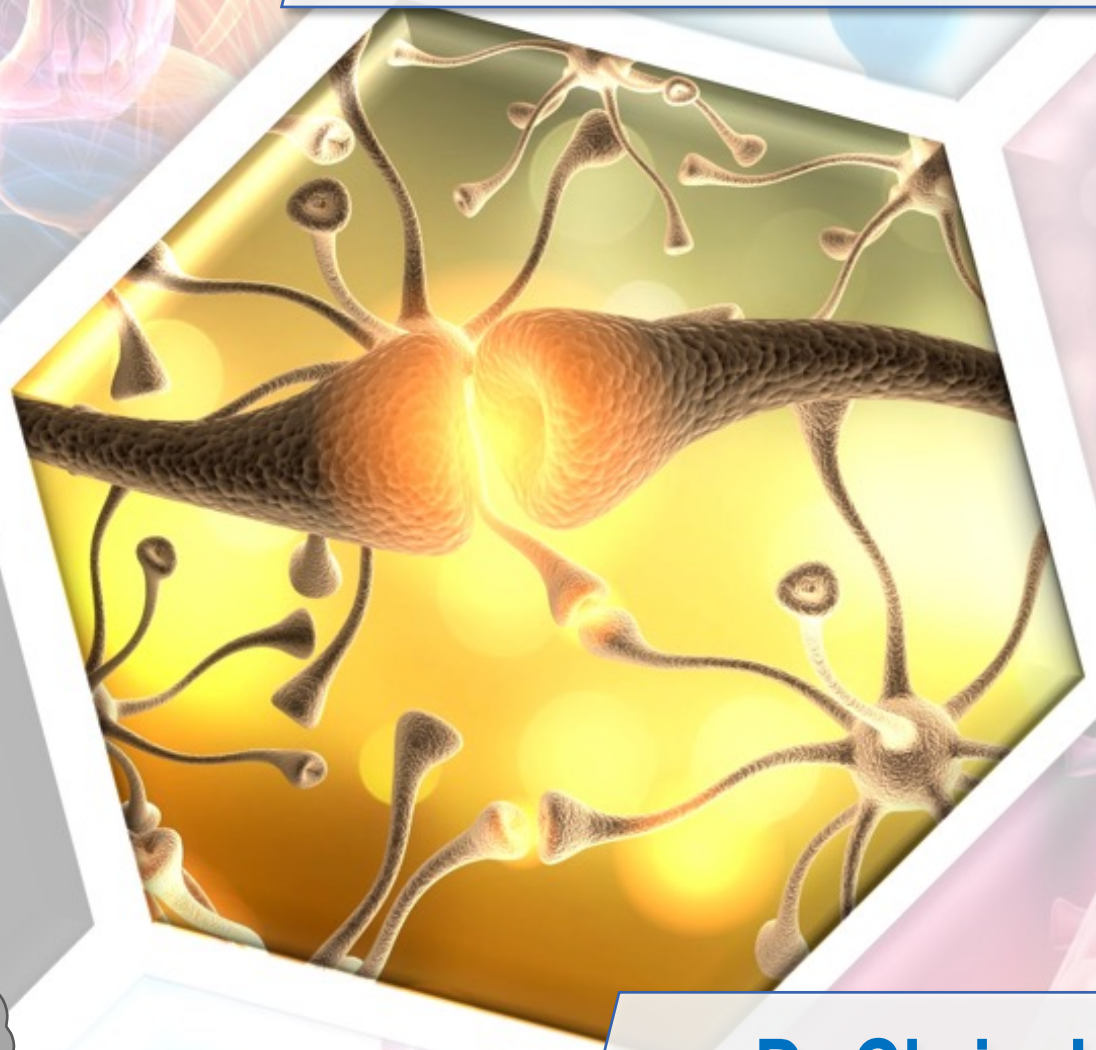
IMPERIAL

Pharmacology of the Nervous System



part 1 of 3

Dr Chris John c.john@imperial.ac.uk

Session Review

QUESTIONS: Go to **www.menti.com** and use the code **8752 3753**

What is pharmacology?

Definition

3 questions

Drug targets/selectivity

Drug targets – classes

Selectivity

Dose/side effects

Dose

Side effects/adverse effects

What is pharmacology?

Before you look at the effects of individual drugs as treatments for specifics diseases/disorders you need an understanding of the core concepts of

pharmacology

What is pharmacology?

Neuro: Epilepsy tutorial (today)

Pharmacology - the study of how chemical agents (drugs) can influence the function of living systems.

A better definition:

A chemical substance that interacts with a specific target within a biological system to produce a physiologic effect

Q: If we use an example of a 'chemical substance', can you answer the three questions opposite?

How do individual drugs produce their effects?

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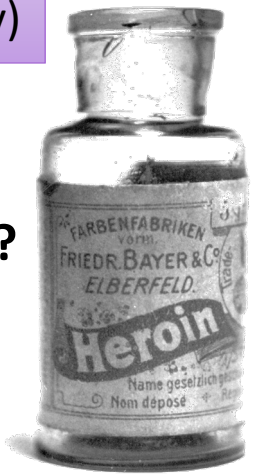

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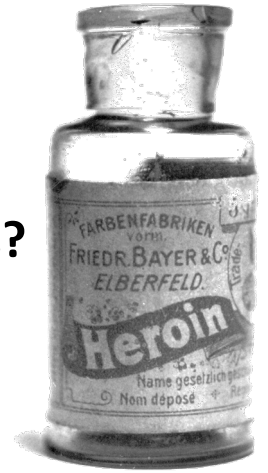

Why do people take heroin?

- Euphoria
- Analgesia (pain relief)
- Cough suppression

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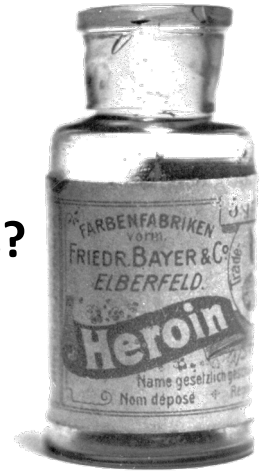

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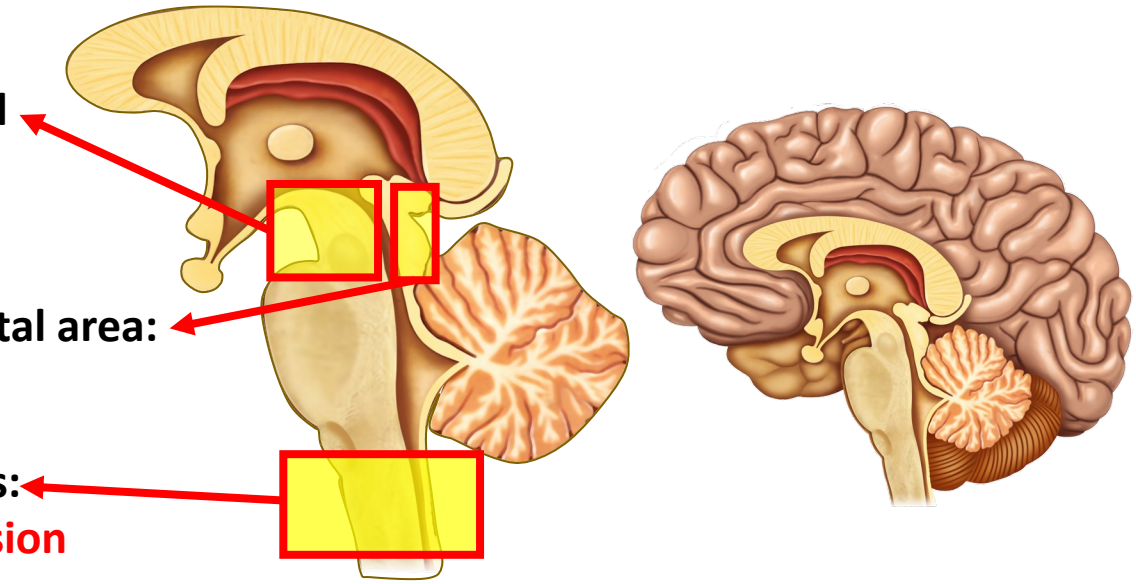

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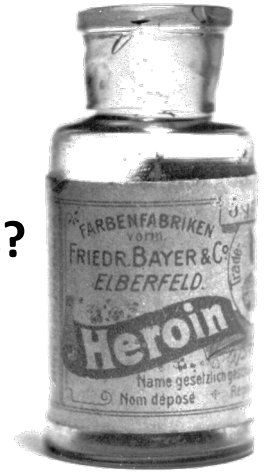
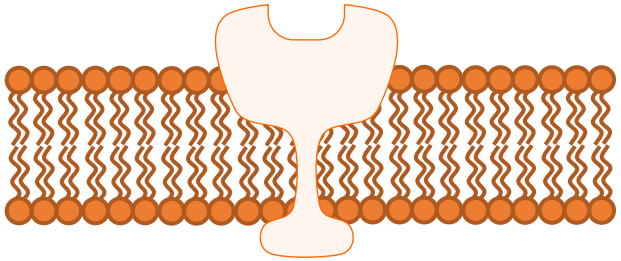
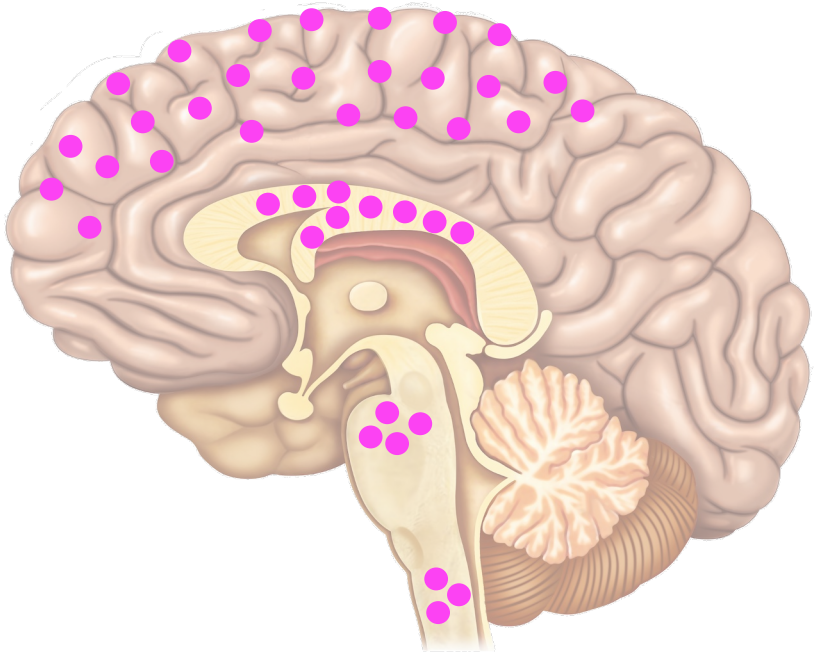




Opioid receptors



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Drug targets/selectivity

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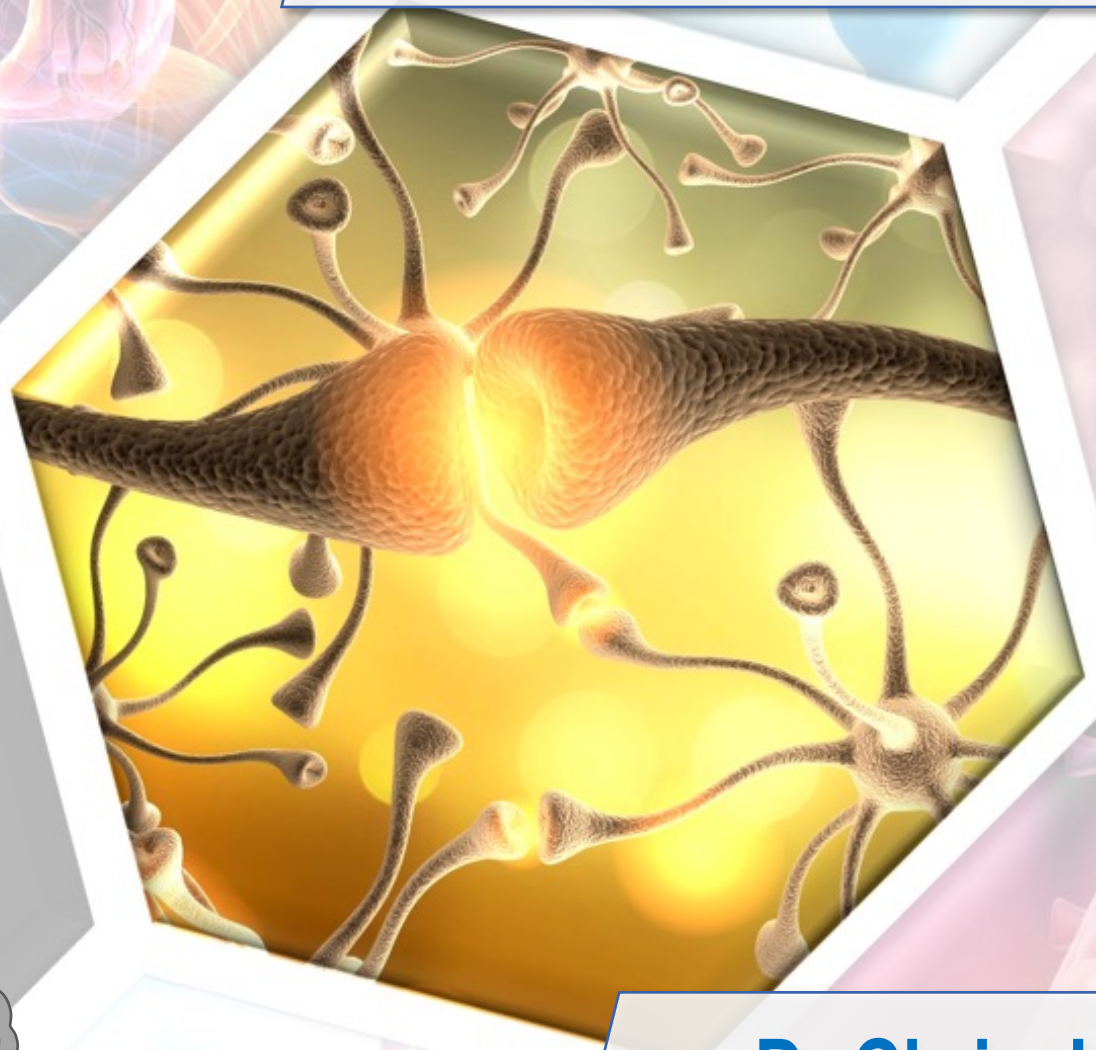

part 2 of 3

Dr Chris John c.john@imperial.ac.uk

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Pharmacology – drug targets

A chemical substance that interacts with a specific target within a biological system to produce a physiologic effect

Majority of drug targets are proteins – **4 main classes**

1) **Receptors**
2) **Enzymes**
3) **Transport proteins**
4) **Ion channels**

Q: Below are 4 of the most commonly prescribed drugs (both locally and globally). Which type of drug target do they act on?

1. **Atorvastatin**
2. **Amlodipine**
3. **Salbutamol**
4. **Citalopram**

(Note – they are not all CNS drugs)

Drug	Target
Atorvastatin	
Amlodipine	
Salbutamol	
Citalopram	

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IMPORTANT POINT

Drugs can act on targets to –

Enhance activation (stimulate an effect)

Or

Prevent activation (block an effect from being produced).

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Enzyme **Receptor**

Transport protein **Ion channel**

Nervous system disorders: Describe the clinical features and treatment options of central and peripheral nervous system disorders.

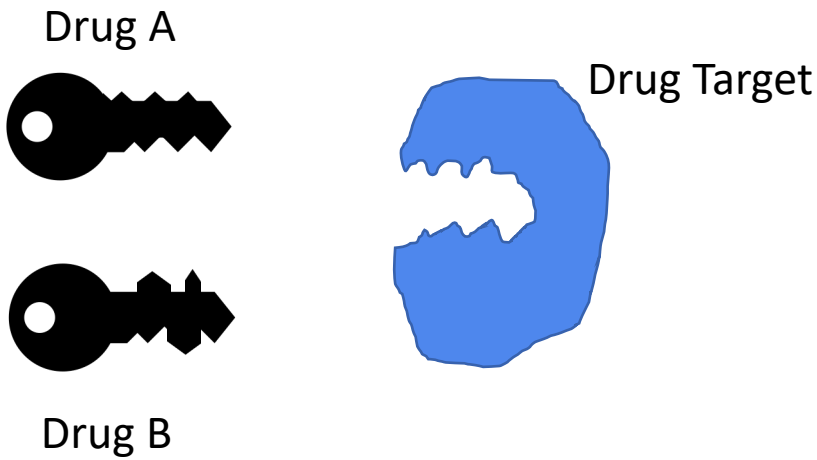
Pharmacology – selectivity

Another concept relating to drug targets =

drug selectivity

To be an effective therapeutic agent, a drug must show a **high degree of selectivity** for a **particular drug target**

Lock & Key Hypothesis



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Consider 3 Central Nervous System Neurotransmitters:
Dopamine, Noradrenaline and Serotonin

Are there structural similarities?

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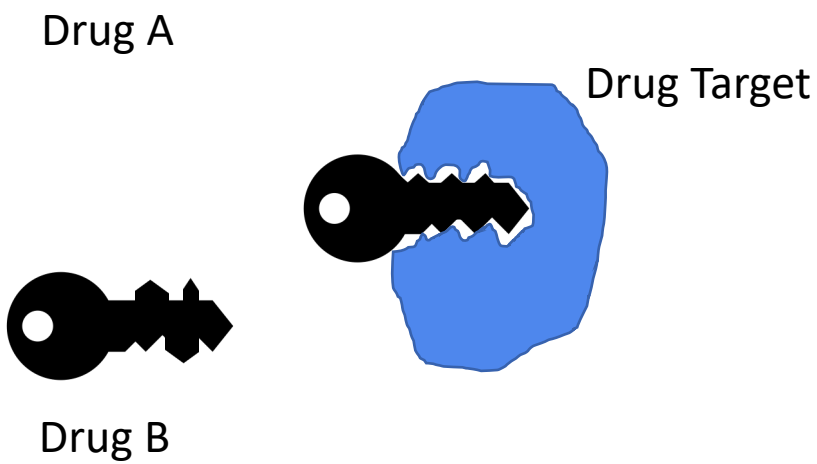
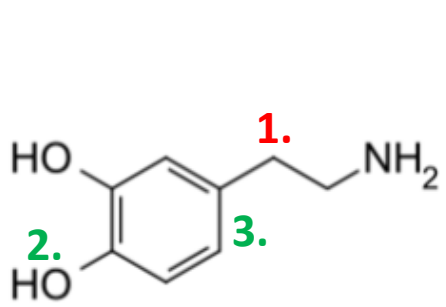
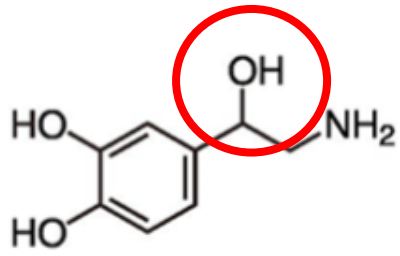
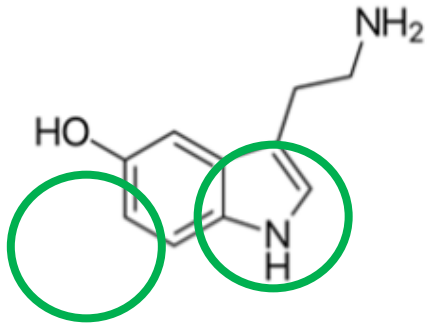




Dopamine



Noradrenaline



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Q. Why might selectivity be more important for drugs than endogenous compounds like dopamine? [**Hint – method of delivery to target**]

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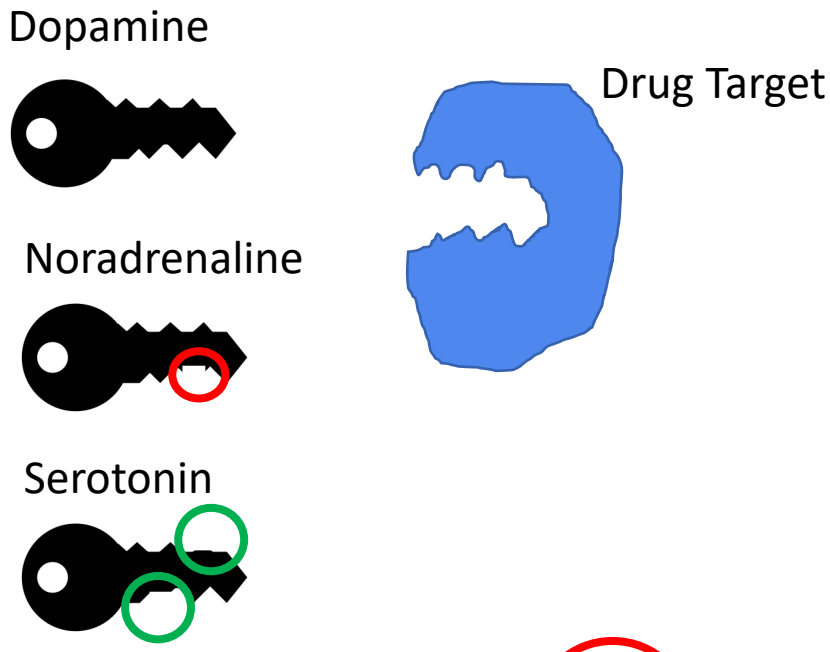

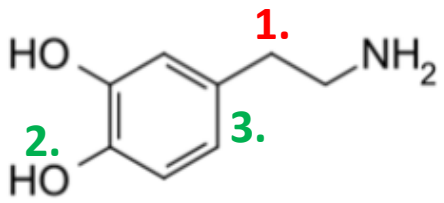

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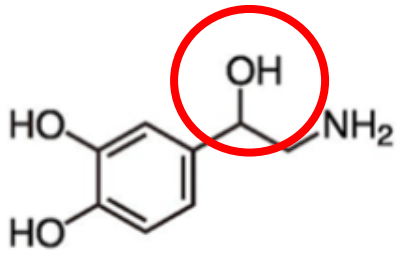

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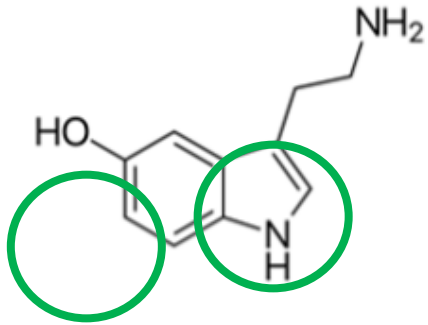

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Lock and key hypothesis

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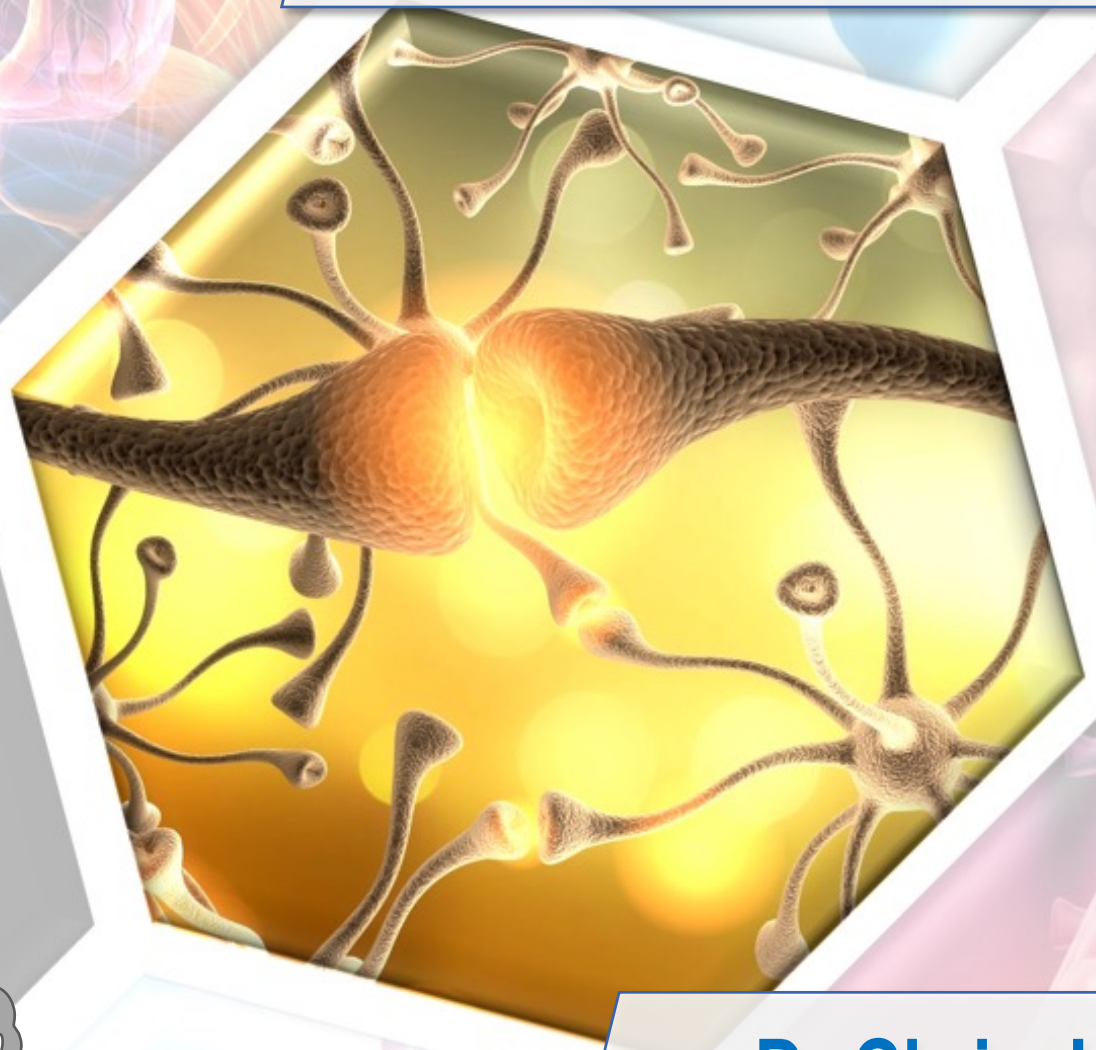

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Pharmacology –side effects/adverse effects

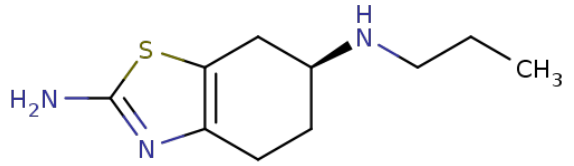
Side effects

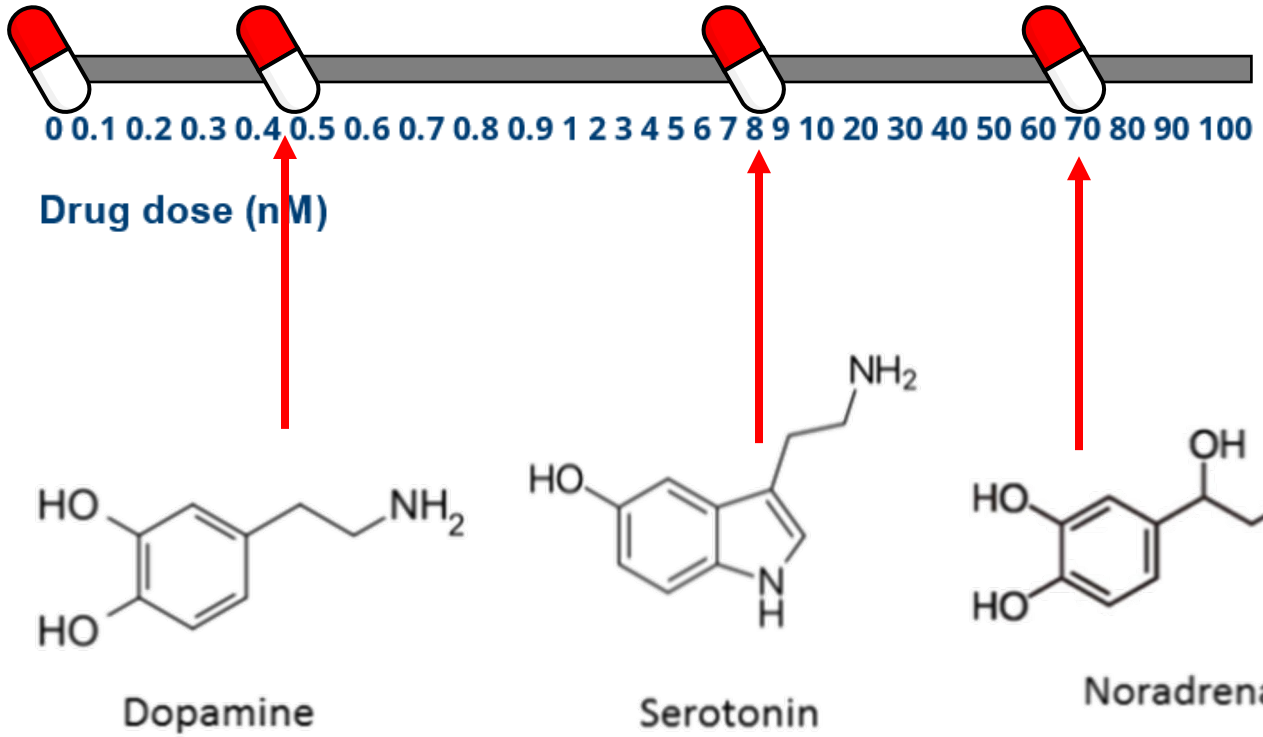
As the name implies, a side effect is an effect produced by the drug that is secondary to the intended effect.

If that side effect has negative health consequences, then it is also termed an **adverse effect**

The two terms are often used interchangeably, since most side effects have some sort of negative health consequence from minor (e.g. runny nose) to major (e.g. heart attack)

Pramipexole – dopamine receptor agonist





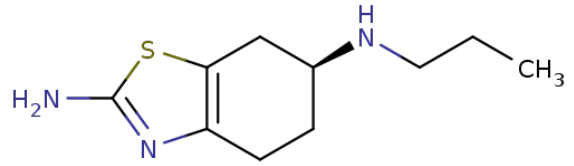
Nervous system disorders: Describe the clinical features and treatment options of central and peripheral nervous system disorders.

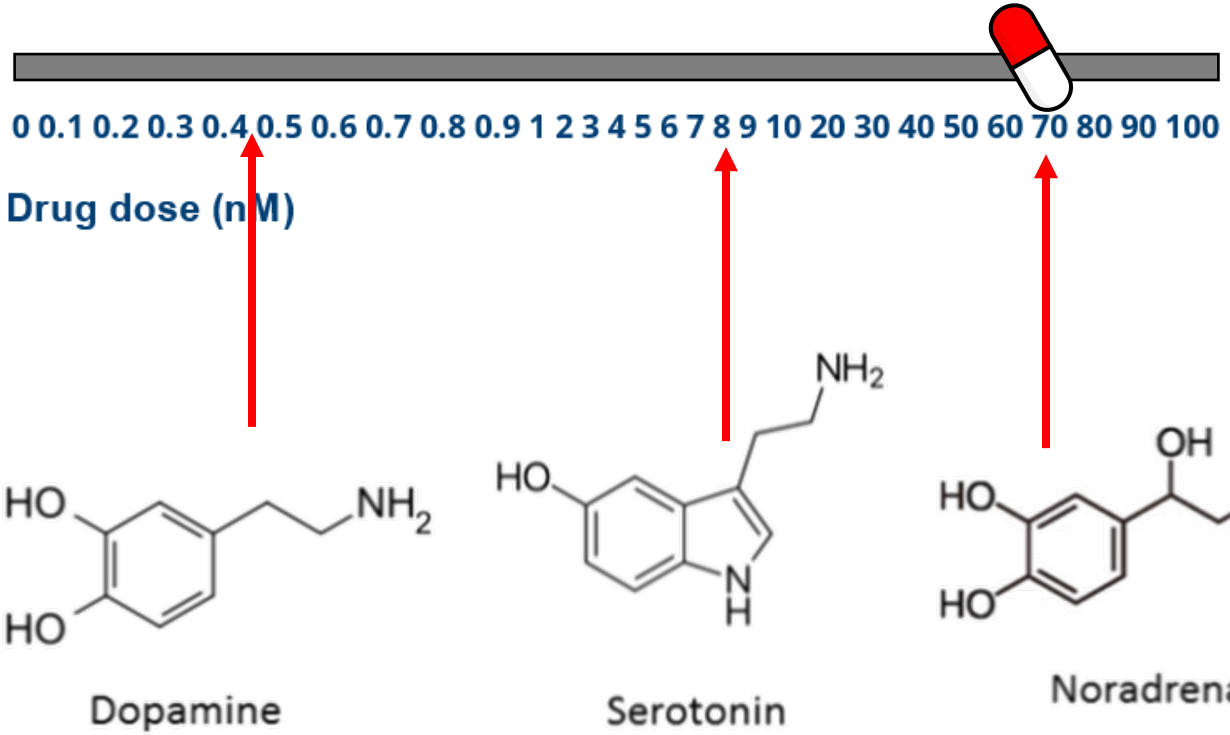
Pharmacology –side effects/adverse effects

Side effects

These can be due to **off-target effects**
(e.g. Pramipexole selectivity)

Pramipexole – dopamine receptor agonist





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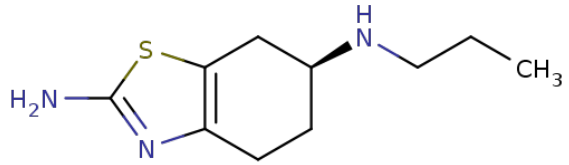
Pharmacology –side effects/adverse effects

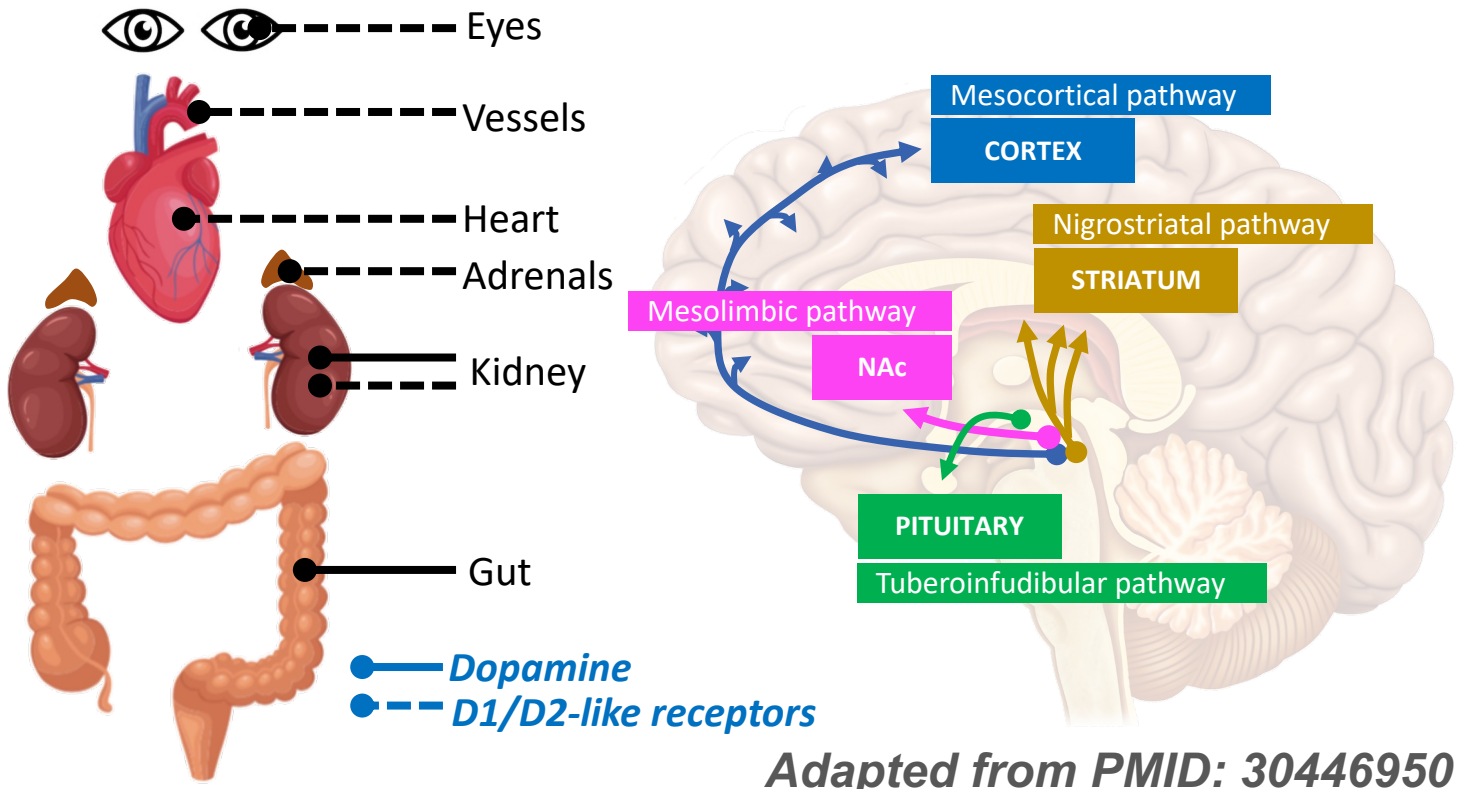
Side effects

Or they can be due to **effects on the same target**

Q: What is the relevance of the figure posted opposite for pramipexole side effects?

Pramipexole – dopamine receptor agonist





Adapted from PMID: 30446950

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Pharmacology –side effects/adverse effects

Side effects

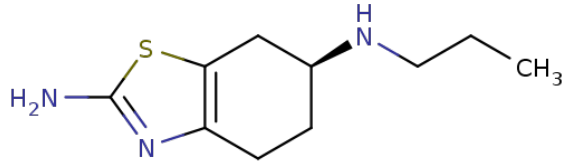
What does it all mean?

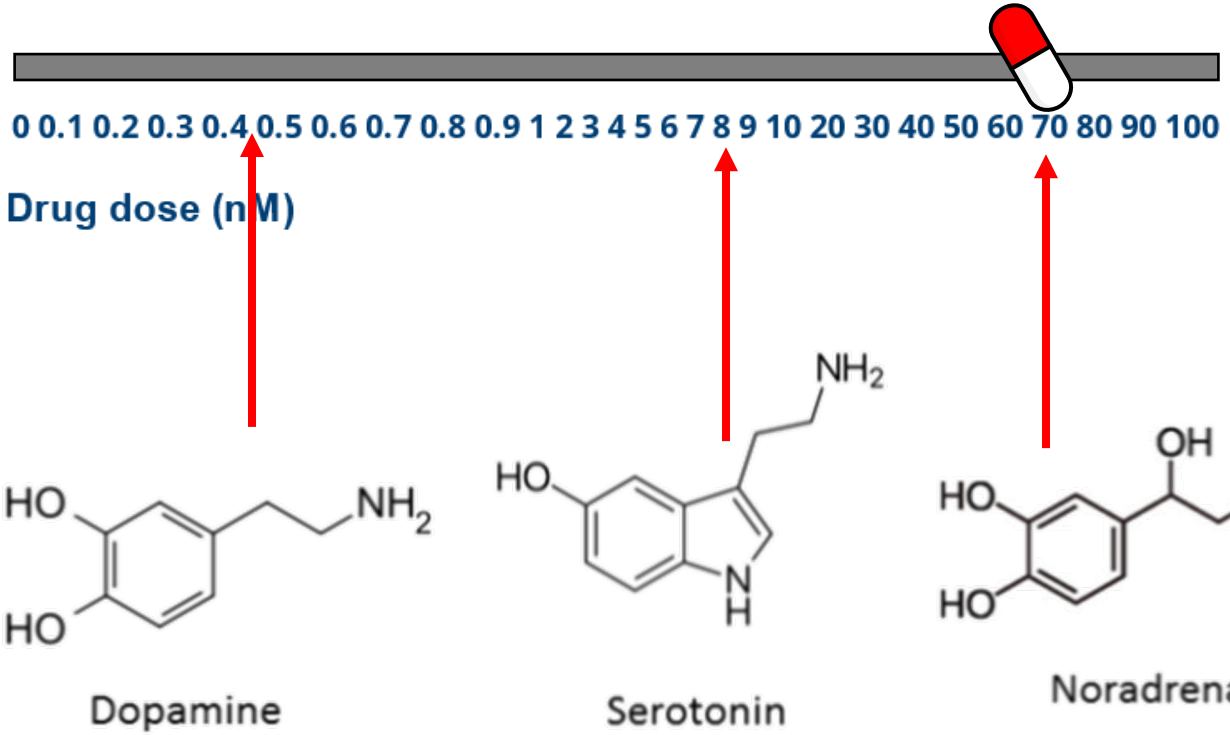
Side effects can be produced by drug action:

a) on **other targets in the same tissue** or **other tissues**
b) on the **same target in other tissues**
c) **dependent on the dose** of drug administered

The ‘safest’ drugs are those where there is a **large difference between the dose required to induce the desired effect and the dose required to induce side effects/adverse effects**

Pramipexole – dopamine receptor agonist





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Lock and key hypothesis

Dose/side effects

Dose

Drug effects are dose related
As dose increases, selectivity is lost

Side effects/adverse effects

Secondary drug effects – can have negative health consequences

Can be due to effects on:
Same target in other tissues
Different targets

Drug safety linked to dose required to induce adverse events