NIVMA 2025

- [x] All About Opioids!
- [x] Building Individualized Premedication Plans
  - Non-Opioid Analgesics
  - Managing Hypotension
  - CPR – RECOVER updates

Non-Opioid Analgesics

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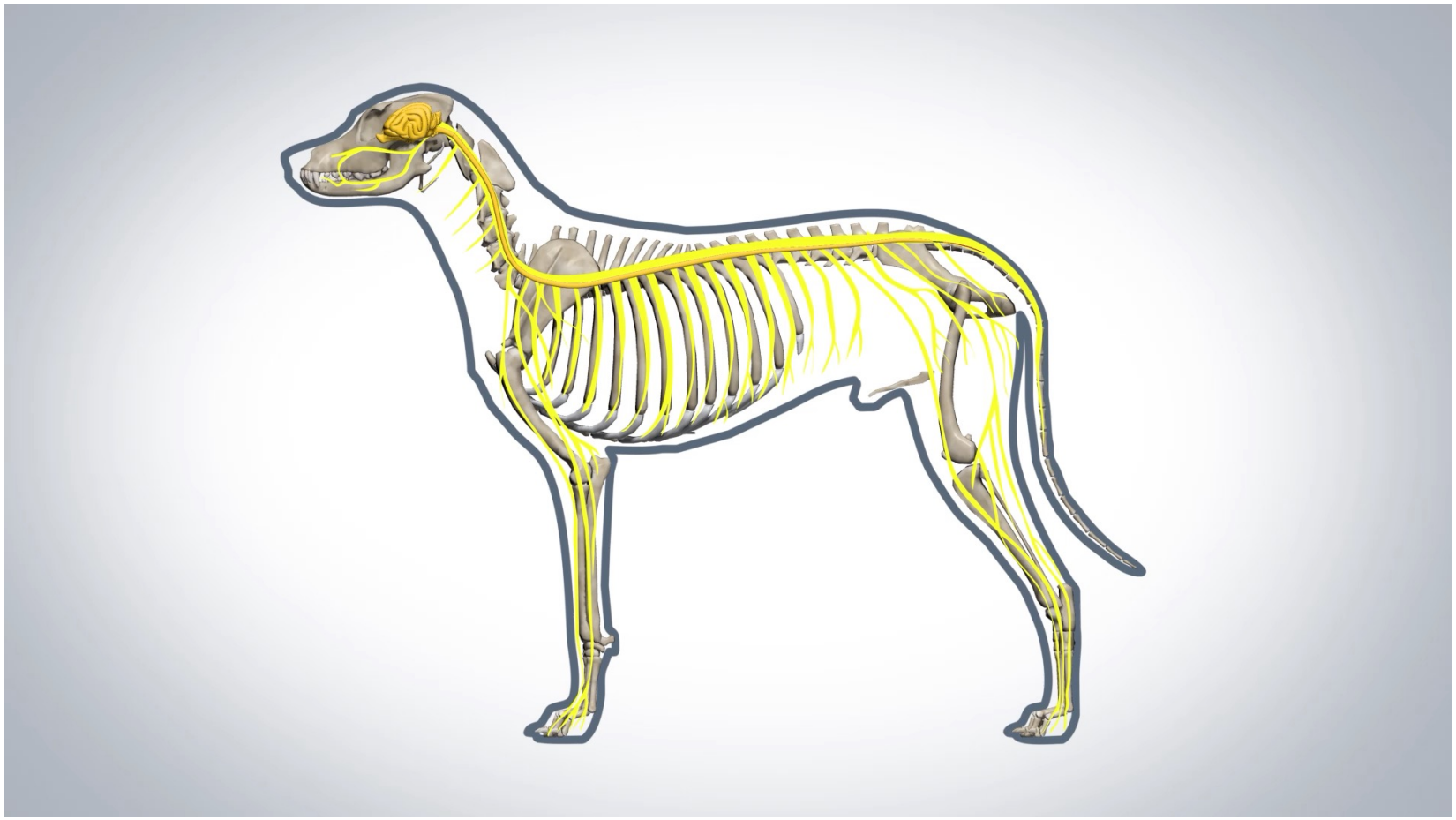
Overview and Objectives

- Overview the basics of the pain pathway
- Review ideal pain management strategies
- Discuss analgesic in-patient options
- Discuss analgesic out-patient options

→ Gain familiarity with a variety of adjunctive analgesic options

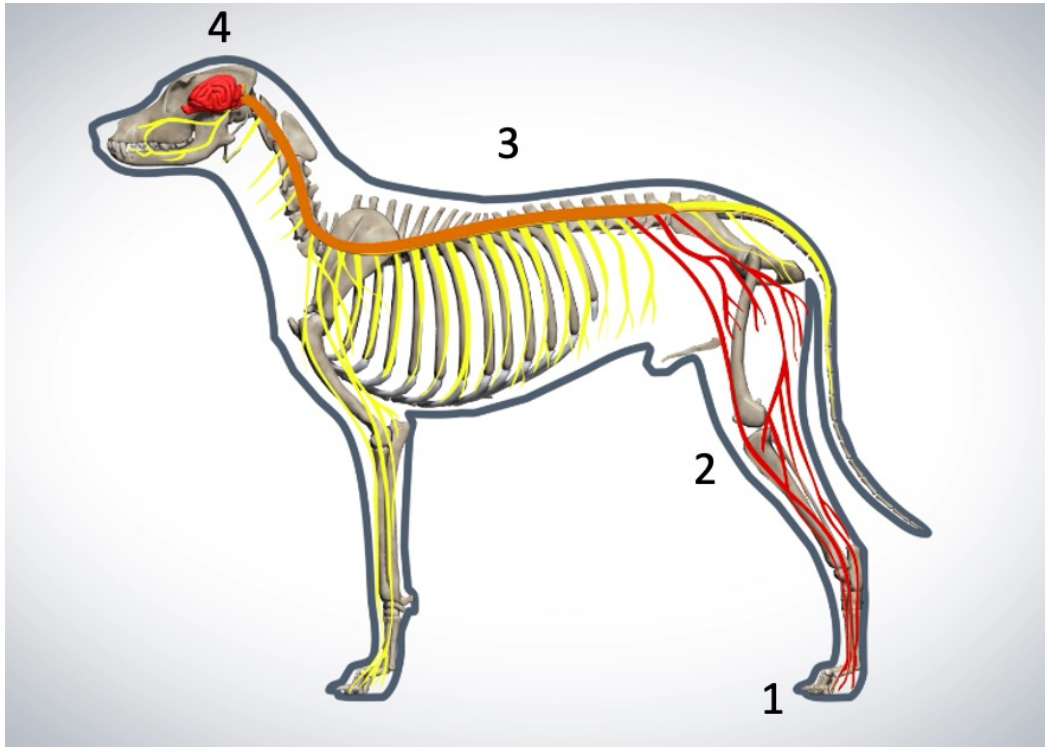
What is happening?



Pain and Nociception

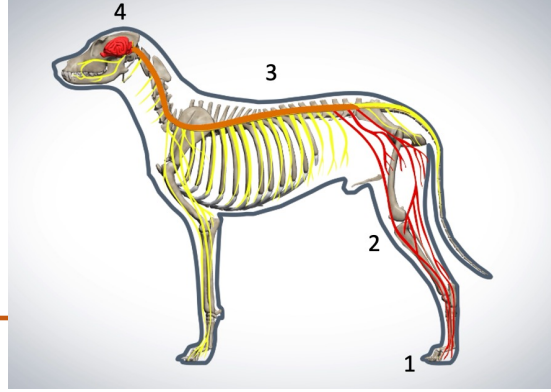
- Nociception – process by which a noxious stimulus is encoded
    1. Transduction
    2. Transmission
    3. Modulation
    4. Perception

→ Pain is the experience resulting from nociception

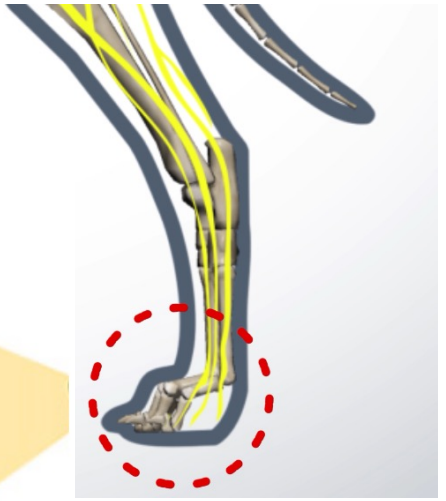


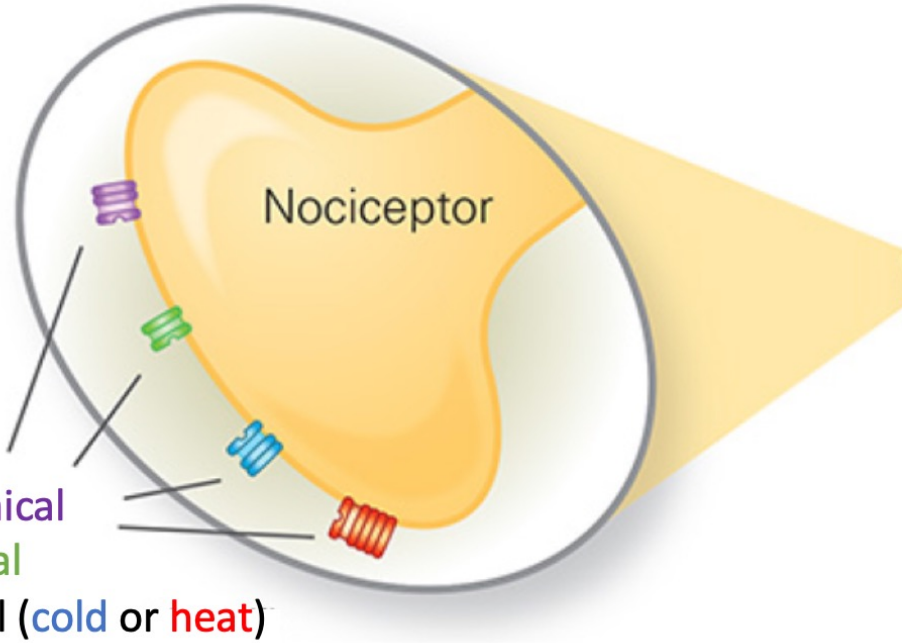
https://www.mdpi.com/1422-0067/19/8/2164#
https://www.nejm.org/doi/full/10.1056/NEJMra1800222

Transduction

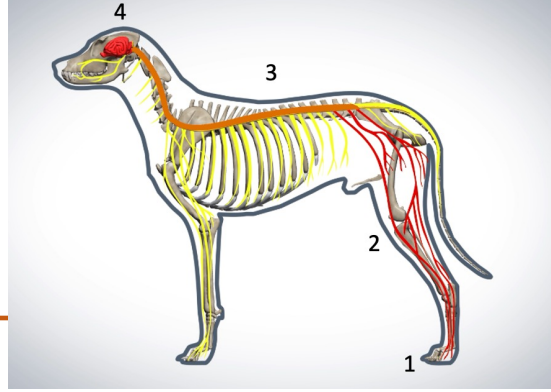


- Noxious stimulus activates transducers on nociceptors
- Only 3 types of noxious stimuli can activate transducers:
  - Mechanical
  - Chemical
  - Thermal (heat or cold)
- High threshold to activate

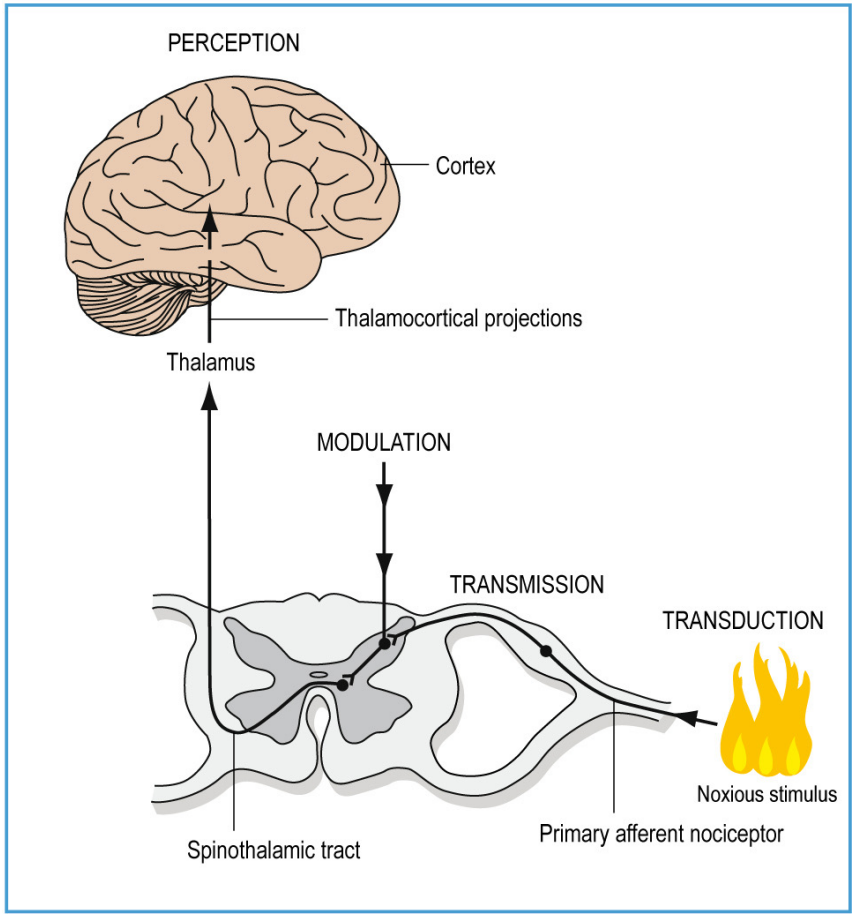




Transmission

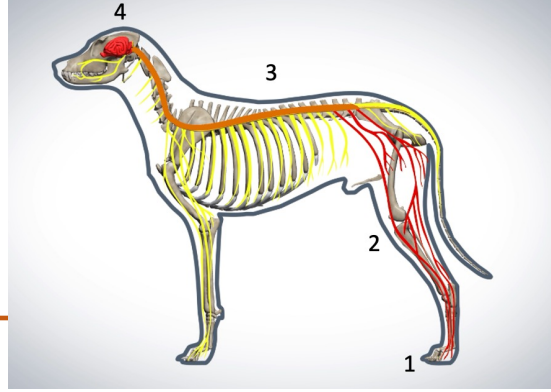


- Action potential travels along the primary afferent neuron (in a sensory nerve) toward the spinal cord

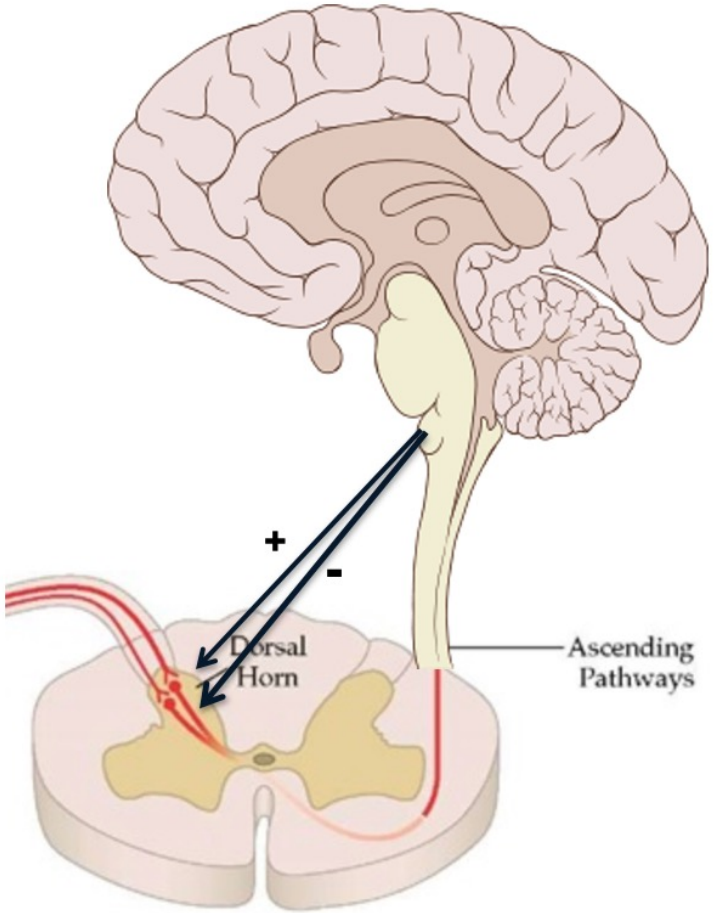


https://www.theveterinarynurse.com/review/article/understanding-the-mechanisms-behind-acute-pain-in-dogs-and-cats

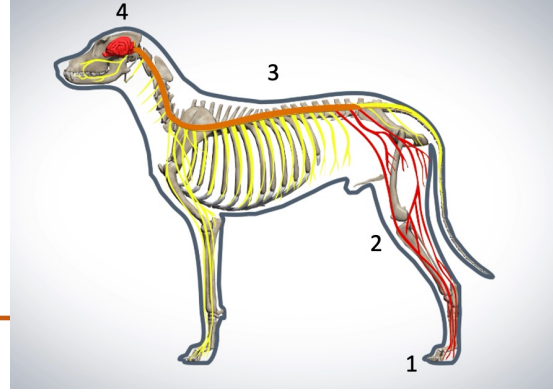
Modulation



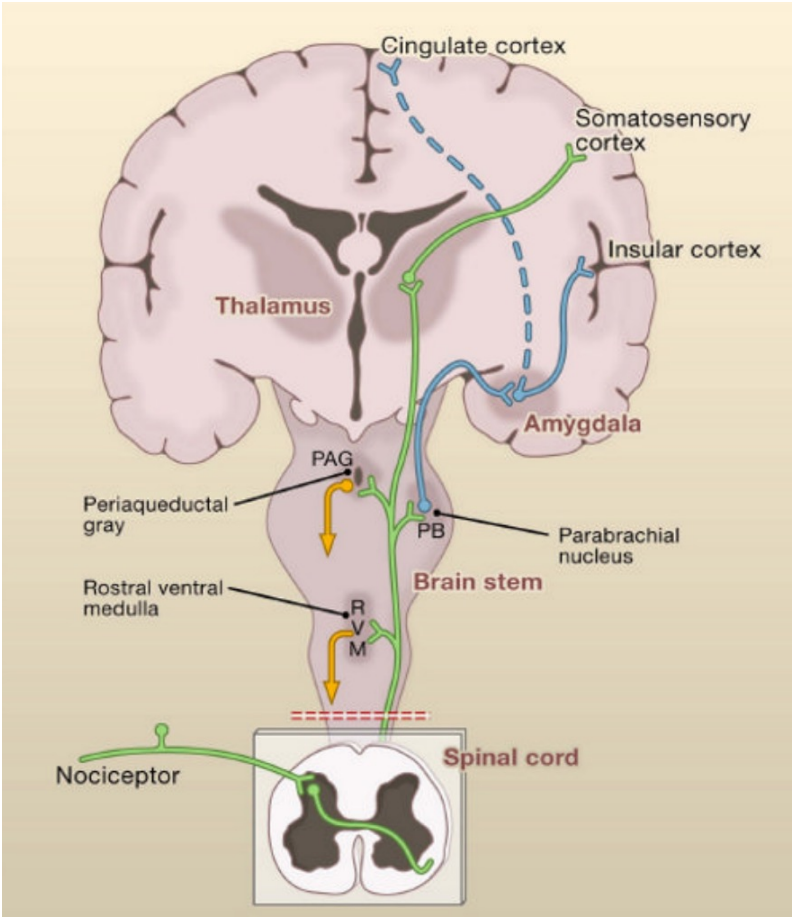
- Primary afferent neuron synapses with second order neuron in the spinal cord
- The signal is relayed and modified
  - Excitatory neurotransmitters dumped into synaptic cleft
  - Descending signals from the brain alter signal



Perception

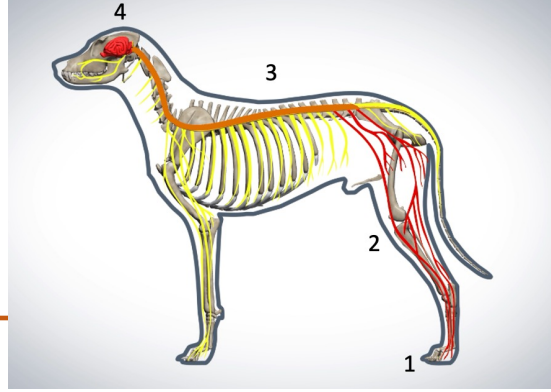


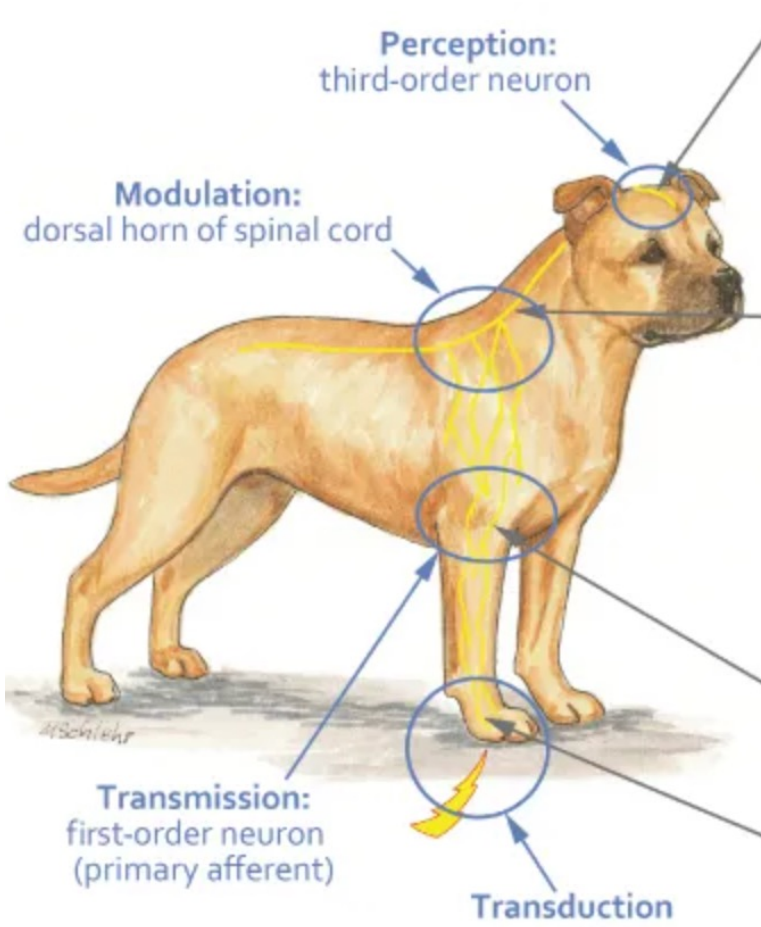
- Nociceptive signal arrives at the brain
  - Sensation perceived
  - Emotional response
  - Behavioral/motivational response
  - Cognitive effects
  - Autonomic response



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2852643/pdf/nihms155644.pdf

Approach to pain management





Perception (cerebral cortex)
- Anesthetics
- Opioids
- α2 Antagonists
- Benzodiazepines
- Phenothiazines
- NSAIDs

Modulation (spinal cord)
- Local anesthetic
- Tricyclic antidepressants
- Cholinesterase inhibitors
- NMDA antagonists
- Opioids
- NSAIDs
- α2 Antagonists
- Anticonvulsants

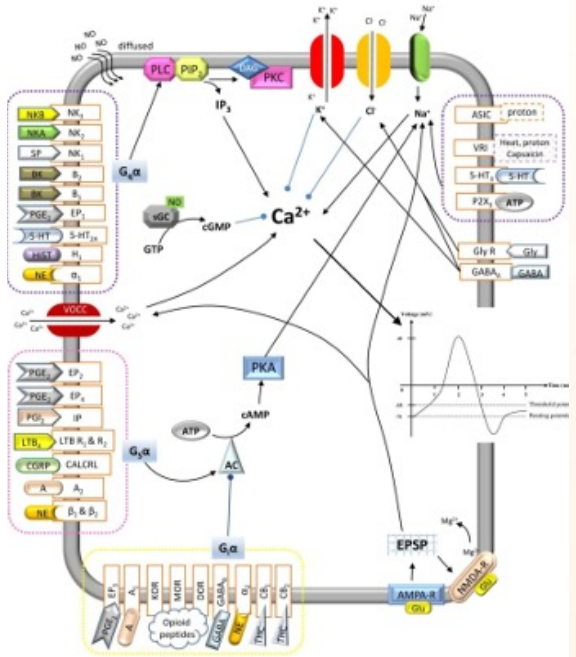
Transmission (sensory nerves)
- Local anesthetics
- α2 Antagonists

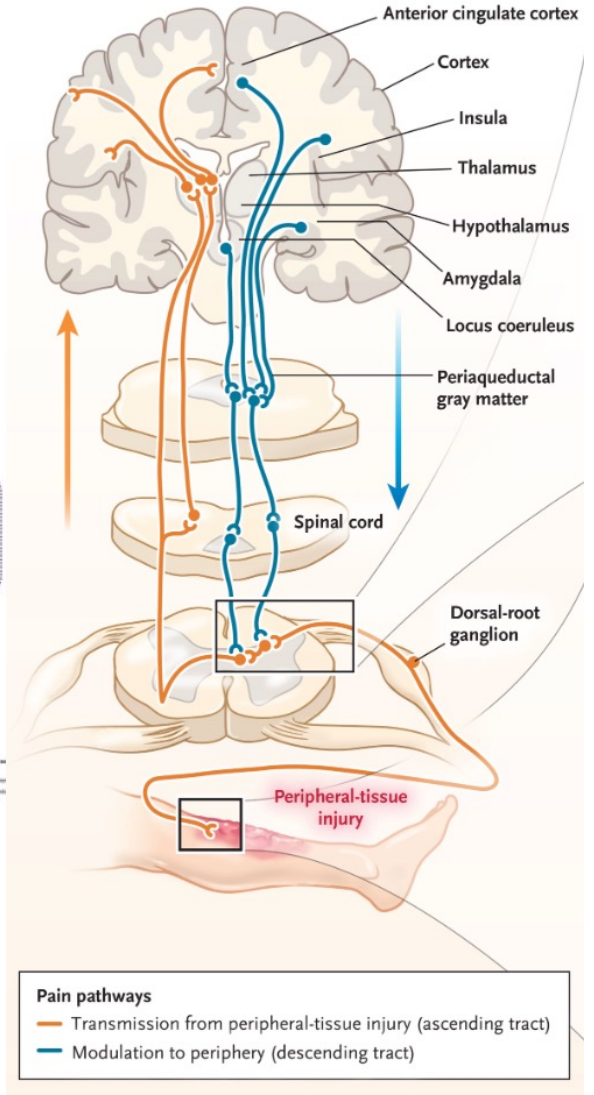
Transduction (sensory nerve endings, nociceptors)
- Local anesthetics
- Opioids
- NSAIDs
- Corticosteroids

https://veteriankey.com/the-prevention-and-management-of-pain-in-dogs/

Disadvantages of a single drug approach

- Pain pathway is too complex for one drug!
  - Insufficient analgesia
- Multimodal approach always recommended
  - Better analgesia
  - Fewer side effects
  - Less chronic pain
- Opioid tolerance can develop rapidly





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https://www.mdpi.com/1422-0067/19/8/2164#
https://www.nejm.org/doi/full/10.1056/NEJMra1800222

In-Hospital Analgesia

- Opioids
- NSAIDs
- Local anesthetics
- IV Lidocaine
- Maropitant
- Ketamine
- Dexmedetomidine

https://operationpetsalive.org/blog/injured-cats-and-dogs-need-your-help/

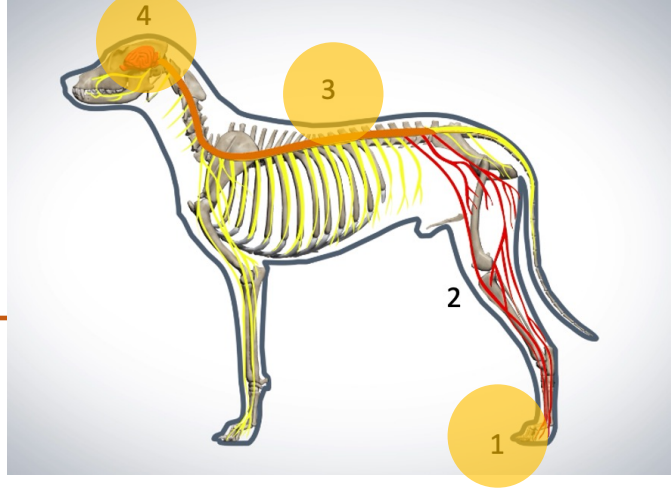
Perioperative Trifecta

Opioids

NSAIDS

Local anesthesia

Opioids



- Analgesia
  - Best analgesia = Full mu agonists
    - Methadone! Mu agonist, NMDA antagonist, 5HT+NE reuptake inhibitor
  - Medium analgesia = Partial mu agonist (buprenorphine)

- 'Standard' durations of action
  - Variable depending on individual, dose and level of pain
  - Regular pain assessments, re-dose as needed
  - First 24-48 hours post-op most painful

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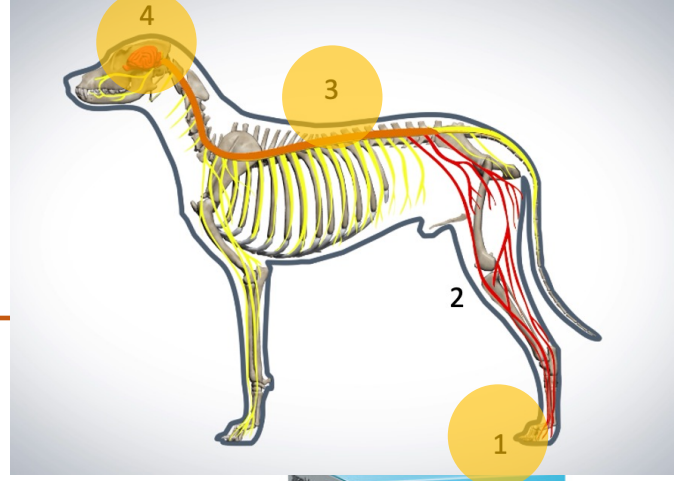
NSAIDs



- Analgesic and anti-inflammatory – act at many levels
- Very effective for post-operative pain
- COX-2 selective often favored
- Generally given after anesthesia
  - COX-2 important during hypotension or hypovolemia
- Possible contraindications:
  - Renal, GI, liver disease
  - Pregnancy

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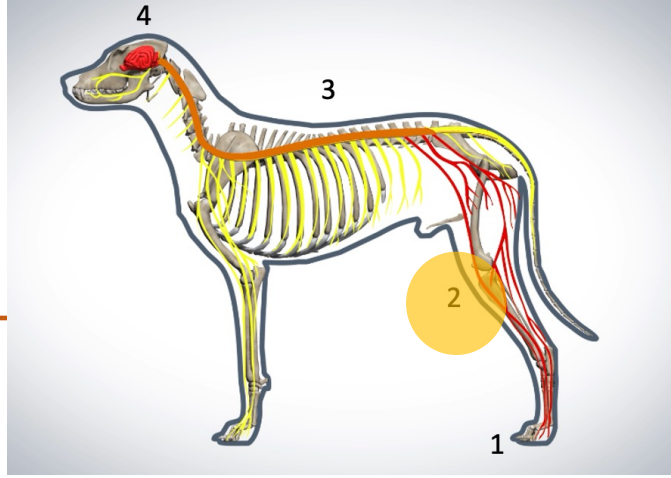
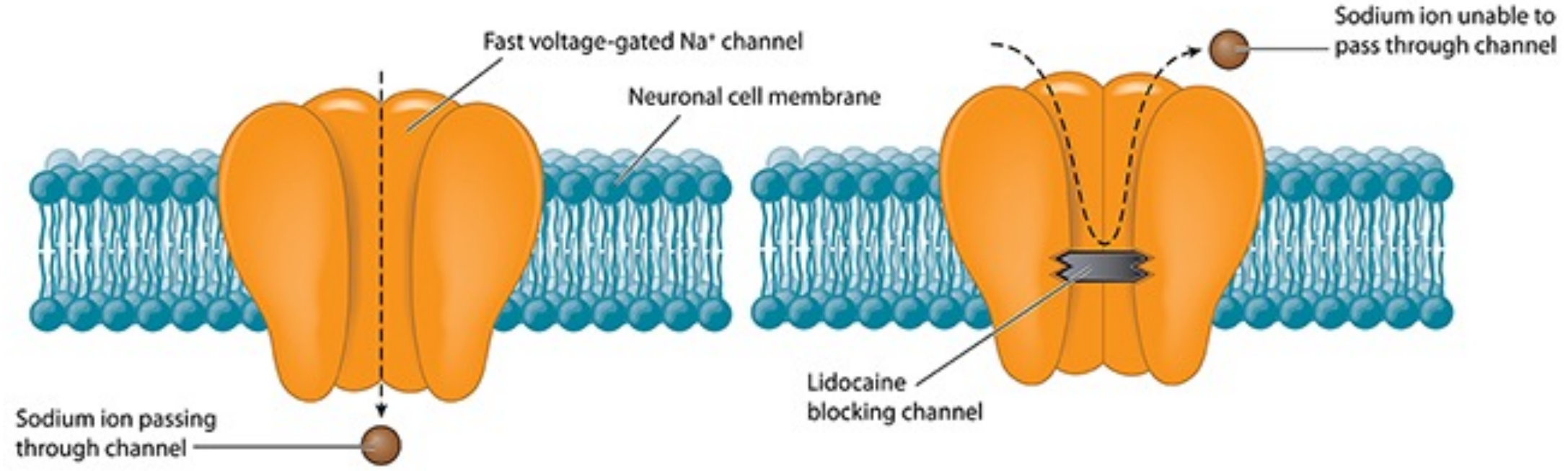
Local Anesthetics



- Sodium channel blockers



→ Best analgesia possible!!

Local Anesthetics

- Infiltration
  - Peri-incisional Nocita or bupivacaine
  - Intra-testicular

- Peripheral nerve blocks
  - So many blocks!
  - Dental blocks
  - Forelimb blocks (RUMM block, brachial plexus block, ring block)
  - Pelvic limb locks (femoral/sciatic nerve block)

- Epidural injections
  - Local anesthetic + opioid
  - Bupivacaine + Morphine 0.1 mg/kg (total mixed volume 0.2 mL/kg)

https://onlinelibrary.wiley.com/doi/full/10.1002/vms3.218
https://www.veterinarypracticenews.com/why-intratesticular-blocks-are-simple-low-cost-and-effective/

Local Anesthetics

- Lidocaine
  - Onset: 5-10 min
  - Duration: 1-2 hr
  - Max dose: 4 mg/kg

- Bupivacaine
  - Onset: 10-15 min
  - Duration: 4-6 hr
  - Max dose: 2 mg/kg
  - Never IV

- Nocita
  - Liposomal bupivacaine
  - Onset: ~30 min
  - Duration: 72 hr

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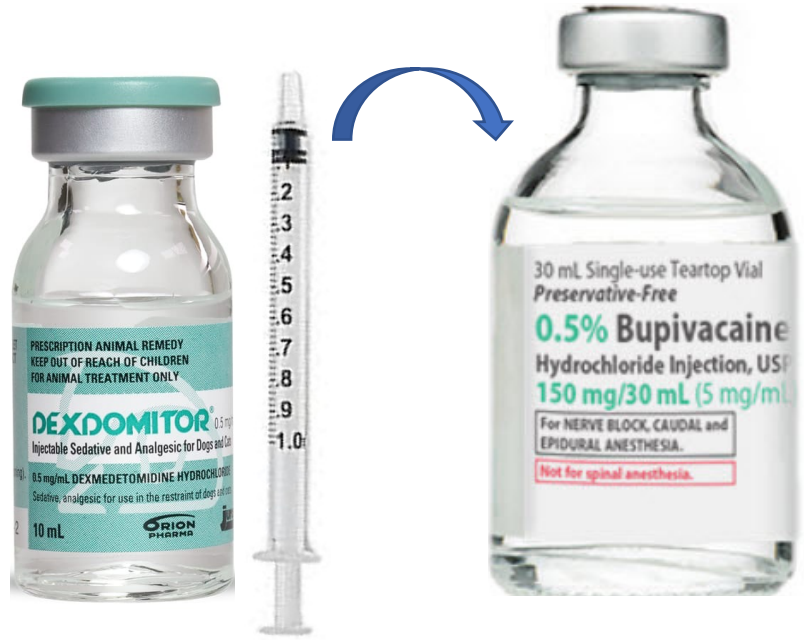
Local Anesthetics – Adjuncts

- Epinephrine
  - Extends analgesia duration with lidocaine (less with bupivacaine)
  - Vasoconstrictor and alpha-2 agonist effects
  - Dose: 5 ug/mL epinephrine in solution
    - 0.5 mL epinephrine (1 mg/mL) into 100 mL bottle of lidocaine
    - CV effects at higher concentrations
  - Duration of action:
    - Lidocaine alone = 1-2 hours
    - Lidocaine + epinephrine = 2-6 hours
  - NOT: Areas without collateral blood supply, epidurals(?)

Local Anesthetics – Adjuncts

- Dexmedetomidine
  - Shortens onset time, extends duration and intensifies block!
  - Dose: 1 ug/mL dexmedetomidine in solution
    - 0.1 mL dexmedetomidine (50 ug) into 50 mL bottle of bupivacaine
  - Duration of action:
    - Bupivacaine alone = 4-6 hours
    - Bupivacaine + dexmedetomidine = 10-24 hours



TIPS & TRICKS

Make a premade mixture!

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IV Lidocaine

- Benefits
  - Analgesia
    - Acute
    - Chronic
  - Reduces inhalant requirements
  - Antiarrhythmic
  - Anti-inflammatory
  - Helps restore normal gut motility
  - Decreases reperfusion injury
  - Antitussive

- Dosing:
  - Bolus: 1-2 mg/kg
  - Loading dose: 1-2 mg/kg IV
  - Infusion: 50-100 ug/kg/min
  - Stop 15-20 minutes before recovery

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https://m.me-zoo.com/main/html.php?htmid=science/science1.html

IV Lidocaine

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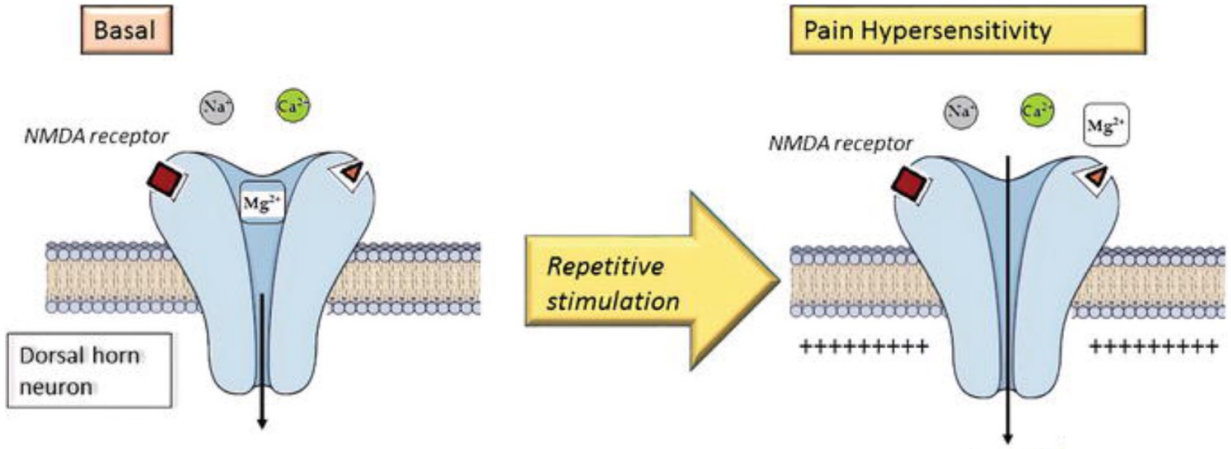
Ketamine

- NMDA antagonist
- Excellent analgesic adjunct
  - Acute pain
  - Chronic pain (neuropathic pain)
- Infusion:
  - Loading dose: 0.5 mg/kg
  - Infusion: 5 ug/kg/min (awake), 10-40 ug/kg/min (GA)
- SQ injection:
  - 0.5-1 mg/kg SQ q 1-3 weeks for chronic pain



https://mycawc.com/how-to-give-subcutaneous-injection-dog-cat/

Dexmedetomidine

- Alpha-2 agonist
- Analgesia, anxiolysis, sedation….and unwanted physiologic effects
  - Cardiovascular effects – Less severe with low analgesic doses
  - Increased urine production
- Dose:
  - Loading dose: 0.5 ug/kg IV
  - Infusion: 0.5-1 ug/kg/hr (awake or GA)

https://www.facebook.com/100044619673828/photos/1181994003297911/

Excellent Resource

- VASG.org

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Case

- Stella – 10 yr FS DSH
  - Stomatitis → Full mouth extractions
  - Mildly increased SDMA
  - BUN + creatinine sneaking up
  - Anxious but sweet girl

  - Anesthesia:
    - Premedication: Methadone 0.3 mg/kg + Alfaxalone 2 mg/kg
    - Induction: Propofol + Ketamine 2 mg/kg IV
    - Maintenance: Isoflurane, maropitant slowly IV
    - Dental blocks….what to use?

Case

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    - Dental blocks….

a) Bupivacaine (4-6 hr)
b) Bupivacaine + dexmedetomidine (10-24 hr)
c) Nocita (72 hr)

Case

- Stella – 10 yr FS DSH
  - Perform bupivacaine + dexmedetomidine blocks
  - Owner elects medical boarding
  - Post-op analgesic plan in hospital?

- ☑ Opioids
- ☒ NSAIDs
- ☑ Local anesthetics
- ☒ IV Lidocaine
- ☑ Maropitant
- ☑ Ketamine
- ☒ Dexmedetomidine

Case

- Stella – 10 yr FS DSH
  - Perform bupivacaine + dexmedetomidine blocks
  - Owner elects medical boarding
  - Post-op analgesic plan in hospital?

Hydromorphone 0.05 mg/kg as needed (q 4-6 hr)
Maropitant 1 mg/kg IV
Ketamine infusion 5 ug/kg/min
…start oral analgesic medications to go home…

Out-Patient Analgesia

→ Chronic pain

- Hard to treat
- Complex mechanisms
- Need multiple drugs

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https://www.reddit.com/r/Dachshund/comments/1jw90j6/wagon_ride_for_a_old_lady_who_over_did_it_on/

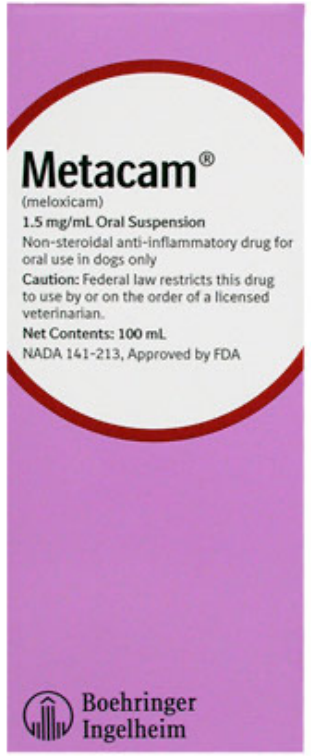
Out-Patient Analgesia

- NSAIDs – Long term
- Gabapentin
- Pregabalin
- Amantadine
- Methocarbamol
- CBD
- Librela
- Non-pharmaceutical options

https://operationpetsalive.org/blog/injured-cats-and-dogs-need-your-help/

NSAIDs

- Excellent for outpatients post-operatively
- Long term use in chronic inflammatory conditions
- Options
  - Standard NSAIDs
  - Grapiprant
  - Acetaminophen



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Long-Term NSAID Use

- Possible treatment for cats and dogs
- Screen for contraindications and adverse effects
- Which is best?

- Dogs
  - No studies to identify safest/most effective
  - Large individual variation
  - Trial different drugs

- Cats
  - Robenacoxib
  - Meloxicam

Long-Term Use in Cats….Really???

- Yes!
- DJD is common in older cats, often pain relief is inadequate
- Fear of NSAID side-effects, nothing labeled in US
- Meloxicam FDA black box warning in cats
  - 0.3 mg/kg for 9 days
  - GI ulcers

Long-Term Use in Cats….Really???

- Meloxicam (Metacam)
  - Oral suspension licensed for cats in other countries (not US)
  - Canine formulation extra-label in US
  - Dose: 0.01-0.03 mg/kg daily, even with kidney disease (0.05 mg/kg licensed in Europe)

Long-Term Use in Cats….Really???

- Robenacoxib (Onsior)
  - Less long-term data
  - 4-12 weeks
    - Multiple studies and countries (3 studies from the US)
    - No difference in adverse effects vs placebo
    - Creatinine slightly higher elevation in robenacoxib group, not worse with CKD
  - Dose: 1 mg/kg daily

Acetaminophen

- NSAID
  - Mechanism not fully known
  - COX-3; weak anti-inflammatory
  - Serotonin or cannabinoid pathways
- Does it work?
  - Limited data
  - Mixed evidence
- Dose: 10-15 mg/kg PO q8hr
- Never give to cats

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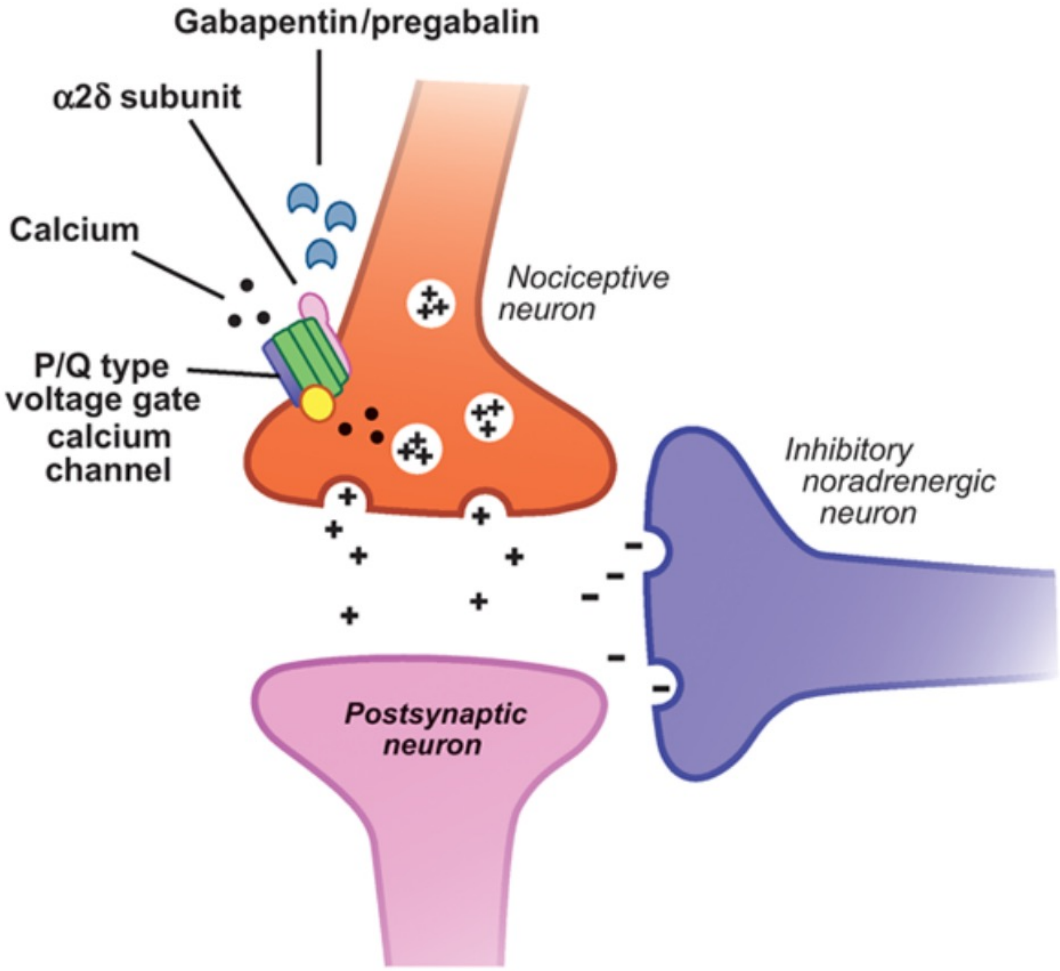
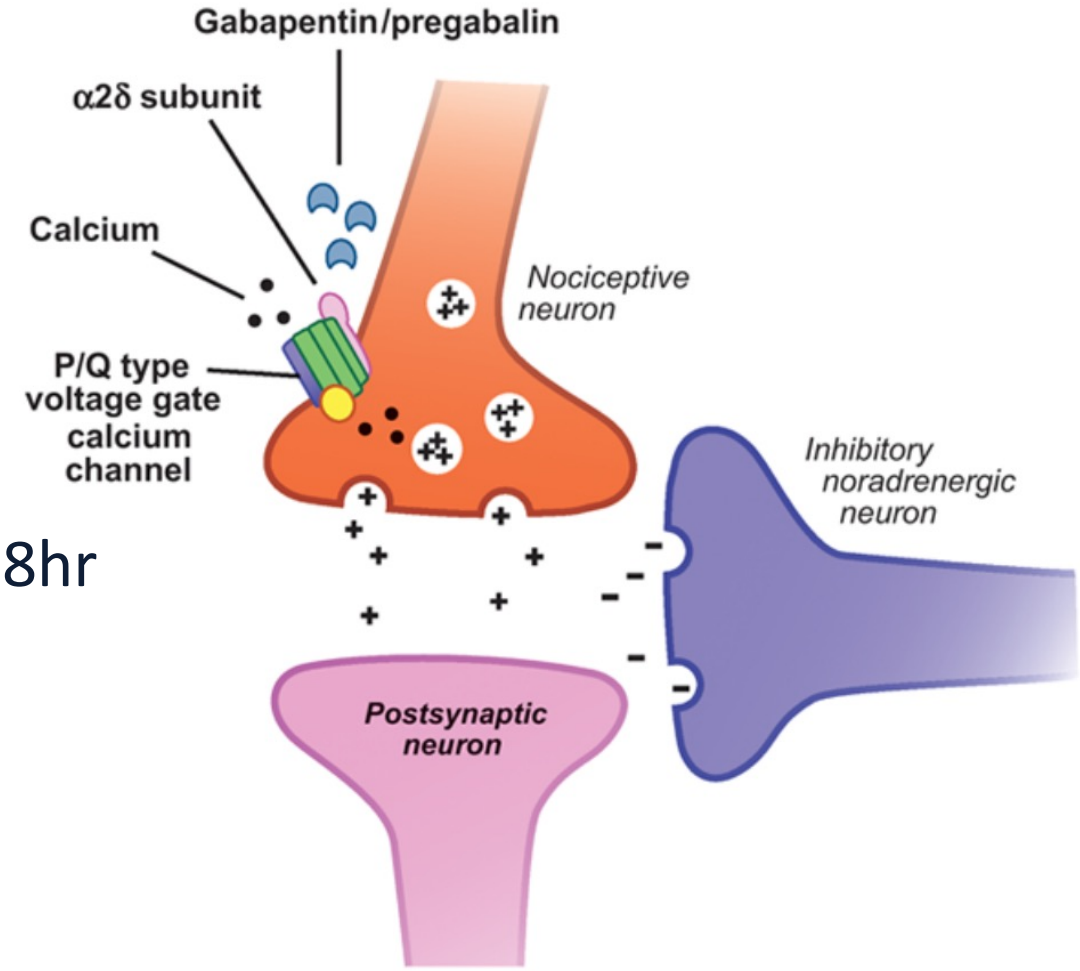
Gabapentin + Pregabalin

- Gabapentinoids
- Mechanism:
  - Binds to voltage-gated calcium channels in which are upregulated in chronic pain states
- Effective for:
  - Chronic pain
  - Neuropathic pain



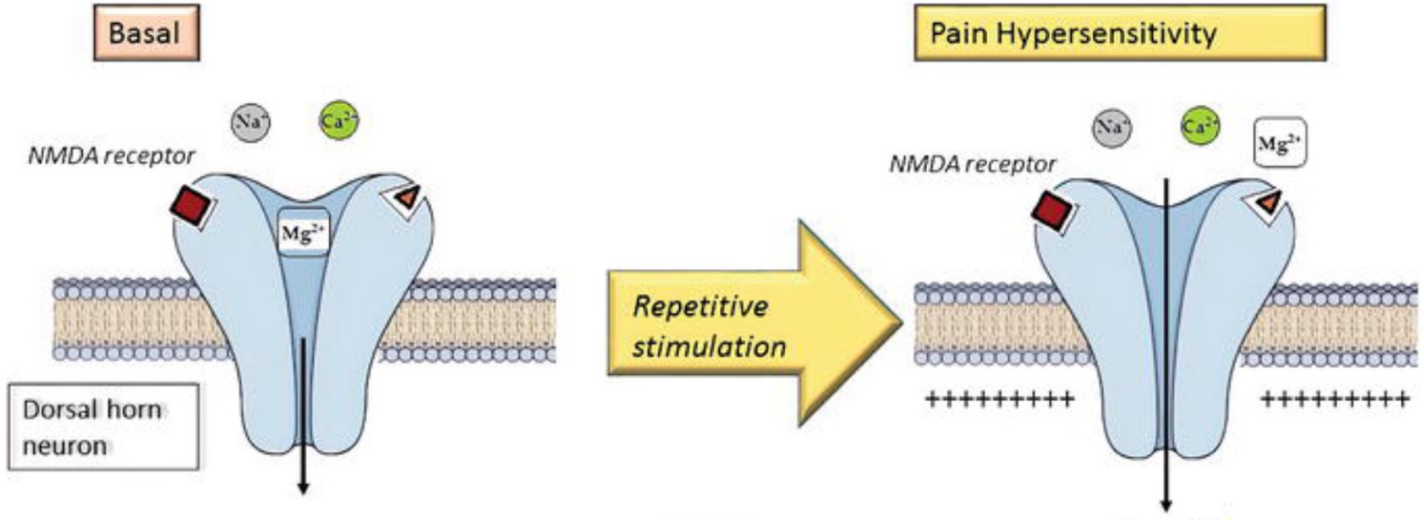
Gabapentin + Pregabalin

- Pregabalin:
  - Similar to gabapentin
  - Longer lasting
  - More expensive
- Dosing:
  - Gabapentin: 5-20 (or higher) mg/kg q8hr
  - Pregabalin 1-4 mg/kg q12hr



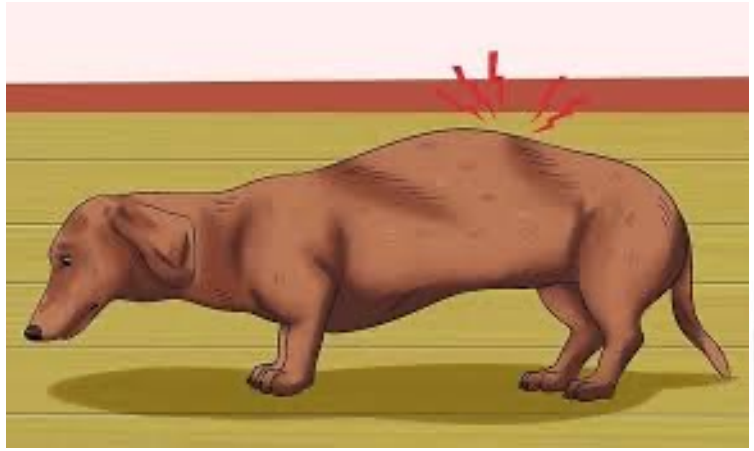
Amantadine

- NMDA antagonist
- “Oral ketamine”
- Effective for:
  - Chronic pain
  - Neuropathic pain
- Used in combination with gabapentin
- Dose: 3-5 mg/kg q 12-24 hr



Methocarbamol

- Centrally acting muscle relaxant
- Not an analgesic drug
- Relieve pain from muscle tension/fasciculation
- Dose: 25-50 mg/kg q8-12hr
- Alternative: Diazepam 0.5 mg/kg



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CBD

- Cannabinoid essentials:
  - Anything with a neural system has cannabinoid receptors
  - Responsible for a wide range of cellular functions – affect every organ
  - Overall function of cannabinoid system:

"Relax, eat, sleep, forget, and protect"

CBD

- Cannabinoid essentials:
  - Anything with a neural system has cannabinoid receptors
  - Responsible for a wide range of cellular functions – affect every organ
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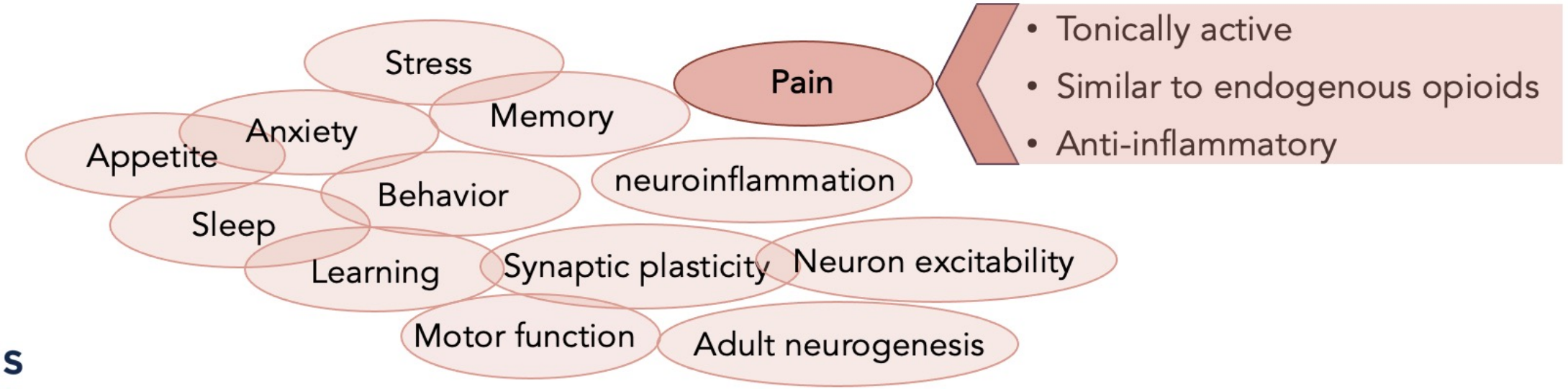
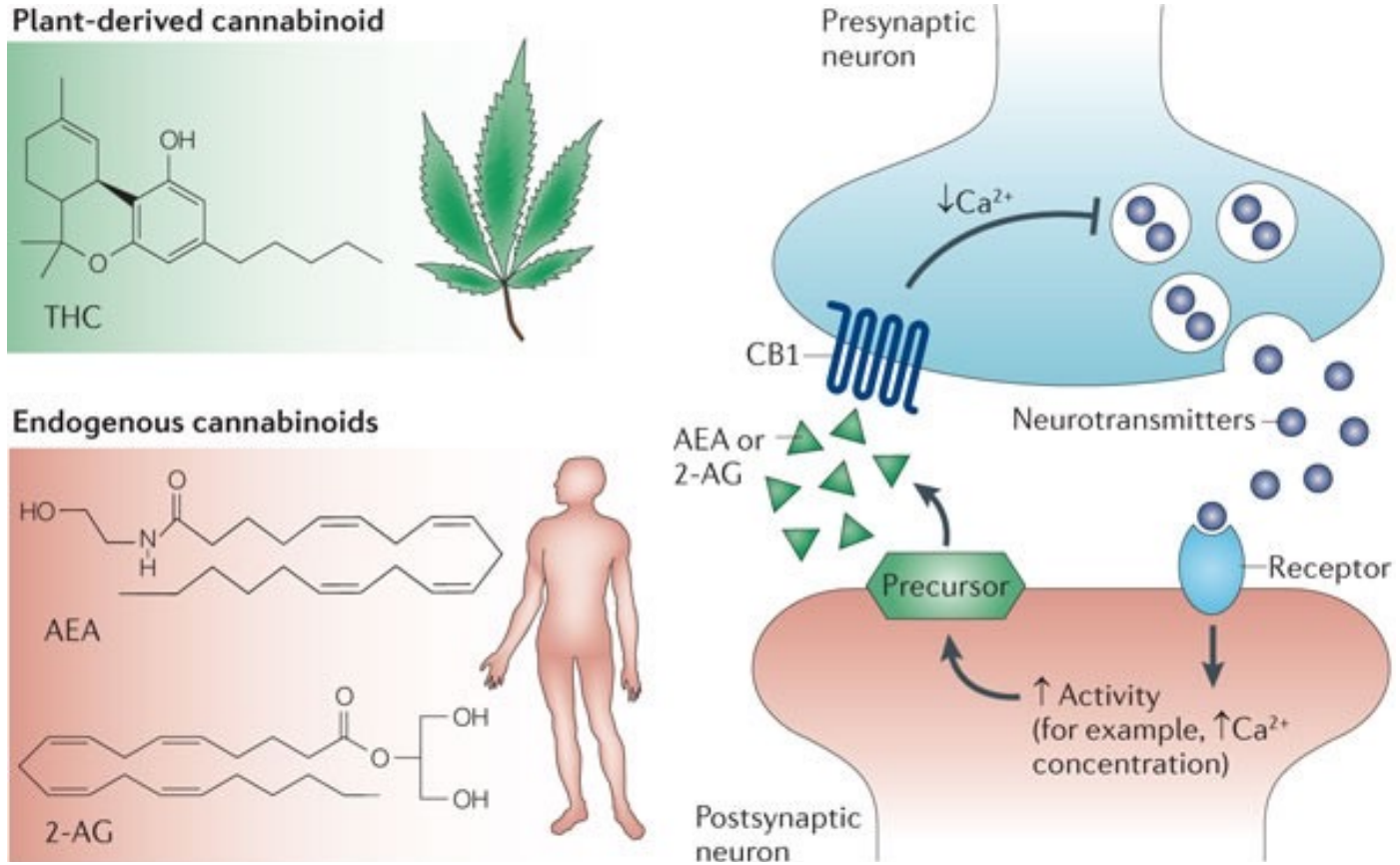


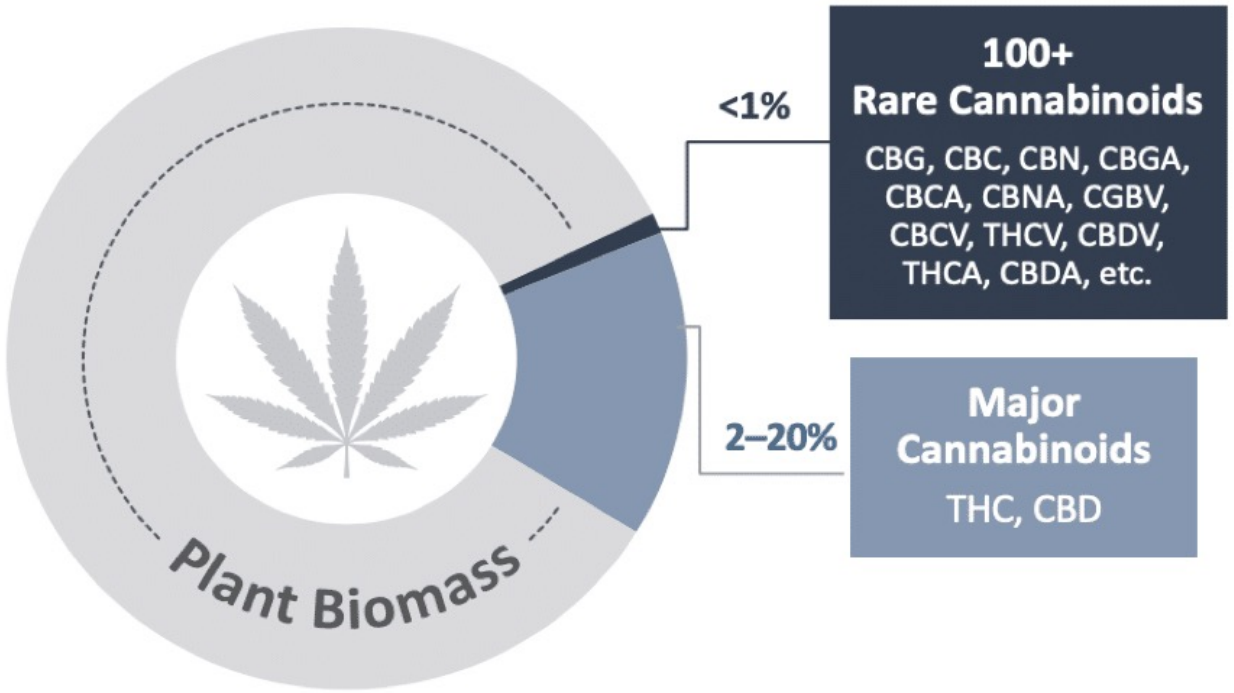
CBD

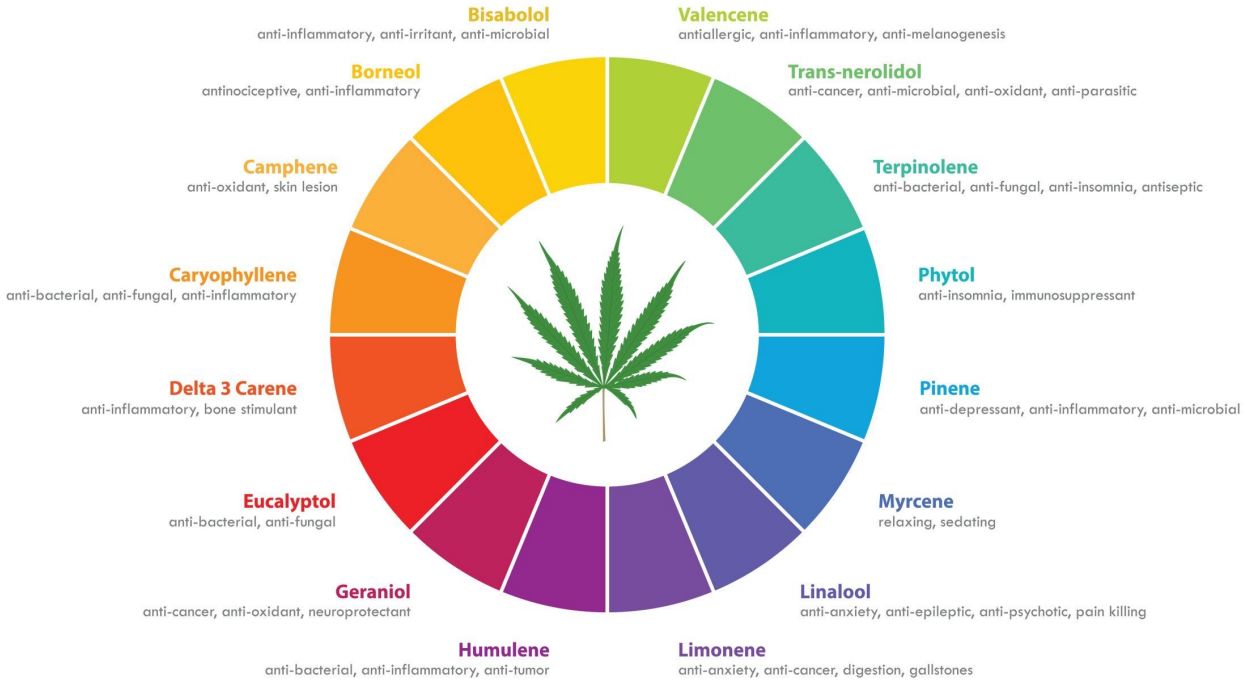
- Cannabinoid essentials:
  - Receptors
  - Endocannabinoids
  - Enzymes
    - Synthesis
    - Uptake
    - Degradation



CBD

- Cannabis – Cannabinoids and Terpenes





→ CBD, ‘whole plant’/’broad spectrum’ products

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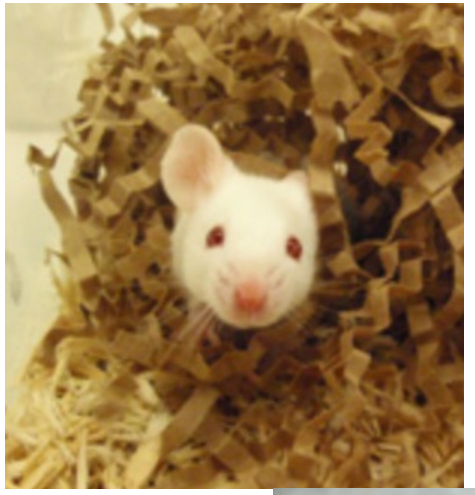
https://papaandbarkley.com/learn/what-are-terpenes-2/
https://www.inmedpharma.com/learn/what-is-cannabinol/

CBD

- Is CBD analgesic?
  - Rodent studies
    - Analgesic, anti-inflammatory
    - Acute, inflammatory and chronic pain
  - Humans
    - Studies are still limited and variable
    - Benefits with THC and/or CBD
    - Neuropathic and advanced cancer pain
    - Limited effect – acute pain, OA pain



CBD

- Is CBD analgesic?
  - Dogs
    - 5 studies on OA pain in dogs – 2 mg/kg PO q12hr
    - Mixed results
    - Questionnaire studies – possible analgesia
    - Most objective study – no effect
  - Cats
    - Case report of positive efficacy with OA pain 0.5 mg/kg q 12 hr
    - No difference in post-op pain score for spay 2 mg/kg before surgery

CBD

- Can I recommend CBD to a client?
  - Marijuana legalization does not apply to animals
  - CBD derived from hemp is not illegal
  - CBD is not FDA approved for animal use as a food or drug

Legally risky

- No medical claims
- Follow label guidelines
- GMP
- Audits
- Third party testing

Librela – Bedinvetmab

- Anti-NGF Monoclonal Ab
- Once a month injection
- Possible adverse effects:
  - Ataxia, seizures, paresis, recumbency, urinary incontinence, polyuria, polydipsia death, euthanasia
- Careful client communication, education and informed consent

Non-Pharmaceutical Options

- Physical therapy
- Diet/body condition
- Acupuncture
- Non-slip flooring
- Soft bedding
- Temperature
- Exercise modification (stairs)

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https://www.fearfreehappyhomes.com/acupuncture-can-it-help-reduce-pet-stress-at-the-vet/

Case

- Wolfie – 9 yr MC Great Dane
  - Osteosarcoma of right front limb
  - Palliative care
  - Current treatment:
    - Meloxicam
    - CBD
  - Still painful…what next?

Case

- Wolfie – 9 yr MC Great Dane
  - Current treatment:
    - Meloxicam
    - CBD
  - Phase in:
    - Gabapentin 10 mg/kg
    - Amantadine 3 mg/kg
    - SQ ketamine injections 0.5 mg/kg
    - Maropitant 1 mg/kg
    - Acupuncture

Take Home Points

- Multimodal pain management is most effective, especially in chronic pain states
- There are numerous analgesic options available for inpatients and outpatients
- Monitor pain levels and adjust medication as needed

Questions, Comments, Discussion?