Opioid Receptors and Classification of Opioid Analgesics

Psychology 472
Pharmacology of Psychoactive Drugs

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Opioid Receptors

- Three Classical types:
  - Mu
  - Kappa
  - Delta

+ Non-Classical
  - Nociceptin

All use a G-protein mechanism of action
Some increase CAMP in MFB
Feel good

Responses Mediated by Opioid Receptors

- **Mu** (μ): Analgesia, respiratory depression, miosis, relaxed euphoria, sedation, sense of tranquility, reduced apprehension and concern, cough suppression, reduced GI motility

- **Kappa**: Spinal analgesia, dysphoria, psychotomimetic effects, miosis, minimal respiratory depression
  
  
  Side Bar: Salvinorin A is a pure kappa agonist psychedelic drug

Functions μ₁

- Cortical analgesia
- Also associated with physical dependence

Function μ₂

- Causes: Euphoria
- Side Effects
  - Respiratory Depression
  - Miosis
  - Reduced GI motility
- Also associated with physical dependence
**Function μ₃**

- Unknown what it does

**Kappa K OP₂ KOP**

- Three types  κ₁, κ₂, κ₃
- Associated with spinal analgesia
- Locations
  - Hypothalamus, periaqueductal gray, claustrum, spinal cord

**Functions**

- Causes
  - Sedation, Miosis, inhibition of ADH release, dysphoria, can also trigger pain arousal (Nociceptin)
- Anxiety and Depression
- Reduced appetite
- Can assist in the development of tolerance to μ agonists
- Opioids create spinal anesthesia

**Delta (δ) OP₁**

- Two types  δ₁, δ₂
- Locations
  - pontine nuclei, amygdala, olfactory bulbs, cortex

**Functions**

- Creates analgesia
- Has antidepressant properties
- Associated with physical dependence

**Nociceptin Receptor OP₄**

- One type identified so far
- Locations
  - Cortex, amygdala, hippocampus, septum, habenula, hypothalamus, spinal cord, probably others
**Functions**

- Thought to be an endogenous antagonist of dopamine transport
- May act directly on dopamine or by inhibiting GABA to affect dopamine level
- Acts as an agonist or antagonist depending on the location of the receptor.
  - Anxiety, depression, appetite
- Also causes tolerance to μ agonists

**Agonists and Friends**

- **Agonist**: Any substance that has affinity for a μ receptor and exerts same effects as morphine (affinity and efficacy).
- **Partial Agonist**: A drug that has affinity but only partial efficacy (limited action).
- **Mixed Agonist-Antagonist**: Binds to opioid receptors (esp. κappa),
  - Causes analgesia in non-opioid-dependent persons,
  - May precipitate withdrawal in opioid-dependent persons.

**Conclusion**

- Several different types of receptors
- Each are activated by different drugs
- Each site causes different effects
- Need to know the receptor types to anticipate potential problems and interactions of different drugs.