

Exercise walk-through

11.6

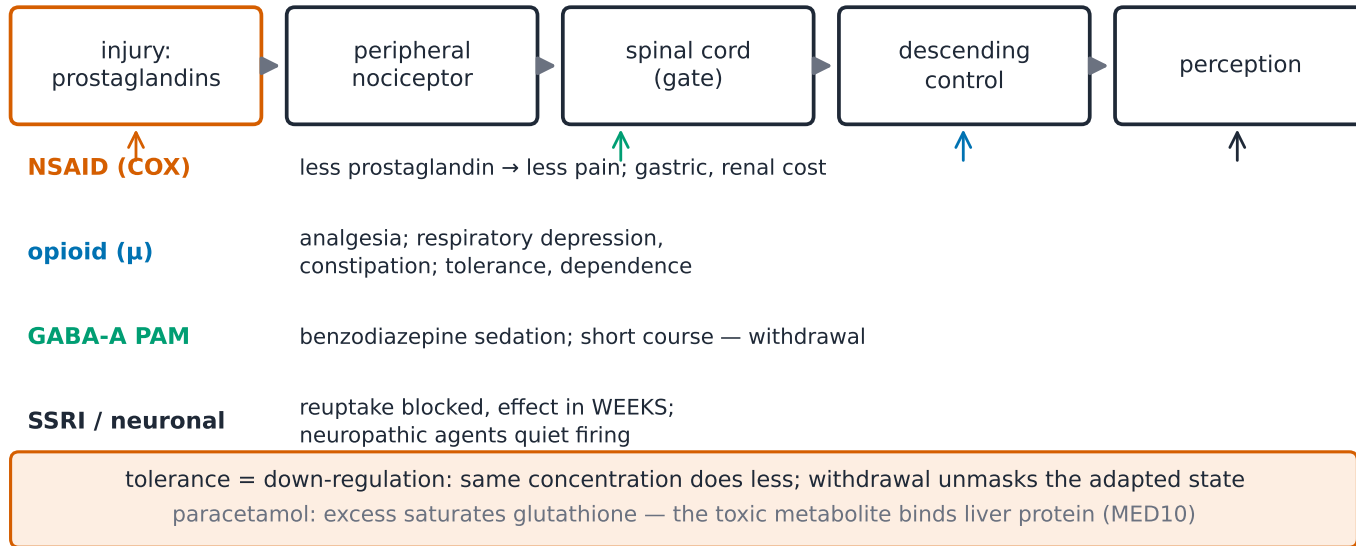
CNS drugs and analgesia

University Medicine

CNS drugs and analgesia: sites along the pain pathway

- 1 **Sites** NSAID at peripheral COX (gastric, renal cost); opioid at μ (respiratory, constipation); GABA-A PAM; SSRI reuptake.
- 2 **Adaptation** Chronic activation down-regulates - **tolerance**; withdrawal unmasks - **dependence** (WHO ladder 1986/1996).
- 3 **Paracetamol** Excess saturates glutathione; the metabolite binds liver protein - MED10 applies.

Drug action sites along the pain pathway



Peripheral COX, spinal gate, descending opioid control - the pathway with its drug sites.

Exercises 2.1-2.3

2.1 Which opioid effect barely tolerises? [3]

2.2 Why do SSRIs take weeks despite immediate reuptake blockade? [3]

2.3 Name the enzyme NSAIDs block and its two isoforms. [3]

Exercises 2.1-2.3

2.1 Which opioid effect barely tolerises? [3]

2.1

- Constipation – the μ effect that hardly tolerises ✓.
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2.2 Why do SSRIs take weeks despite immediate reuptake blockade? [3]

2.2

- Clinical effect needs receptor adaptation, not just the block ✓.
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2.3 Name the enzyme NSAIDs block and its two isoforms. [3]

2.3

- Cyclo-oxygenase: COX-1 (housekeeping) and COX-2 (inflammatory) ✓.

Exercise 3.1

3.1 Three fictional pains: prostaglandin-mediated inflammation; severe post-operative pain; neuropathic burning.

Match each to its first-line mechanism site (peripheral COX; μ receptor; neuronal excitability agents) with one cost named for the first two (gastric; respiratory) ✓. Explain why combinations from different sites add ✓. [8]

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3.1

- Inflammation: NSAID at peripheral COX – gastric cost ✓.
- Post-operative: opioid at μ – respiratory price ✓.
- Neuropathic: agents on neuronal excitability – neither site alone ✓.
- Different sites → additive without overlapping toxicity ✓.

Exercise 3.2

3.2 A fictional patient on long-term benzodiazepines stops abruptly.

Explain what tolerance was (receptor adaptation: same dose, less effect), what dependence is (the adapted state uncovered by withdrawal), and why the course is kept short by design ✓. Contrast the paracetamol overdose mechanism (glutathione saturated; metabolite binds liver protein – MED10) as a dose-related toxicity instead ✓. [7]

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- Tolerance: down-regulation – same concentration does less ✓.
- Dependence: withdrawal unmasks the adapted state ✓.
- Short courses by design limit the adaptation ✓.
- Paracetamol: dose-related – glutathione saturated, liver protein bound (MED10 necrosis) ✓.