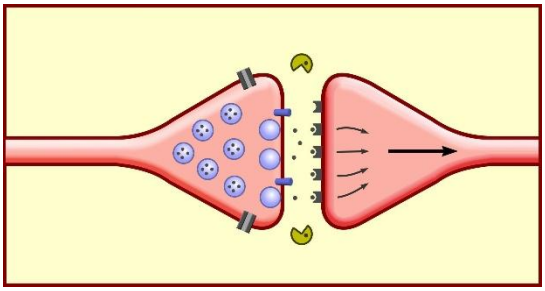
Section two – how we think medicines help ADHD

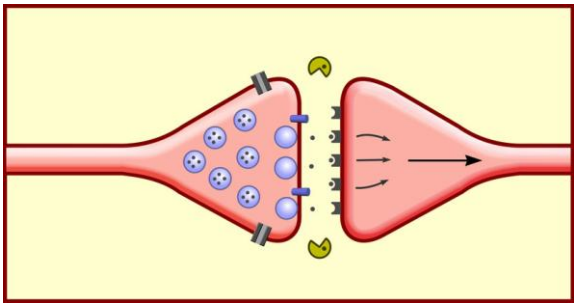
a. How we think the symptoms of ADHD (Attention Deficit Hyperactivity Disorder) happen

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

Routine or usual communication between cells in their networks



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



Networks in the frontal lobe of the brain control and manage motor drive in the brain. The frontal lobe is also the last network of the brain to fully mature. In ADHD these networks may be late to fully mature and so there is less control over 'drive' in the brain. A young brain may then not have enough control over its actions.

Stimulants such as methylphenidate, lisdexamfetamine and other amfetamines can boost the frontal lobe and help make the most of its controlling role.

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

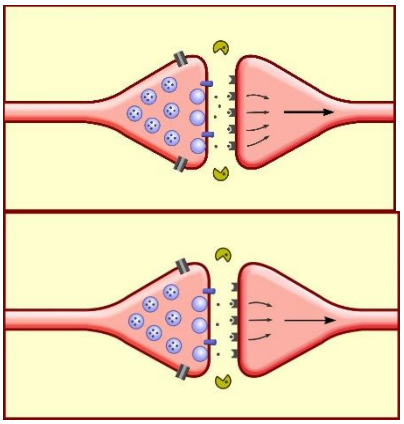
Genes can play a part in this too. If you have the DRD2 gene (as some people with ADHD have) it seems to make dopamine receptors less sensitive. This is same effect as having too little dopamine.

Even if this lack of effect from dopamine and/or noradrenaline is only in one area of the brain, almost all networks 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 help ADHD

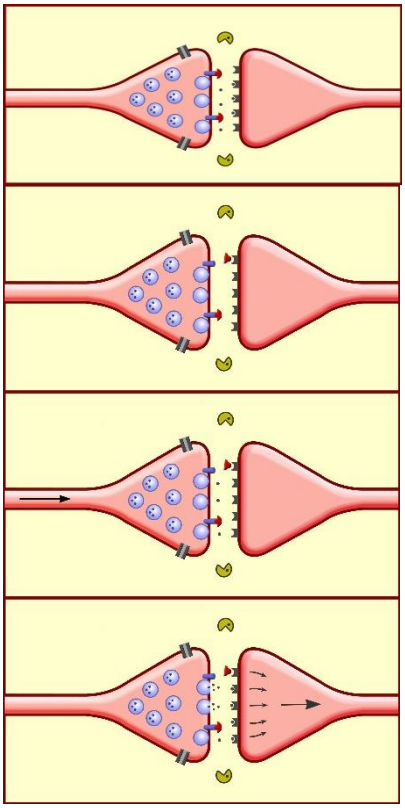
Stimulants include methylphenidate, dexamphetamine/dexamfetamine, Adderall® and lisdexamfetamine.

Normal nerve activity



Too little activity in some networks of the brain e.g. the networks that help it to concentrate (frontal lobe), can mean the brain can't focus well enough on anything and gets distracted. It can also mean that the brain is constantly searching for something exciting to boost its 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 helps 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 concentrate and feel more relaxed.

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

Not enough dopamine and/or noradrenaline in some networks 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 networks of the brain might cause:

Stimulant effects:

- Reduced appetite (sometimes called anorexia, but is not anorexia nervosa)
- Aggression - if the dose is too high
- Poor sleep – this is why it is often best to take stimulants in the morning. On the other hand, a few people find taking a small dose at night helps them concentrate on something enough to get them off to 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)
- Reduced appetite (sometimes called anorexia, but is not anorexia nervosa)
- Poor sleep.

d. How we think atomoxetine helps

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 in these networks, which increases attention and decreases impulsiveness and hyperactivity in people with ADHD. This effect on noradrenaline can also boost dopamine, which might also be lacking in some networks of the brain in ADHD. An important thing to remember is that **atomoxetine is NOT a stimulant**.

Normal nerve activity

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

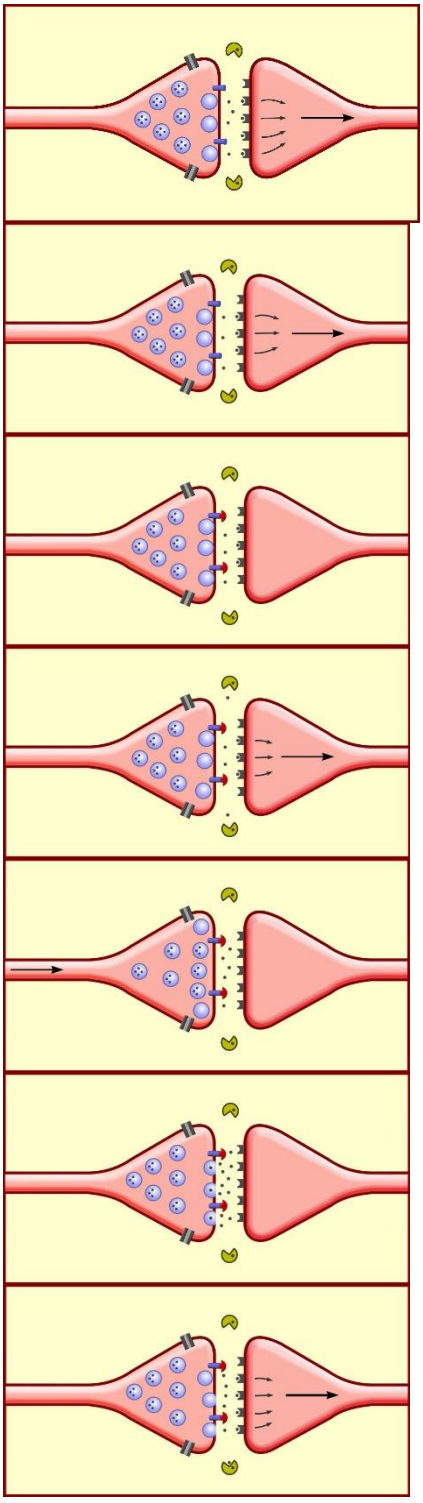
One way to help the brain is to block the reuptake (recycling) of noradrenaline. Increasing noradrenaline can also help increase dopamine.

This is what atomoxetine does. It blocks the reuptake of noradrenaline. How this helps 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 concentrate more and feel more relaxed.



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

Atomoxetine increases the amount of noradrenaline in some networks 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)
- Reduced appetite (sometimes called anorexia, but is not anorexia nervosa)
- 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 some of 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 too.

An ultra-fast CYP2D6 enzyme:
- Is generally even rarer but also varies depending where your some of 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
- Breaks down atomoxetine really quickly and you get few side effects, but little effect.

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

- Drugs don't cure ADHD but can help the person to concentrate and so help at 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 usually decrease the desire 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. However, 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 through schooling, qualifications, 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.

If you would like to read a bit more you could do no better than buy the book "Brain and Mind Made Simple" by Professor David Nutt, which walks you through the complexities of how the brain and mind work, and what happens when things go wrong, without assuming any prior knowledge, and also in a very readable and entertaining style. Go to the Drug Science website for the details of how to purchase (currently £22.95 inc. P&P to UK). If you buy it through Drug Science directly then the proceeds of the sale help support the Drug Science charity more than buying through other sources.