The scan reveals where the tracer binds, and the intensity of the radioactive signal in each brain area is related to the level of the molecule being studied.

Neurotransmitter receptors come in multiple forms, or subtypes, and each subtype has multiple variations. Some tracers bind to one particular subtype or more specifically to one variation of a subtype. To date, we know of at least five subtypes of receptor for dopamine – D_1 to D_5. Genetic mutations in the D4 subtype of the dopamine receptor (DRD4), for example, are linked to ADHD, Parkinson's disease and schizophrenia, as well as drug use and personality traits such as aggression and impulsiveness. PET and SPECT can be used to examine exactly how alterations in the DRD4 receptor are linked to these conditions and behaviours.

OTHER WAYS TO IMAGE

Many different imaging methods are in use and development

One imaging technique that is now widely used by researchers is calcium imaging. When neurons fire, the concentration of calcium ions inside them increases. This can be detected in slices of brain tissue or in live animals, using fluorescent dyes that are sensitive to the concentration increases combined with two-photon microscopy (a type of microscopy used particularly to image living cells). This technique requires an operation to expose the brain and is not used in humans.

Near-infrared spectroscopy (NIRS) is a method that detects changes in blood flow around the brain. It works by transmitting light with a wavelength of 700–900 nanometres through the head; the light passes through skin, bones and brain tissue but is absorbed differently by oxygenated and deoxygenated blood. The person being scanned wears a cap containing lasers or light-emitting diodes; this allows people to do more things while their brain is examined because they are not enclosed in a scanner. NIRS is cheaper than fMRI and is particularly useful in small babies, whose skulls are thinner than those of children or adults and transmit the light used by NIRS better.

Other techniques include functional electrical impedance tomography by evoke response (fEITER). This uses electrodes attached to the head, which transmit electrical currents that are interrupted by the brain's electrical activity. Researchers recently used fEITER to image how brain activity changes when people lose consciousness under anaesthesia.

University of Durham, Simon Fraser/Science Photo Library

HANDS-ON RESEARCH

Researchers can alter your brain function

Some techniques enable researchers to alter activity in the living human brain. One of these is transcranial magnetic stimulation (see above), which uses a figure-of-eight-shaped coil placed on the scalp to deliver magnetic pulses to parts of the brain directly under the coil. This can be used in the lab to interrupt brain activity, to see how different brain regions contribute to certain functions. In the clinic, transcranial magnetic stimulation can also be used to assess brain damage in people who have suffered a stroke and to aid their rehabilitation.

Deep brain stimulation is an invasive surgical procedure in which thin wire electrodes are implanted into the brain. By passing current through the wires from a control box outside the head, you can alter the activity of the region where the wires are implanted. Deep brain stimulation can help alleviate some symptoms of Parkinson's disease, and so far it has been used to treat about 90 000 patients with the condition. It is also being used to treat other conditions, such as depression and obsessive–compulsive disorder, as well as drug addiction.

FAST FACT

A 2011 study suggests that the increase in general intelligence seen during adolescence can be attributed to increases in mental speed. Source: **Coyle TR et al. Psychol Sci 2011;22(10):1265–9.**

Mythbusting

We've all heard the one about people using only 10 per cent of their brain, but is this just a myth or proven fact? Like any respectable science publication, we've gone directly to the published evidence to help you separate scientific fact from brainy baloney.

IS IT TRUE THAT...

...LEARNING CAN PHYSICALLY ALTER THE BRAIN?

Neuroscientists believe that learning and memory change the physical structure of the brain. Animal research shows that forming a new memory involves the strengthening of synapses in a network of neurons. The same is probably true of humans, although we still do not have the techniques to observe these changes directly in the human brain.

Eric Boucher/Shutterstock

Learning can cause other changes in the brain, some of which can be seen in the human brain using various imaging techniques. In 2004, for example, researchers used MRI to show that learning to juggle for three months increases the density of grey matter in parts of the visual cortex specialised for processing complex visual motion. More recently, another group of researchers showed that learning to juggle also leads to changes in the brain's white matter tracts. Using diffusion tensor imaging, they found that it increases the density of white matter underneath the intraparietal sulcus, which is involved in several mental functions, including memory for where things are in space and perceptual–motor skills (such as hand–eye coordination).

Learning to read as an adult also causes significant changes in brain structure. In a unique study, researchers in London and Spain examined the brains of former Colombian guerrillas who learned to read Spanish after returning to mainstream society. Using MRI, they detected increases in the volume of grey matter in the left frontal and temporal lobes, both of which contain areas specialised for processing language.

...WE ONLY USE 10 PER CENT OF OUR BRAINS?

Many people think that we only use 10 per cent of our brains and that we can harness the rest to boost our mental abilities. This is the most popular myth about the brain, and there is no scientific evidence for it – we almost certainly use all of it. The brain is a very hungry organ, consuming nearly one-quarter of the body's energy, despite accounting for just 2 per cent of body mass. From the point of view of evolution, it just doesn't make sense to have a large organ that consumes so much energy if only 10 per cent of it is actually needed.

...BRAIN GYM MAKES YOU SMARTER?

The makers of Brain Gym claim that particular physical activities enable students to access parts of the brain that they normally do not use, and that pushing "Brain Buttons" on parts of the body, or performing certain repetitive movements, can improve blood flow to certain parts of the brain or improve certain brain functions.

www.braingym.org/faq states: "Our primary evidence comes from the countless anecdotal stories reported to us since 1986." They also publish three publications of their own research. Several scientists have explained publicly why they think some of the claims do not stand up scientifically (on **senseaboutscience.org,** for example). A 2007 paper by Dr Keith Hyatt from Western Washington University found that "a review of the theoretical foundations of Brain Gym and the associated peer-reviewed research studies failed to support the contentions of the promoters of Brain Gym".

However, regular aerobic exercise is good because it makes the heart work harder and increases blood flow to the brain. There is evidence that it improves cognitive function and memory, and can be linked to academic achievement. Regular exercise throughout life may help to protect the brain against the changes that occur with age, and could slow these changes down. In mice and rats, exercise also causes the growth of new brain cells, but we still don't know whether this also happens in humans.

...THERE'S A JENNIFER ANISTON NEURON?

While examining the brains of people with epilepsy who were about to undergo neurosurgery, researchers discovered neurons that respond specifically when people look at pictures of celebrities like Jennifer Aniston and Halle Berry or famous landmarks like the Eiffel Tower. The cells also fired when the patients thought about the celebrities. They are located near the hippocampus, which is crucial for memory formation. Each cell is probably part of a network that encodes the memory, or concept, of the celebrity or landmark and probably contributes to hundreds of other networks, each of which encodes a different memory or concept. It is unlikely that single neurons map directly and uniquely onto single people or objects.

MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain

...A BIGGER BRAIN IS A CLEVERER BRAIN?

It was once thought that having a bigger brain makes you more clever, but that isn't true. Women's brains are, on average, 9 per cent smaller than men's (and so contain fewer neurons), but women are not less intelligent than men; the size difference just reflects the fact that women's bodies are generally smaller. Brain size and intelligence are definitely linked, however, but we still don't know exactly how. What seems to be more important than overall size is how the neurons are connected to each other.

Albert Einstein's brain (right) illustrates just how complicated the relationship between brain size and intelligence is. Einstein is often said to be one of the most intelligent people that ever lived, and researchers naturally believed his brain might provide important clues about what made him so clever. When he died, they were surprised to discover that his brain was actually quite small. It weighed 1.23 kg, or about 200 g lighter than the average of 1.4 kg, and the temporal lobes – which contain areas that are specialised for speech and language – were also smaller than average.

Scientists who examined Einstein's brain did find some unusual differences that help to explain why he was so intelligent. For example, his parietal lobes, which are important for mathematical abilities and visual and spatial functions, were about 15 per cent wider than average. They also had an unusual pattern of grooves and ridges, and certain regions of the parietal lobes had more glial cells per neuron than normal.

Einstein's brain. *Wellcome Images*

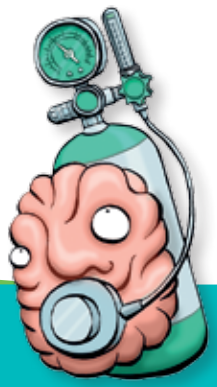
...THE SIDES OF OUR BRAIN DO DIFFERENT THINGS?

Another popular myth about the brain is that the left hemisphere is 'logical' and the right hemisphere is 'artistic'. This probably comes from early studies of people with brain damage and from work on 'split-brain' patients, in whom the connections between the left and right hemispheres were destroyed to prevent epileptic seizures from spreading throughout the brain. It's true that the left and right hemispheres each contain areas that are specialised for different functions, but most things we do involve the coordinated activity of the two hemispheres.

...ABUSE AND LOVE CAN CHANGE THE BRAIN?

There is plenty of evidence that childhood neglect and abuse can cause changes in the brain that have long-lasting effects. Most of it comes from research on animal behaviour, but there is evidence for this in humans as well.

In recent years, it has been found that growing up in poverty has a direct effect on children's mental abilities. One study showed that children raised in impoverished conditions have a reduced capacity for working memory – the ability to store small amounts of information for short periods of time – in comparison to better-off children. A follow-up study showed that this is probably because stress affects the way in which children's brains develop. More recently, it has been found that childhood abuse stunts growth of the hippocampus, part of the medial temporal lobe that is crucial for memory formation.



FAST FACT

The human brain accounts for 2 per cent of the total mass of the body, but 20 per cent of its oxygen consumption at rest. Source: **www.ncbi.nlm.nih.gov/books/NBK28194/**

...WE'RE BORN WITH ALL THE BRAIN CELLS WE'LL EVER HAVE?

Thomas Deerinck, NCMIR/Science Photo Library

Nerve cells and glial cells, SEM

Neuroscientists had always believed that the adult brain could not produce new cells and that we are born with all the neurons we will ever have. This viewpoint slowly began to change in the 1970s, when scientists discovered that the brains of rats and songbirds produce new cells throughout life. This is now widely accepted as being correct, and many scientists also take it for granted that the same is true for the adult human brain.

Actually, though, there's still very little evidence for it. According to the latest estimates, the brain contains about 86 billion neurons and roughly the same number of glial cells. As far as we know, the vast majority of these cells are produced in the womb – during early pregnancy, about 250 000 brain cells are produced every minute. The rest are produced during a short period of time after birth – maybe as little as a few months, or as much as a year.

As a result, the brain produces at least twice as many cells than it actually needs to work properly. Neurons begin to die before we have even been born and continue to die every day of our lives. Researchers have estimated that about 85 000 neurons die every day in the cerebral cortex. That's equivalent to one every second.

Know your mind

New techniques and developments in brain imaging can bring big improvements for patients, including a quicker or more accurate diagnosis and better ways to monitor the effectiveness of treatments. However, these developments can also raise tricky ethical, legal and social questions. Read our examples below, based on situations that could arise today (or have already), and see what you would advise for the people involved.

INCIDENTAL FINDINGS

Imagine your friend is doing a PhD and you have volunteered to participate in a brain scanning study as part of her research. You visit her in the lab and she gives you instructions about what you need to do while she scans your brain. When the results come in, your friend's supervisor looks at your scans and spots something abnormal.

What should she do?

According to a recent survey, this happens to a small number of people. In 2009, neurologists reviewed the results of 31 MRI studies carried out between 1950 and 2008, involving about 35 000 people. According to their results, abnormalities were found in up to 1 in 50 people who had their brains scanned for a non-diagnostic reason. These were more common in older people and included several different types of brain tumours, as well as abnormalities in blood vessels that might indicate an increased risk of stroke.

A similar situation is found in genetics research. The cost of DNA sequencing has decreased significantly in recent years, and it is now common for researchers to sequence and compare the entire genomes of many thousands of people. As a result, they are more likely to identify genetic mutations and variations that predispose people to certain diseases or behaviours.

DISCUSS:

Do researchers have a duty to share this kind of information with you? And would you want to know if your brain scan revealed an abnormality? Often, people participate in scientific research anonymously, so the researchers don't know whose results they are analysing. Is this right? What should guidelines suggest should be done when researchers think they have found something unusual about one of their participants?

UNLOCKING CONSCIOUSNESS

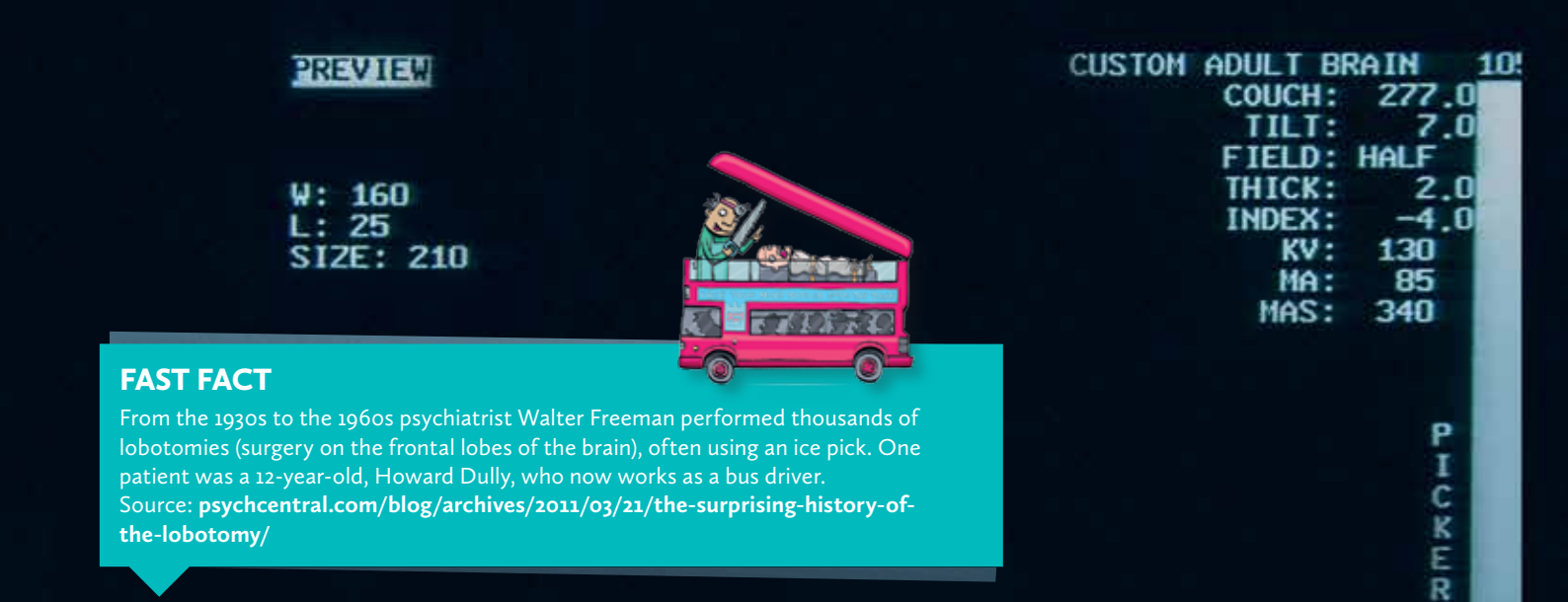
Researchers have devised a clever way of using fMRI to try to communicate with patients diagnosed as being in a vegetative state. To do so, they place a patient in the scanner and ask them simple questions. The patient is told to imagine playing a game of tennis if they want to answer "yes" and to imagine walking around their house if they want to answer "no". These thoughts produce different patterns of brain activity, which can be detected by the scanner: imagining playing tennis activates the premotor cortex, which is involved in planning movements, whereas imagining walking around a house activates the hippocampus and surrounding areas, which store maps of the environment and memories of how to navigate them.

Until recently, it was thought that patients in a vegetative state were completely unable to follow instructions like this. Using this method, however, researchers have found that at least one in ten of them can willfully modify their brain activity in this way and apparently answer simple questions correctly. Follow-up work has led some researchers to conclude that close to 20 per cent of patients who are thought to be vegetative are actually conscious.

DISCUSS:

The apparent ability to communicate with these patients raises some difficult ethical questions. Most of these patients are unresponsive and cannot communicate in any other way, so who should be responsible for giving the researchers permission to do this? Patients who can answer questions in this way probably have a better chance of recovering, but brain scans are expensive. How should the researchers decide which patients to test? And what questions should they ask the patients they do scan?

MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain



FAST FACT

From the 1930s to the 1960s psychiatrist Walter Freeman performed thousands of lobotomies (surgery on the frontal lobes of the brain), often using an ice pick. One patient was a 12-year-old, Howard Dully, who now works as a bus driver.
Source: **psychcentral.com/blog/archives/2011/03/21/the-surprising-history-of-the-lobotomy/**

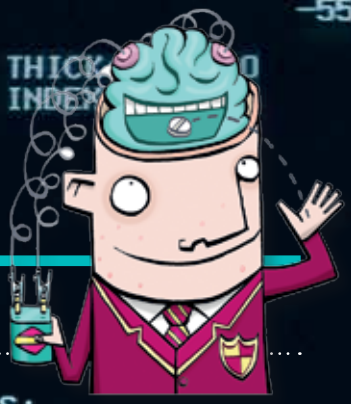
BRAINS TO BLAME

Brain injuries often affect a person's behaviour and personality, causing them to do things that they may not otherwise do. One example is the US schoolteacher who began visiting prostitutes and collecting child pornography, then molested his 12-year-old stepdaughter. The man was eventually charged and remanded in custody. He then started complaining of severe headaches, which got so bad that he was taken to hospital. A brain scan showed that he had a large tumour in his frontal lobe. Doctors removed the tumour and his inappropriate sexual behaviour stopped. But about a year later, the tumour grew back, and the behaviour returned. **www.newscientist.com/article/dn2943-brain-tumour-causes-uncontrollable-paedophilia.html**

Drug treatments can also cause profound changes in behaviour. The drug L-dopa, for instance, which is given to patients with Parkinson's disease, can sometimes lead to compulsive gambling or impulsive sexual behaviour.

DISCUSS:

Are people responsible for their actions in cases like this? Should they be punished in the same way as others, or should their brain damage or drug treatment be taken into account? And is there an ethical problem with prescribing a drug when it is known to have side-effects, like L-dopa? According to research published last year, judges are more lenient towards violent criminals who are known to be genetically predisposed towards violence. Do you think this is right?



SELF-IMPROVEMENT

Adam is in the first year of a university degree in economics. His exams are approaching, but he hasn't done much revision. He wants to enhance his brain function using psychostimulants and brain stimulation, so he can cram in as much as possible in the little time he has left before they start. He knows someone who can get him some 'smart drugs' – modafinil, a stimulant given to people with narcolepsy, which enhances wakefulness and has memory-boosting effects, and methylphenidate (sold as Ritalin), a stimulant given to children with ADHD, which enhances attention.

Adam thinks that taking modafinil might help him to stay up all night, giving him precious extra time for last-minute revision, and that methylphenidate might help him to stay focused on his work for much longer than normal. He also knows that he can further boost his capacity to learn and retain information using transcranial direct current stimulation (tDCS), a simple technique that involves applying small electrical currents to the brain, via electrodes on the scalp that are attached to a 9-volt battery. He can buy a cheap tDCS kit online and apply it himself.

DISCUSS:

Do you think it's OK for Adam to enhance his mental functions in this way? Would it give him an unfair advantage over other students who have worked hard throughout the year? What would you do if you were in his position? And how is this different from drinking coffee to keep yourself alert? If you were a potential employer, would these actions influence the value you placed on his grades?

Real voices

Three people talk about the role of brains in their lives. Meet Jessica Collis, who is being treated for OCD; Conor Mallucci, a surgeon who uses brain imaging; and Dr Marius Kwint, a cultural historian.

JESSICA COLLIS

Greengrocer's assistant being treated for a neurological condition (OCD)

Who are you?
I'm 18 and I have worked at a greengrocer's since I finished sixth form about a month ago. I have obsessive–compulsive disorder (OCD), which means I have to do certain things a lot, like washing my hands, checking things and sometimes self-harming.

When did you find out you had OCD?
I knew for a while before I was diagnosed a few months ago. I got really bad during my GCSEs; I used to check everything – fire alarms, burglar alarms, corners of rooms. I think I've had it since I was about five, but it's only been confirmed recently.

How does it affect your life?
There are a lot of things in the house I don't like touching: the side of the chair, the TV controls, a wall in my bedroom, light switches. The main things I do are check things and wash my hands, but when I'm really low I punch my leg over and over, and sometimes I scratch my arm until it breaks the skin. I have a thought in my head that my arm itches and I have to keep scratching it. I haven't done those things for a while, though.

How do other people react?
I've only been able to tell about five people face-to-face because I don't know what to say. I recently made a friend on the OCD UK forum. That really helps because I can learn from his experiences. I always thought I was the only person, so it's good to talk to someone else who understands what I'm going through.

It really annoys me when celebrities and other people talk about 'having OCD'. Everybody thinks it's just hand washing and making sure everything is straight. They don't realise it affects you a lot and can make you feel really down.

How do you think it will be in the future?
I just started CBT (cognitive behaviour therapy) yesterday. It was my first one, so we just talked about everything, and [the CBT specialist is] going to try to help me get better. I want to be more confident so I can go out more without worrying about my OCD. I think in the future I would like to go out to schools and talk about OCD so more people understand.

I know I'm not supposed to be like this, but I can't help it. I'm hoping I will get a lot better soon, now I'm getting the help and support that I need.

CBT is a highly effective treatment for OCD. For more info on this and the condition itself, see **www.ocduk.org/**, call 0845 120 3778 or email support@ocduk.org. Read an extended Q&A with Jessica and her mum at **www.wellcome.ac.uk/bigpicture/brain**.

CONOR MALLUCCI

Paediatric neurosurgeon at Alder Hey Children's Hospital, Liverpool.

What you do?
I am a consultant paediatric [children's] neurosurgeon at Alder Hey Hospital in Liverpool. I was appointed when I was 31 and I'm now 46, so I've been doing it for 14 years. My main interest is paediatric brain tumours, and that's what I do 90 per cent of the time.

How do you use MRI?
All kids with brain tumours need MRI [magnetic resonance imaging] scans at some point before their operation. It's standard practice. When you take out a paediatric brain tumour, you've only got the surgeon's word for it that it's been removed. You need to confirm that with a post-operative [after the operation] MRI scan. This would be done the next day, and if there is some residual tumour, you'd then have to discuss whether to take the child back to theatre within the next couple of weeks to remove that residual tumour. The vast majority of brain tumours do better, and the patient's chances of survival are much improved, if you remove them completely.

How is intraoperative MRI different?
Intraoperative [during the operation] MRI brings the scanner into theatre. When we think we've completed a resection [removal], we keep the head open and move the patient into the scanner, which is next to theatre, through a special transport system. While the head is still open, we do an intraoperative MRI scan. Then we discuss the results, and if we are happy with the scan we go back and close the patient. If we're not happy, we do more surgery. In the past couple of years, we've done more surgery in 30 per cent of cases.

What are the advantages?
It means we can be sure that we've done exactly what we wanted to do – that we've resected the whole tumour – at the time of the first surgery without having to wait until the next day for the post-operative scan.

Using intraoperative MRI reduces the chance of having to bring the child back for repeated surgery over the next couple of weeks. We used to have a 12 per cent return-to-theatre rate within six months for further surgery. That rate is now zero per cent.

What are the disadvantages?
The problem with intraoperative MRI scanners is that they're extremely expensive, and paediatric brain tumours are rare. It's an expensive luxury, which is paramount to the parent of a child with a brain tumour but not necessarily to the NHS.

How would you sum up your job in a single sentence?
It has to be the best job in the world and the most privileged job in the world.

MORE ONLINE: www.wellcome.ac.uk/bigpicture/brain

DR MARIUS KWINT

Cultural historian and curator of Wellcome Collection's Brains *exhibition*

What do you do?
I'm a cultural historian with particular interests in the relationship between art, science and visual culture. I study changing attitudes to the world: how culture changes over time and in different places. I lecture at the University of Portsmouth.

How did you become a cultural historian?
I did a degree in cultural history at Aberdeen University. It was an interdisciplinary degree, and Scottish universities allow you to do a mixture of subjects in the first couple of years, so I studied a combination of science, the arts and the social sciences. My A-levels weren't all that promising, but I knuckled down for my degree – it really interested me and it was a new, experimental course – so I did pretty well and managed to get a grant to do a PhD at Oxford.

How did you get involved with the *Brains* exhibition?
I was invited by the senior curator of the Wellcome Collection, James Peto, and the Head of Public Programmes at the Wellcome Trust, Ken Arnold, to guest curate it. My interest in the brain stems from an exhibition that I worked on in 2005 in Zurich. The exhibition was on branching forms – anything that has a tree shape that isn't actually a tree (e.g. a brain cell). I co-wrote a paper with a neuroscientist, Richard Wingate, on that subject. That helped give me a bit of understanding of the nature of brain anatomy.

What was the exhibition about?
The exhibition explored not so much what the brain is or what it does, but rather 'what we do to it'. I wanted to focus on things that only an exhibition could show: objects and images. We concentrated on collecting brain matter, which has been central to brain science since the 18th century, when preservation techniques (i.e. pickling body parts in alcohol or formaldehyde) were developed.

What problems did you face?
We had to consider the ethics of exhibiting human specimens and also the human tissue regulations, which govern what you can and can't display to the public. But Wellcome Collection has a human tissue authority license and lots of experience in these matters. The specimens were properly handled and complied with ethical requirements to protect the anonymity of the subjects. All the brains we showed had been collected a long time ago, in some cases more than 100 years before.

Who would you swap brains with?
Mary Shelley. She had tremendous experiences and an extraordinary imagination and was able to say so many interesting things about science in her novel *Frankenstein*.

For more on Wellcome Collection's *Brains: The mind as matter* exhibition, see **www.wellcomecollection.org/brains** and the related article at **www.wellcome.ac.uk/bigpicture/brain**.

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