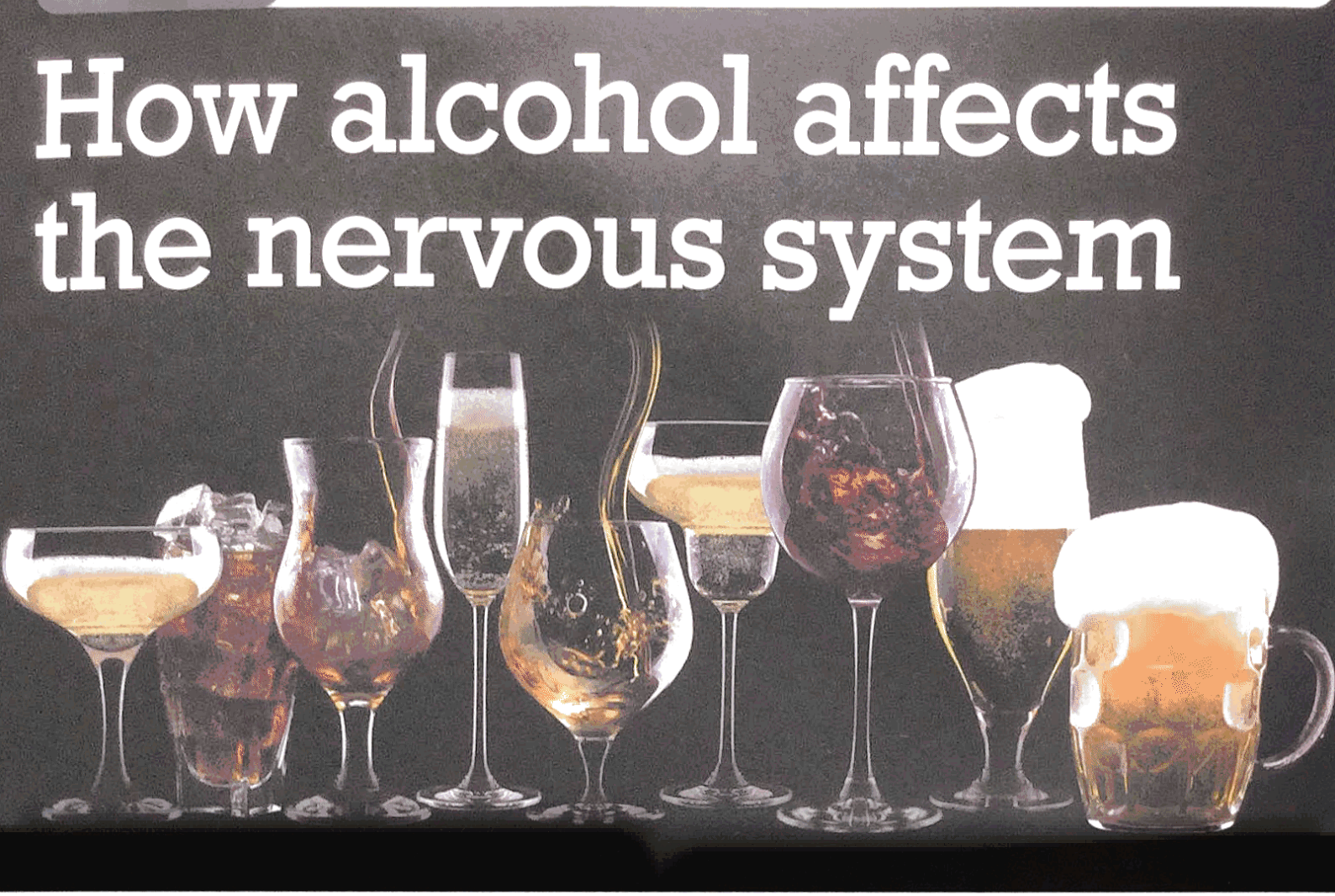
How alcohol affects the nervous system



Our understanding of how alcohol causes a rollercoaster of emotions is limited but many of the short-term effects of alcohol are thought to be due to its actions on the brain. Neuroscience researcher Oliver Freeman focuses on how alcohol alters behaviour by altering the transmission of signals between brain cells

Key words

Synapse
Dopamine
Neurotransmitter
Synaptic transmission

Drinking alcohol is a popular pastime in the UK. Many people love a drink to unwind, to celebrate or to commiserate, but alcohol is also a dangerous drug. Alcohol affects the brain mainly because of the chemistry of ethanol (see Figure 1), the active constituent of alcoholic drinks. The brain is protected from most of the chemicals that enter our body by the blood–brain barrier — a fatty barrier that surrounds blood vessels in the brain (see Biological Sciences Review, Vol. 25, No. 1, pp. 2–5). However, ethanol dissolves in fat quite easily so it can pass through this barrier.

Once in the brain, ethanol has marked effects on the communication between brain cells and can play havoc with our normal behaviour and decision making. So, to understand how alcohol affects the nervous system, we must first understand how brain cells communicate with each other.

Communication between cells (neurones) in the brain relies on the passage of electrical signals — nerve impulses — from one cell to another. When an electrical impulse comes to the end of one neurone, it cannot simply jump across to another neurone. Instead it is converted to a chemical signal in order to move between the neurones, and is converted back into an electrical signal in the next neurone. This process is known as synaptic transmission, because the signal is transmitted across the junction between the neurones — the synapse.

Synaptic transmission

Synaptic transmission relies on the conversion of an electrical signal in the pre-synaptic neurone (the one sending the message) into a chemical signal, and the ability of this chemical signal to form an electrical signal in the post-synaptic neurone (the one receiving the message). The chemical signal is called a neurotransmitter.

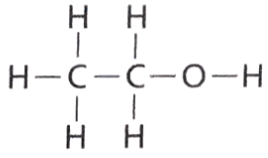


Figure 1 The chemical structure of ethanol

Synaptic transmission begins with a nerve impulse — an action potential — in the pre-synaptic neurone passing along its axon until it reaches the pre-synaptic axon terminal. The action potential causes the voltage across the cell membrane to change. This opens **voltage-gated calcium channels** in the membrane, which allow calcium ions (Ca^{2+}) to enter the terminal (see Figure 2). Voltage-gated ion channels are proteins containing a pore, which are embedded in the membrane. The pore is selective for a certain type of ion, in this case calcium ions, and is opened/closed in response to a change in voltage. The change in voltage opens the pore and allows calcium ions to move into the cell by diffusing down their concentration gradient.

Once they have entered the cell, calcium ions bind to vesicles containing neurotransmitter. Vesicles are small bags that package chemicals in order to move them around the cell (see Figure 3). The binding of calcium ions to vesicles causes them to fuse with the pre-synaptic cell membrane, releasing neurotransmitter into the **synaptic cleft**. The neurotransmitter travels across the synapse by diffusion, and binds to **ligand-gated ion channels** on the post-synaptic neurone membrane. Ligand-gated ion channels also contain a pore but instead of opening in response to a change in voltage, they open when a specific chemical, called a ligand, binds to them. In this case, the ligand is the neurotransmitter.

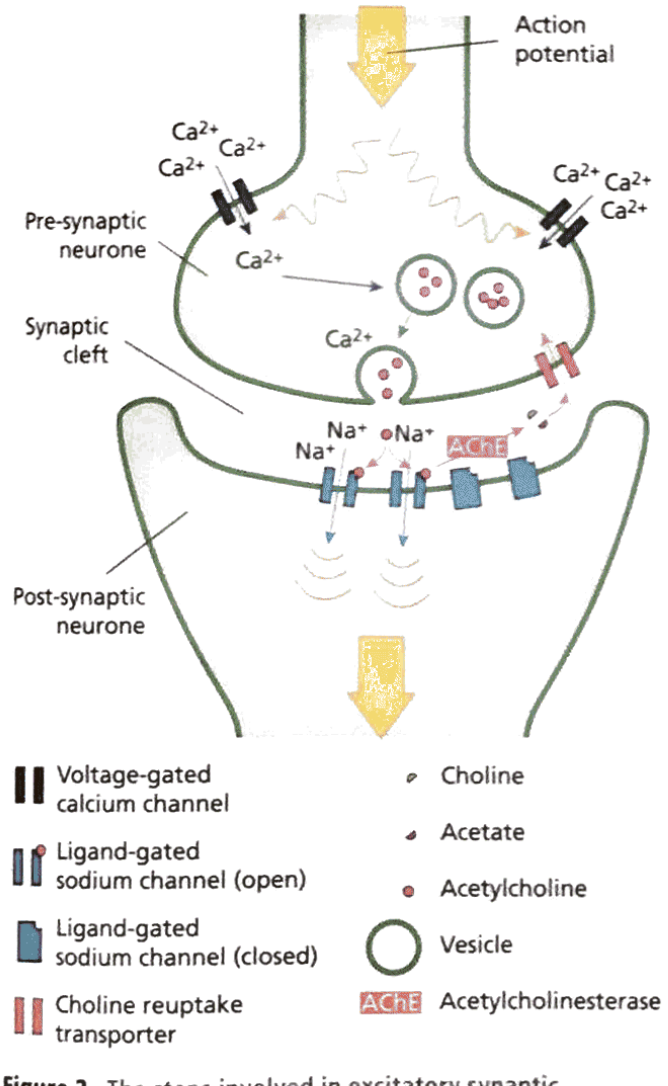


Figure 2 The steps involved in excitatory synaptic transmission with acetylcholine (ACh)

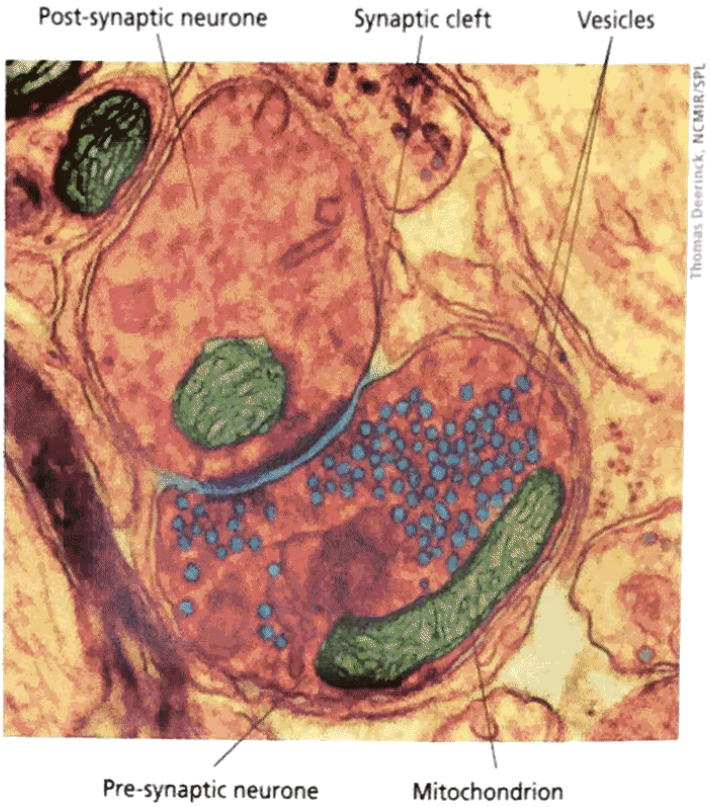


Figure 3 Coloured transmission electron micrograph of a synapse in the brain (×40 000)

An important aspect of synaptic transmission is to 'turn off' the chemical signal once it has acted on the post-synaptic neurone. Neurotransmitters can be broken down by enzymes in the synaptic cleft into smaller, inactive products, which are then taken back into the pre-synaptic neurone by **reuptake transporters**. Figure 2 shows the enzyme acetylcholinesterase (AChE) breaking down acetylcholine to acetate and choline.

Neurotransmitters and their actions

There are dozens of different types of neurotransmitters, which help different types of neurones to send different messages. A few of the major ones are listed in Table 1, together with their roles in the brain.

Different neurotransmitters can exert different effects. Some, such as acetylcholine and glutamate, are excitatory. This means that their action on the post-synaptic neurone is

Table 1 Some common neurotransmitters found in the brain

Neurotransmitter	Action	Description
Glutamate	Excitatory	By far the most common neurotransmitter in the brain; important for learning and memory
GABA	Inhibitory	The most common inhibitory neurotransmitter in the brain; reduces anxiety and stress
Dopamine	Excitatory	Important for motivation and reward; many drugs of addiction affect the 'feel-good' dopamine system
Acetylcholine	Excitatory	Important at the neuromuscular junction for initiation of voluntary muscle contraction

Terms explained

Ligand-gated ion channels Ion channels that are opened by the binding of a chemical ligand.

Reuptake transporters Membrane proteins that carry neurotransmitter from the synaptic cleft back into the pre-synaptic neurone.

Synaptic cleft The gap between pre- and post-synaptic neurones.

Voltage-gated calcium channels Ion channels that are opened by a change in voltage.

to make it *more* likely to fire an action potential by allowing entry of positively charged sodium ions (Na^+), as illustrated in Figure 2. In contrast, other neurotransmitters, such as gamma-amino butyric acid (usually shortened to GABA), are inhibitory. Binding of GABA to ligand-gated ion channels on the post-synaptic neurone causes opening of pores specific to chloride ions (Cl^-). Entry of these negatively charged ions into the post-synaptic neurone makes the post-synaptic neurone *less* likely to generate an action potential.

How alcohol disrupts the brain's balance

Alcohol is described as a central nervous system depressant. What this means in a scientific sense is that it decreases excitatory activity and increases inhibitory activity. Excitation and inhibition in the brain are normally finely balanced. When this fine balancing act is tampered with, brain function suffers.

To explain how alcohol causes increased inhibition in the brain we can look at an example of how ethanol, the active ingredient of alcoholic drinks, affects the activity of the neurotransmitter GABA. GABA is the most common inhibitory neurotransmitter in the brain and GABA activity is known to suppress emotions such as worry, stress and anxiety. Patients showing behaviours such as anxiety or insomnia are often prescribed drugs that increase GABA activity because this helps them to relax.

The results of these drugs — a calmer and sleepier patient — mirror what you may see in a person who is drinking alcohol. The action of ethanol on inhibitory GABA activity involves both the pre-synaptic and post-synaptic sides of the synapse. First, ethanol increases the amount of GABA released from the pre-synaptic neurone in response to an action potential. This is thought to be because ethanol increases the likelihood of GABA-containing vesicles fusing with the membrane of the pre-synaptic terminal. Second, ethanol boosts the binding of GABA to its ligand-gated ion channels on the post-synaptic membrane, making the pores more likely to open following GABA release, and leading to


Alcohol can have negative effects

increased entry of chloride ions and more inhibition of the post-synaptic neurone.

As well as increasing inhibition in the brain, ethanol causes a decrease in excitatory activity. Glutamate is the commonest excitatory neurotransmitter in the brain — it is used at 90% of synapses — and is crucial for learning and memory. Ethanol acts on glutamate receptors on the post-synaptic membrane to prevent the binding of glutamate. This means that glutamate cannot trigger the opening of ligand-gated ion channels and excitation cannot occur in the post-synaptic neurone. This may partly explain the characteristic memory loss suffered after a night of heavy drinking.

Why does drinking alcohol feel good?

The alcohol-induced imbalance of excitatory/inhibitory activity not only explains the general drowsiness and slow reactions of a person who is drinking alcohol but also, we believe, why drinking alcohol feels good. The parts of the brain responsible for generating 'feel-good' signals are known as the reward system and are located in the striatum (see Figure 4). This system normally acts to reinforce beneficial behaviours, such as eating. It also becomes more active following consumption of alcohol. This finding suggests that alcohol may directly excite a part of the brain that makes us feel good.

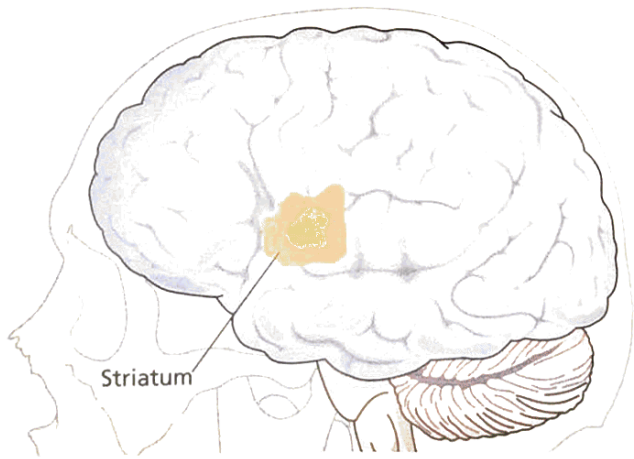


Figure 4 A drawing from a brain scan, showing regions that are more active (orange areas) when someone has been given alcohol. This corresponds to the striatum, which contains the reward system

Further reading

S-cool the revision website for A-level biology has information on nervous and hormonal control at synapses: **http://tinyurl.com/k5bvgve**

To download a pdf about the effects of drugs on synapses and how altered synapses may affect the brain during adolescence go to: **http://tinyurl.com/ksehy97**

Box 1 Negative effects of alcohol

Although many people enjoy alcohol responsibly, there are common cases of alcohol having negative influences.

- Drinking alcohol can cause disruption of sleep, weight gain, bad skin, stomach problems, liver damage and more.
- Doctors recommend drinking no more than two or three units per day for women (roughly a 175 ml glass of wine) and three or four units per day for men (roughly 1½ pints of 4% beer).
- Alcohol dependence is a serious problem in the UK with the NHS estimating that 9% of men and 4% of women show signs of alcohol dependence. Alcohol causes dependence due to its effects on the dopamine reward system.
- The NHS currently spends £3 billion a year on alcohol-related health problems.

Statistics from **www.drinkaware.co.uk**

The major neurotransmitter in the reward system is dopamine. However, scientists have thus far failed to find a direct action of ethanol on synapses that use dopamine as a neurotransmitter. Instead it is more likely that effects of ethanol on the reward system again involve GABA. It is thought that the reward system is normally kept in check by GABA inhibition. When this inhibition is suppressed, the reward system becomes more active and thus drinking alcohol feels good.

BiologicalSciencesReviewExtras

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Although alcohol in moderation can make us feel good, it can also be extremely damaging, both for the individual and for society (see Box 1). Alcohol-related diseases, such as liver disease, are increasing in the UK, including in young people. Alcohol can be addictive, with serious consequences for individuals and their families. Drunken behaviour can lead to violence, vandalism and antisocial behaviour.

We are only beginning to understand how alcohol has such widespread effects on the brain. Its actions on synaptic transmission can lead to a wide range of behavioural changes. Used in moderation, many people feel that it is an acceptable social drug, but until we fully understand how it works to alter brain function, we should continue to treat it with caution and respect.

Point for discussion

- Do you think alcohol usage should be controlled more than it currently is?

Oliver Freeman is a PhD student in neuroscience at the University of Manchester. He is currently investigating why diabetic patients develop nerve damage, and new ways to improve the diagnosis of early damage. He blogs about the brain at **thebrainbank.scienceblog.com**