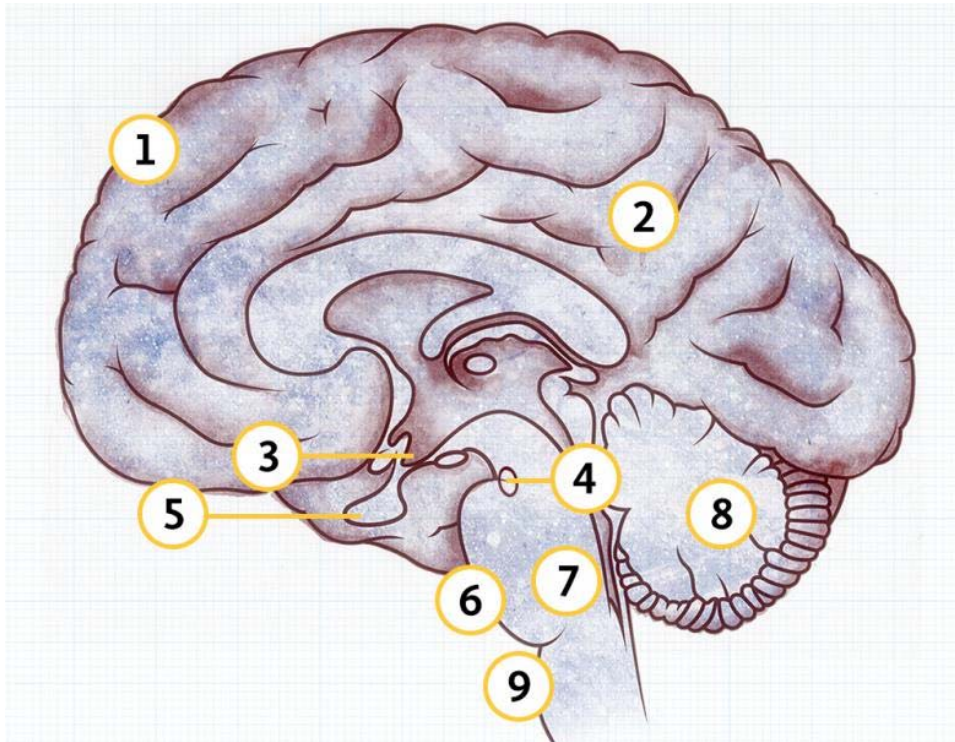


# Inside your brain

## You and your brain

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.



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1. Cortex: The thin, folded structure on the outside surface of the brain.
2. Cerebral hemispheres: The two halves of the brain, each of which controls and receives information from the opposite side of the body.
3. 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.
4. Substantia nigra: The 'black substance' contains cells that produce the neurotransmitter dopamine and the pigment melatonin, giving it a black appearance.
5. Hypothalamus: The interface between the brain and pituitary gland. It controls the production and release of hormones.
6. Spinal cord: A large bundle of millions of nerve fibres and neuronal cells, which carries information back and forth between the brain and the body.
7. Medulla oblongata: Controls vital involuntary functions such as breathing and heart rate.
8. 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.
9. Cranial nerve nuclei: Clusters of neurons in the brain stem. Their axons form the cranial nerves.

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 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 impulses called action potentials. Neurons use a change in the number of action potentials that they 'fire' to change the information they are transmitting. 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.

## Exploring the nervous system

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.

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 towards 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.

# The chemicals of the brain

**Beneath every thought, dream or action lies a remarkable chemical dance.**

Molecules called neurotransmitters are in constant flux throughout the brain. Manufactured and released by the billions of neurons a human brain possesses, they orchestrate how we feel, act and react.

Special cells called neurons are responsible for information transport through the brain. To relay this information, they use small chemicals called neurotransmitters, which are released from one neuron and received by another, using special docks – or receptors – to recognise the neurotransmitter and pass the information on to the cell body.

## **Dopamine: Pleasure, reward and motivation**

Without pleasure we would not be here. Eating, sex and happiness are all things that feel good – as a consequence, we seek them out. Of all the neurotransmitters in the brain, dopamine is the one most associated with pleasure (though endorphins also play a large part). Everything that makes you feel good is down to dopamine and the effect it has on the brain. Moreover, every known addictive substance affects dopamine release in what's known as the brain's 'reward pathway', the equivalent of a neurological circuit connecting experience with feeling good. Dopamine also plays a role in positive reinforcement and dependency, making a person more likely to repeat pleasurable actions and become addicted to substances that give this feeling.

Regulating dopamine's effects throughout the brain are its receptors, of which there are five known main variants: D1–D5. Alongside pleasure, these receptors ensure the involvement of dopamine in a range of activities, from movement and attention to memory. Drugs, such as cocaine and amphetamines, lead to a sharp, temporary rise in dopamine within the brain.

Unfortunately, things aren't quite as simple as that. With more and more research it is becoming increasingly apparent that dopamine isn't just a 'happy' neurotransmitter. Some research actually suggests that we shouldn't think about dopamine as a 'pleasure' stimulator, but rather as a 'motivation' stimulator, as it increases the person's motivation to repeat an action even when not associated with a pleasurable feeling. It also has a whole range of functions inside and outside the brain, showing just how important this little chemical is.

## **Glutamate: What goes up...**

Glutamate is the brain's 'on switch'. Known as an 'excitatory neurotransmitter', this tiny molecule does pretty much what it says on the tin – wherever it finds a receptor to dock with, it causes the hosting neuron to become excited. An excited nerve is one that's more likely to 'fire', resulting in the release of its own unique mix of neurotransmitters.

Glutamate receptors are a varied bunch, and can be split into two main families. Ionotropic receptors are so-called because they form channels for ions to move through when glutamate binds to them. Ionotropic glutamate receptors are: NMDA (which ketamine binds to and blocks its activity), kainate and AMPA.

Metabotropic glutamate receptors act a little more indirectly. Chances are, you're already an expert on glutamate as it crops up in foods either alone (it tastes savoury), or in its flavour-enhancing form – monosodium glutamate, or MSG.

## **GABA: ...must come down**

GABA (gamma-aminobutyric acid) is the neurotransmitter acting as glutamate's lazy twin, its sole purpose being to slow things down, dampen and inhibit nervous activity. Like glutamate, the GABA receptors are split into two types. GABA A receptors respond to GABA binding by allowing the flow of ions across nerve membranes. The GABA B receptors involve intermediaries in the process.

Drugs that stimulate these receptors tend to slow the brain down, so it's no surprise to discover alcohol affects these receptors. Drugs activating GABA receptors are found everywhere – liquid ecstasy, or GHB, has become well known as a 'date rape drug' while other activators, such as the benzodiazepines, are used in clinical contexts to help people get more sleep or lessen anxiety. These drugs are easy to overdose on, and produce tolerance (ie you need to take

more and more to achieve the same effect). This means they aren't used as much as they could be clinically, because they're quite dangerous.

### **Serotonin: Feeling groovy**

Ninety-five per cent of the body's serotonin is actually in the gut, but the 5 per cent in the brain has a big effect on mood – a person's overall state of mind, how they feel about themselves and the external world at a point in time. As you might expect, laying the burden of something as complex as mood on a single molecule could be oversimplifying things a little, but remarkably, this simple molecule does have a big impact on your mind.

The link between serotonin and how you feel is down to the large variety of serotonin receptors throughout the brain. Part of the reason the behavioural effects of this single neurotransmitter can be so complex is due to the number of different serotonin receptor types and the range of effects they can have.

These effects include causing the levels of numerous other neurotransmitters to be increased or decreased throughout different brain regions. Like a throwing a pebble into a lake, serotonin causes ripples of effect.

A lack of serotonin in the brain is associated with depression, which is why drugs called SSRIs (selective serotonin reuptake inhibitors), such as fluoxetine (Prozac), are commonly prescribed to help treat depression. Such drugs can cause an increase in the overall levels of serotonin in the brain leading, in many cases, to diminished symptoms.

Certain recreational drugs, such as MDMA (ecstasy) and LSD (acid), can also stimulate serotonin receptors, leading to altered or extreme moods. MDMA has two major effects on serotonin: causing it to be released as well as blocking the receptors involved in its reabsorption, meaning higher levels of serotonin remain in the synaptic cleft. This means that other receptors for serotonin continue to be active, creating the feeling of extreme happiness that MDMA is known for. However MDMA also depletes the levels of serotonin in the brain, at least in the short term. This is likely responsible for the 'comedown' phenomenon; after the positive effects of the drug wear off, many users are left feeling down.

LSD has a very similar structure to serotonin, meaning that it fits into and activates certain serotonin receptors. This means that brain processes related to serotonin release are constantly activated, producing feelings of happiness. LSD also affects many other areas of the brain to produce its other, psychedelic effects.

### **Acetylcholine: Remember me?**

Among other things, acetylcholine appears to play an important role in learning and memory. The neurons that produce this neurotransmitter – cholinergic neurons – are found in several regions of the brain, where, when stimulated, they release their stores of neurotransmitter onto waiting neurons. But to have any effect, those neurons need to have the right receptors: in this instance, the nicotinic and muscarinic receptors.

Nicotinic receptors, named after one of their most potent activators, nicotine (the reason cigarettes are so addictive), allow ions to quickly pass through them when either acetylcholine or nicotine binds to them. Muscarinic receptors (from muscarine, a receptor stimulant and poison extracted from certain mushrooms) act on a slower time frame than the nicotinic receptors. One of the most common blockers of the muscarinic receptors is atropine, a natural compound found in certain plants, such as deadly nightshade or mandrake.

### **Cannabinoids: Natural highs?**

There's no doubt that the brain responds to cannabis – the question is why would the brain evolve the ability to bind to this drug? In fact, the active component of the cannabis plant (tetrahydrocannabinol – THC) is a natural mimic of compounds that the human body actually makes on its own.

This group of THC-like chemicals made within the body are endocannabinoids. These are fatty chemicals able to move freely between cells until they find their receptors – CB1 and CB2. Once these are activated, a number of pathways are activated, resulting in a diverse array of effects, from reduced experience of pain to movement of the digestive tract, as well as having an effect on mood.

### **Opioids: Poppy-derived painkilling**

The colourful poppy is the source of the alkaloid drug, opium (an opiate – literally meaning ‘poppy tears’), a property that led to the eventual discovery of the numerous opioid receptors that bind such compounds within the nervous system. One well-known opiate commonly used today for the treatment of severe pain is morphine (after Morpheus, the Greek god of dreams).

Distributed throughout the nervous system, the opioid receptors, OP1–OP4, are involved in all of the calming effects we might expect, such as pain relief and reduction in anxiety – but these are taken to extremes by recreational drugs such as heroin. The natural partners to the opioid receptors are the endorphins, released during certain activities, such as running (they’re thought to be responsible for the ‘runner’s high’), pain and orgasm.