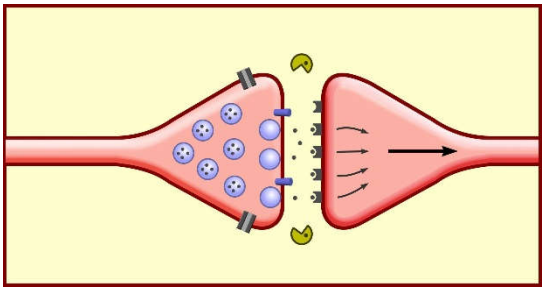
Section two – how we think medicines work for ADHD

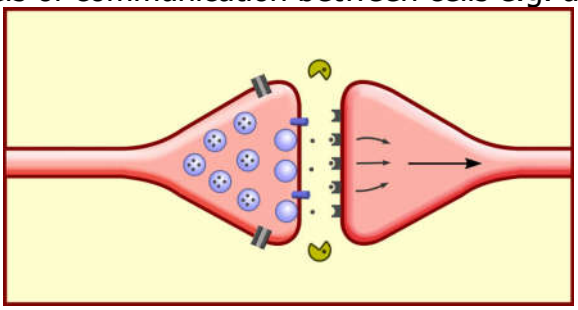
a. How we think the symptoms of ADHD (Attention Deficit Hyperactivity Disorder) happen

Dopamine and noradrenaline are two of the many chemical messengers in the brain. They play a part in controlling concentration and reward. It seems that too little activity from dopamine (and noradrenaline) in some parts of the brain can mean the brain can't focus on anything and doesn't feel calm.

Routine or usual communication between cells



Lower levels of communication between cells e.g. as in ADHD



Not enough dopamine and/or noradrenaline in the reward parts of the brain mean the brain may often be looking for something exciting to boost dopamine and noradrenaline to make it feel 'normal'. This can lead to the symptoms of ADHD such as being easily distracted, impulsive, taking risks, smoking and reward seeking.

Genes can play a part in this too. If you have the DRD2 gene it seems to make dopamine receptors less sensitive. This is same effect as having too little dopamine.

Even if this lack of effect from dopamine and/or noradrenaline is only in one area of the brain, almost all parts of the brain are interconnected and interact with, and react to, each other. So, a change in one area will affect another.

b. How we think the stimulant treatments work for ADHD

*The stimulants include **methylphenidate**, **dexamphetamine/dexamfetamine** and **lisdexamfetamine**.*

Normal nerve activity

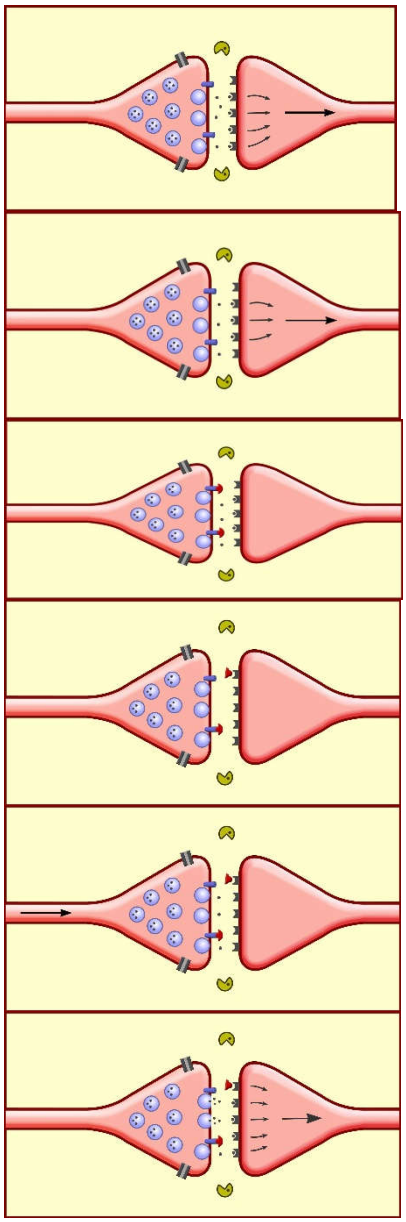
Too little activity in some parts of the brain e.g. the parts that help it to concentrate, can mean the brain can't focus on anything. It seems that can also mean that the brain is constantly searching for something exciting to boost dopamine and noradrenaline and to then feel more normal.

One way to help the brain is to block the reuptake (recycling) of dopamine or noradrenaline

This is what the stimulants do. If the recycling is blocked it boosts the amount of dopamine and noradrenaline.
Dexamfetamine (and lisdexamfetamine) may also increase the amount of dopamine and noradrenaline released.

How this works is that the next message is downbeat as before. Dopamine and noradrenaline are released but are boosted by some dopamine and noradrenaline left over from the previous message.

The message is thus stronger. By boosting dopamine and noradrenaline this helps the brain feel more normal and helps it concentrate.



c. How and why you can get side effects from the stimulants

Not enough dopamine and/or noradrenaline in some parts of the brain might lead to some of the symptoms of ADHD. The stimulants boost dopamine and noradrenaline and would help correct this. However, too much in other parts of the brain might cause:

Stimulant effects:

- Reduced appetite (Anorexia)
- Aggression
- Poor sleep
- Feeling nervous.

Noradrenaline can be quite activating, including on the heart, and can lead to:

- Increased heart rate (although nearly all of the noradrenaline increase occurs in the brain)
- Loss of appetite (anorexia)
- Poor sleep.

d. How we think atomoxetine works

Noradrenaline is vital in the areas of the brain that control or regulate attention, concentration, mood and thinking. Atomoxetine increases the amount of this noradrenaline, which increases attention and decreases impulsiveness and hyperactivity in people with ADHD. This effect on noradrenaline can also boost dopamine, which might be lacking in ADHD. An important thing to remember is that **atomoxetine is NOT a stimulant**.

Normal nerve activity

Too little noradrenaline activity in some parts of the brain e.g. the parts that help it to concentrate, can mean the brain can't focus on anything. It seems that can also mean that the brain is constantly searching for something exciting to boost it.

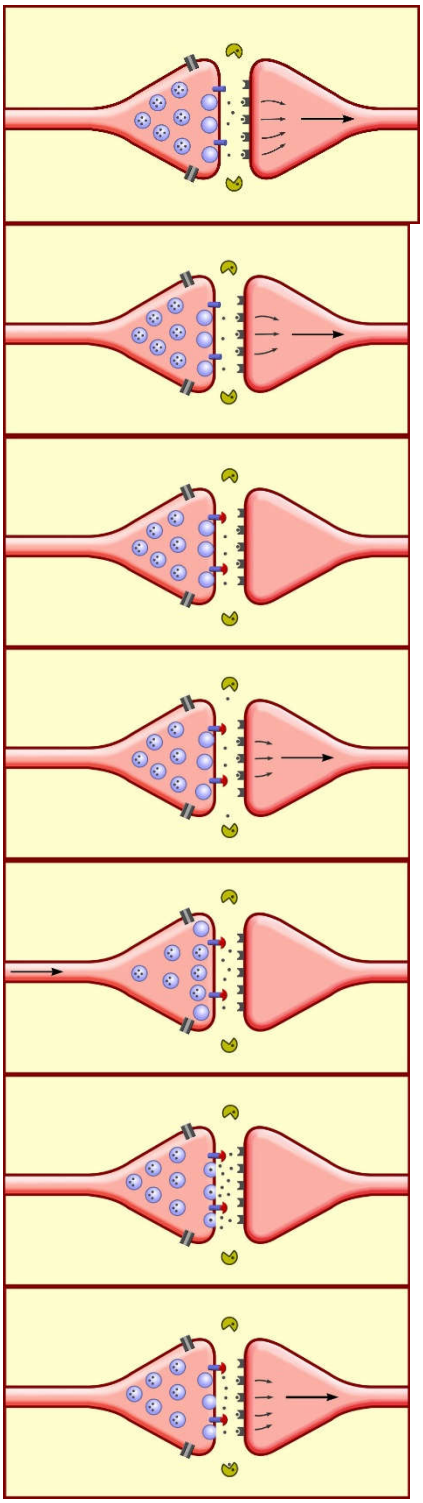
One way to help the brain is to block the reuptake (recycling) of noradrenaline. Increasing noradrenaline can also help increase dopamine.

This is what atomoxetine does. It blocks the reuptake of noradrenaline. How this works is that the next message is downbeat as before.

The message arrives and noradrenaline is released.

This is boosted by some noradrenaline left over from the previous message and from some stimulation of noradrenaline receptors. More activity means more or stronger messages being passed. This boosts noradrenaline, which in turn can boost dopamine (but not enough to risk any abuse).

Boosting noradrenaline (and dopamine) helps the brain feel more normal and helps it concentrate.



e. How and why you can get side effects from atomoxetine

Atomoxetine increases the amount of noradrenaline in the brain, and also some serotonin and dopamine, which can help the symptoms.

Noradrenaline can be quite activating, including on the heart, and can lead to:
- Increased heart rate (although nearly all of the noradrenaline increase occurs in the brain)
- Loss of appetite (anorexia)
- Poor sleep

Too much serotonin can lead to:
- Nausea and vomiting.

You might also get more (or less) side effects if one of your liver enzymes (the one called CYP2D6) breaks down atomoxetine slower or faster than other people. In day-to-day life having a slow or fast CYP2D6 enzyme doesn't normally make any difference at all, but it can do if you are taking a drug broken down by this enzyme.

A slow CYP2D6 enzyme:
- Is not common but varies depending where your genes have come from
- Occurs in about 2% (1 in 50) Turkish people, about 9% (1 in 11) white British Caucasians (9%) through to 19% (1 in 5) black South Africans
- Will mean that your body will not break down atomoxetine as well, so you get higher levels in the body for the same dose. This can lead to more side effects and at lower doses.

An ultra-fast CYP2D6 enzyme:
- Is generally even rarer but also varies depending where your genes have come from
- Occurs in about 1% (1 in 100) white British Caucasians, about 10% (1 in 10) Spanish people through to about 30% (1 in 3) of Ethiopians
- Will breaks down atomoxetine really quickly and you get few side effects, but little effect.

f. Some other facts you may want to know about medicines for ADHD

- Drugs don't cure ADHD but can help even out any low activity of chemical messengers in the brain and allow the person to concentrate and help school, work and driving
- They do **not** increase the chances of someone abusing drugs later in life, compared to people with ADHD who are undiagnosed who thus untreated. The opposite seems to be true as medicines for ADHD decrease the need for people with ADHD (who tend to be impulsive and risk-taking) to self-medicate, or treat themselves with stimulants, alcohol, cannabis etc.
- They do **not** seem to lose their effect, as long as you keep taking them. Younger people may need higher doses as they get older and bigger
- There are no known long-term side effects
- Stimulants can be stopped and restarted
- No one actually wants to give medicines to younger people if they are not needed but younger people who have ADHD can be held back by their symptoms. This can have a life-long effect on school, qualification, social skills and jobs. If ADHD medicines can help a person get as good an education as possible that is good. The effects of a poor education last a life-time.