Week 2 – Pharmacology

Psychopharmacology

- Psychopharmacology: the branch of psychology concerned with the effects of drugs on the mind and behaviour

Why study psychopharmacology

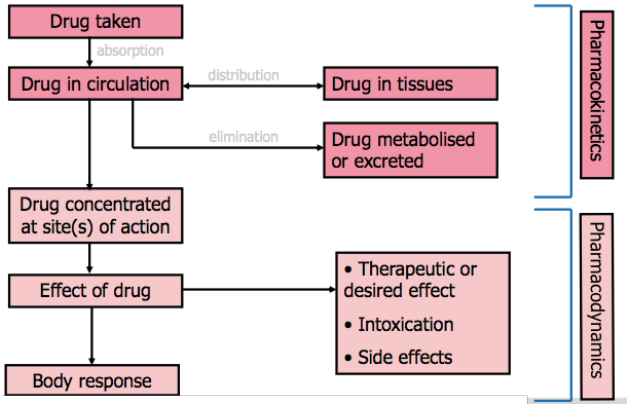
- Knowing the correct dose of a medication – clinical effect
- Predicting side effects
- Every drug has both clinical and side effects
- Predicting how two or more drugs may interact in the body
- Helping to prevent and treat overdoses
- Pharmacogenetics: predicting harmful effects and personalised medicine
- Treatment of drug addictions

Effects of drugs on our body vary according to:

- Age: impact on brain development
- Gender
- Body composition: higher body fat (women) = alcohol absorbed quicker = drunk faster
- Health: e.g. antidepressant on depressed/non-depressed person
- Route of administration
- Amount and frequency used
- Personality: i.e. impulsivity
- Mood: sad + alcohol = more sad
- Expectations: what you think will happen, is more likely to happen
- Environment

Pharmacokinetics & Pharmacodynamics

- ***Pharmacokinetics:*** what the body does to the drug
- ***Pharmacodynamics:*** what the drug does to the body



Pharmacokinetics

Modes of administration:

- Oral (most common but less effective for some drugs, (e.g. heroin and nicotine))
- Intranasal (snorting)
- Inhalation (gasses and smoke)
- Injection
- Suppositories (rectum or vagina)
- Sublingual/buccal (under the tongue/on the cheek)
- Transdermal (through the skin; i.e. adhesive patch, like nicotine)

Absorption: the rate at which the drug enters the blood stream

- Oral – slow absorption; unpredictable potency
- Lungs – most rapid; maximum potency
- Injection – rapid; some loss of potency
- E.g. Cocaine (powder) vs. crack (crystals)

Distribution

- Delivery of the drug to organs in the body
- Only a small portion of the drug actually interacts with the brain – it depends on blood flow and solubility (e.g. water vs. fat soluble drugs)
- Drug dose is specified in terms of mg of drug per kg of body weight (mg/kg)

MDMA distribution

- Ecstasy molecules that have entered the blood stream from the stomach and small intestines then travel to the liver
- In the liver, some of the ecstasy is metabolised to inactive compounds and the rest is varied through the veins to the heart
- Once in the heart, the ecstasy is pumped to the lungs along with the blood, which becomes oxygenated and then returns to the heart
- Now, oxygenated blood carries the ecstasy from the heart to the brain and to other organs in body that have a high blood flow
- Normally **there is a barrier between the blood vessels in the brain and brain matter**, which excludes many drugs from entering the brain. However, ecstasy is predominantly in its nonpolar form in blood and therefore it crosses the barrier into the brain very easily

Blood brain barrier

- Determines which drugs reach the brain in the cerebrospinal fluid
- Capillaries in the CNS have tight junctions between **endothelial cells** – too small for some drugs to pass through
- Capillaries in the CNS are also surrounded by astrocytes which are a component of the blood-brain barrier
- The psychoactive potency of a drug is linked to how easily it can cross the BBB (e.g. heroin vs. morphine)

Metabolism

- Metabolism involves breaking the drug down into smaller molecules or changing fat soluble drugs into water soluble drugs
- Usually renders a drug ineffective, but many drugs have active metabolites
- The liver is the key organ involved in metabolism-first pass the filter; that's why routes bypass the liver – more powerful effect

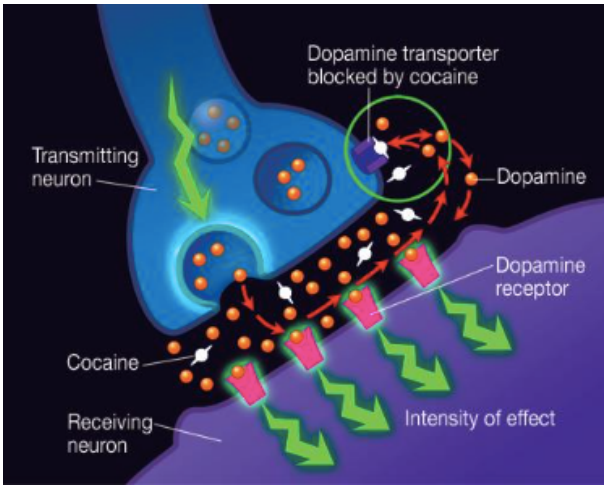
Excretion

- Elimination of the drug and metabolites from the body; usually excreted in urine but also breath, swear and faeces
- Plasma half-life: time it takes plasma concentration of a drug to reduce by half-shorter half-life=higher potency + more addiction
- Drugs with a short half-life more likely to be abused because of their rapid onset & offset of 'peak' effects (e.g. nicotine/cocaine)

- Treatment applications:
    - Methadone has been used to effectively and safely treat opioid addiction; Methadone is used as a substitute drug in the treatment or morphine and heroin addiction; Methadone's effects last 4-6 times as long as those of heroin, so people in treatment need to take it only once a day;
    - Properly prescribed methadone is not intoxicating or sedating, & its effects do not interfere with ordinary activities like driving
    - Medication is taken orally & it suppresses narcotic withdrawal for 24 to 36 hours; it relieves the craving associated with heroin addiction
    - Methadone is medically safe, even when used continuously for 10 years of more
- Toxicity (intoxication) occurs when drugs are consumed at rates that exceed the capacity of the body to breakdown and excrete the drug. This results in cumulative blood concentrations (e.g. ethanol)

Pharmacodynamics

Drug Action



- Drugs can affect the body by:
    - Mimicking the actions of neurotransmitters (NT) and occupying NT receptor binding sites, taking the place of the NT (e.g. nicotine)
    - Decreasing the activity of enzymes that destroy NTs (MAOIs)
    - Altering the reuptake of a NT (e.g. cocaine)
    - Changing the amount of NT released (e.g. amphetamines)
    - Interfering with ion channels (e.g. benzodiazepines)
    - Distribution of cellular membranes (e.g. ethanol, general anaesthetics, topiramate)
- ***Agonists:*** bind to a receptor site and have the same (or similar) effect as the NT (e.g. methadone) and heroin similar to beta-endorphin, nicotine similar to acetylcholine)
- ***Antagonists:*** bind to a receptor site, but lack the effect of the NT; antagonists block the NT from binding to its receptor (e.g. naltrexone blocks the effect of beta-endorphin and morphine)
- Treatment applications
    - Agonists: methadone (Mu Opioid receptor agonist)
    - Antagonists: Rimonobant (CB1 receptor antagonist)

Reinforcement

- People use drugs because they are reinforcing (the drug-taking behaviour is rewarded by the experience of positive drug effects)
- Linked to the **release of dopamine in the mesolimbic dopamine system** (links midbrain, limbic structures & forebrain

Tolerance

- Decreased effectiveness of a drug as a consequence of repeated administration
- Necessary to increase the dose of a drug in order to maintain its effectiveness

Dependence

- Varies in degree and intensity
- Tolerance and withdrawal (physical dependence)
- Compulsive behaviour – drug seeking (psychological dependence)

Withdrawal

- Physiological changes that occur when the drug use is stopped or decreased; Withdrawal can be arrested by re-administering the drug, or a drug with a similar action (cross-dependence)
- *Psychological dependence:* compulsivity taking a drug in the absence of physical withdrawal symptoms (e.g. opioids result in both forms of dependence, but psychological dependence outlasts physical withdrawal symptoms

Drug interactions

- *Addictive:* sum of the individual effects of each drug (e.g. Valium and alcohol)
- *Hyperaddictive/synergistic:* combination is greater than the sum of their individual effects (e.g. Synergy between barbituarates and alcohol)
- *Potentiation:* a drug which has little effect alone will magnify the effect of the drug it is taken with (e.g. Talwin and triplennamine)