A5 Neuropharmacology

- Re read the synapse section of the SL notes

A5 A Some neurotransmitters excite nerve impulses in postsynaptic neurons and others inhibit them. (p 541 – p 542)

REMEMBER: some neurotransmitters like acetylcholine are ___EXCITATORY_________ and when they bind to receptors on the post synaptic membrane they cause depolarization_____ (an increase in the membrane potential which leads to an action potential)**sometimes called cholinergic synapses. (sodium ion – Na + channels open)

Some neurotransmitters are ___INHIBITORY_________ like GABA, and cause a ___DECREASE_______in membrane potential called ___HYPERPOLARIZATION_____. This makes iT ___MORE DIFFICULT____________ for depolarization to occur and for _____THE THRESHOLD_________ to be reached. This is done by opening ___chloride________________ channels, as __________chloride ions (Cl-)_____ move in the membrane becomes more ___negative__
A5 B Nerve impulses are initiated or inhibited in postsynaptic neurons as a result of summation of all excitatory and inhibitory neurotransmitters received from presynaptic neurones. (p 542)

Presynaptic neurons each release a neurotransmitter (usually a single release is not enough to reach threshold and trigger an Action Potential)

The post synaptic membrane has receptors and the effects of the different neurotransmitters are “summed” up and the neuron fires/or does not fire. The combination of ions will either reach threshold membrane potential or not.
Many different slow-acting neurotransmitters modulate fast synaptic transmission in the brain. (p 542 – 543) This statement was worth a mark.

Acetylcholine and GABA are FAST acting (one millisecond) and cause ion protein channels to open immediately in one post synaptic neuron. Their effect is immediate and brief. The mechanism is simple as it involves only the conformation change of ONE receptor molecule.

Slow acting neurotransmitters act SLOWLY and LAST longer b/c they are involved in a cascade of rxns, (or a SERIES of events) within the post synaptic neuron. They appear to MODULATE or regulate the action of FAST acting neurotransmitters. Slow acting neurotransmitters diffuse and can affect MULTIPLE neurons, ex. dopamine and serotonin are slow acting, Glutamate is fast acting.
A5 D Memory and learning involve changes in neurones caused by **slow-acting neurotransmitters.** *(p 543)*

Slow acting ______NEUROTRANSMITTER________________________ play a role in ___MEMORY____________________ and learning as they release _____SECONDARY_____ messages within a _______POST SYNAPTIC MEMBRANE_____. These SECONDARY messages may increase the number of receptors (in post synaptic membrane) to _INCREASE___the rate of ion movement, this is basically __REMODELLING__ the synapse, or THEY MAY increase neurotransmitter production or lead to changes in shape OF RECEPTORS

**Slow Acting Neurotransmittors effect or modulate other chemical processes**

- increase the number of connections/synapses (leading to making memories easier to recall or actions easier to repeat)
- short term memory depends on changes in the strength of existing neural connections
- ltp (ltp) long term or long life potentiation is a lasting increase in strength of synaptic transmission (glutamate is a fast acting neurotransmitter that leads to long term potentiation).
- Ltp is a persistent strengthening of a synapse based on activity
Psychoactive drugs affect the brain by either increasing or decreasing postsynaptic transmission. (p 543)

Know the Effects on the nervous system of two stimulants and two sedatives

*Video: Mouse brain/* requires a flash plug in try firefox web browser [https://learn.genetics.utah.edu/content/addiction/mouse/](https://learn.genetics.utah.edu/content/addiction/mouse/)

**Stimulants: (p546)**—increase synaptic transmission

_____EXCITATORY_ drugs act to ___INCREASE__________ or amplify transmission by increasing ___NEURON________firing.

a. Cocaine: increases dopamine response leading to increased feelings of pleasure/euphoria. (cocaine blocks the dopamine reuptake so that continual excitation occurs-dopamine is a neurotransmitter that increases feelings of well being- it is where the root word of “dope” comes from)

   b. Amphetamines (speed) increases neurotransmitter release, increases alertness and heart rate.

C. MDMA: /ecstasy- blocks the reuptake of serotonin, serotonin levels rise, serotonin also acts to promote feelings of well being.

**Sedatives: **___INHIBITORY__________drugs that _________DECREASE______post synaptic transmission by blocking nerve impulse transmission.
a. Alcohol: enhances the effects of inhibitory neurotransmitter: GABA, slows reaction time, alters/slurs speech, hazy/unclear thinking

b. THC (tetrahydrocannabinol): blocks CANNABOID receptors in the brain, binding to them and inhibiting the release of excitatory neurotransmitters - those have an overall sedative effect

c. Benzodiazepines: ex Valium slows down the action of the brain, increases the effects of GABA, decreases anxiety, slows breathing, drowsiness, impairs motor coordination
Anesthetics act by interfering with neural transmission between areas of sensory perception and the CNS. (p 544-545)

The effect of anesthetics on awareness. (p 545)

Anesthetic cause a reversible loss of sensation in all (general anesthetic) or part (local anesthetic) to block feelings of pain.

General anesthetics result in total unconsciousness and loss of awareness so there is no awareness of surgery. If doses are not high enough, patients may retain some awareness.

Local anesthetics: patient is still aware/awake, not unconscious.

Anesthetics interfere with/block sensory perception to the brain/central nervous system.

Anesthetics prevent propagation of Action Potentials on the post synaptic membranes.

They are reversible.

They allow for continuation of vital physiological functions such as breathing.

Ex. Giving birth a local, spinal block is given to block pain but breathing is normal, (less drugs to effect baby).

A stimulant increases the activity of the nervous system to make a person more alert, (increases heart rate, Blood pressure and body temperature)

The effect of stimulants MATCH the sympathetic nervous system and cause the body to act as if the sympathetic nervous system were activated)

Ex. Caffeine, nicotine, cocaine, amphetamines
A5 H Addiction can be affected by **genetic predisposition**, **social environment** and **dopamine secretion**. (p 547)

**What is addiction?** The __CHRONICALLY____________ relapsing disorder which is characterized by:

a) ___COMPULSION_______ to seek and take drugs,
b) ___LOSS OF CONTROL___ in limiting intake
c) ______NEGATIVE________ emotional state when drugs aren’t taken

**Affected by:**

a. **genetic predisposition:** inheritance of some genes
   (___POLYGENIC___ factors-more than one gene contributes to this) may increase the chances of addiction

Ex. DRD2 gene: dopamine receptor, some alleles of this gene have been linked to increase in alcohol consumption
Ex. _ENZYMES______ used to dispose of drugs maybe produced in ___LOWER_____ amounts, leading to _________INCREASED CHANCE OF ADDICTION____

Ex. Genetic predisposition to ___RISK TAKING______(more complex /difficult to understand)

b. **social environment** can affect addiction
EX. Poverty..high need to escape life’s circumstances
Exposure at a young age to drug use/abuse, ex parents (drug use becomes normalized)
Peer pressure, a group of peers is taking drugs
Stress/ traumatic life experience
Media portrayal of drugs as glamorous/no side effects
Lack of education to know the effects
little/ no hope for future
c. **dopamine secretion**: Cocaine (and nicotine, alcohol) affect the ___DOPAMINE____ secreteting ___SYNAPSE_________________, so these drugs lead to ___INCREASED______feelings of _________________PLEASURE________(as dopamine is a neurotransmitter that acts in the reward pathway of the brain, leading to feelings of pleasure). This makes these drugs difficult to ___ABSTAIN_____from

OVER time with cocaine abuse, _____DOWN REGULATION____can occur. The_____NUMBER_________ of ____DOPAMINE RECEPTORS on the POST SYN MEMBRANE_________ decreases, so even normal pleasurable experiences do not lead to feelings of pleasure) as there are fewer receptors. (drawing below) This makes is difficult to stop taking a drug.

WATCH THIS video: [https://www.youtube.com/watch?v=Tqwo9dmIXAQ](https://www.youtube.com/watch?v=Tqwo9dmIXAQ)
Assessing risks associated with scientific research—patient advocates will often press for the speeding up of drug approval processes, encouraging more tolerance of risk. (4.5) (p545)

**drug testing ensures that doses are appropriate, route of administration is effective and that side effects are minor. This takes MANY years.**

Usually a control group (given the drug) and a placebo group (not given the drug) are used to determine effectiveness.

Skipping these steps/speeding them up means that some harmful effects may not be discovered until large numbers of patients are given the drug.

? if a disease is terminal with certain death people may campaign for early release (AIDS)

? has been some cases where cancer treatments drugs were processed speedily and people died of side effects, some people NOT given the drug actually survived

Your thoughts 😊:
Applications

Endorphins can act as painkillers (p543)

_______PAIN____ receptors detect stimuli (ex heat, puncture) and pass the nerve impulse along a _______SENSORY___neruon to the____CNS__ and then ___CEREBRAL CORTEX____________ where we experience the sensation of pain

_______ENDORPHINS____ are your body’s own opiate compounds made by the __PITUITARY____gland that_______BLOCK_____________ transmission of impulses at synapses (nerve connection) involved in pain perception by _______BINDING TO RECEPORS__ in the synapses of the pathway

(Endorphins are neuropeptides that act as neural transmitters) (Could be a fast response to pain that is acute and localized, and/or a slower response that is a throbbing sensation over a larger area) (Exercise leads to the production of endorphins)
**Skills**

Evaluation of data showing the impact of MDMA (ecstasy) on serotonin and dopamine metabolism in the brain. (p544) Do data based if you have time. I posted the original article

![Graphs showing changes in dopamine and serotonin levels over time.](image)

**Figure 2**


MDMA binds to and _____BLOCKS_____________ serotonin __________REUPTAKE_______ proteins

MDMA has a greater effect on serotonin levels than dopamine levels, as it binds to ________SEROTONIN______reuptake protein_____________ preferentially.

MDMA does work at both serotonin and dopamine transporters, it binds to the transporter and ___COMPETITIVELY INHIBITS_____ and blocks the reuptake of the serotonin and dopamine.