FWRA Analgesia Review

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Nociception vs. Pain

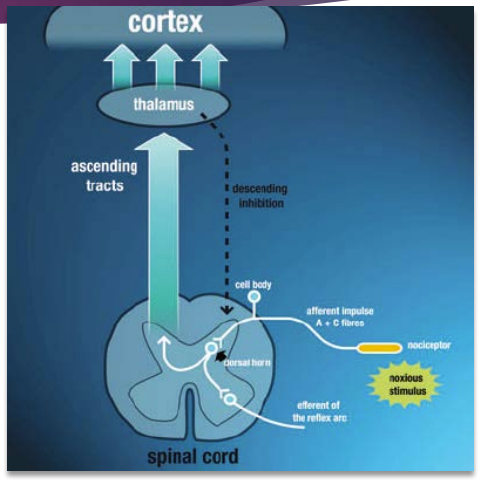
- Nociception: sensory nervous system's response to certain harmful or potentially harmful stimuli
- Pain: unpleasant sensory AND **emotional experience** associated with actual or potential tissue damage.

Who has Pain?

- Vertebrates: nociceptors, spine, brain
- The "cortical" processing gear is a little different between vertebrate orders.
- Does different mean no pain?

Pain Physiology 101
How Pain Travels

- Signal Transduction = stimulus hits a pain receptor (nociceptor)
- Signal Transmission = message travels from the receptor axon to spinal cord
- Modulation = spinal cord to brain (thalamus)



Journal of Small Animal Practice (2012) 53, 377–386 DOI: 10.1111/j.1748-5827.2012.01243.x

Pain Perception

- Governed by **3** major parts of the brain
  - The thalamus: Sensory integration
  - Brainstem: internal pain relief mechanisms
  - Cortex: defines pain and suffering

WHERE WE DIFFER: Cortex

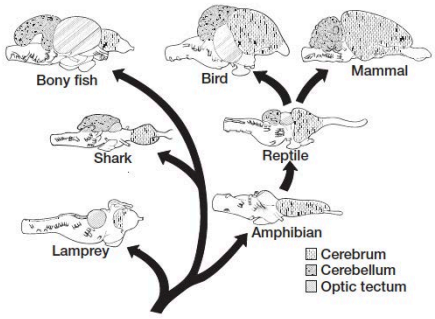


FIGURE 16.33 Evolution of the vertebrate brain. Note the phylogenetic enlargement of the cerebrum and cerebellum.

Kardong 2011. Vertebrate Comparative Anatomy & Function

Types of Pain

- Somatic: skin, muscle, bone = well localized
- Visceral: slow burning, poorly localized
- Neuropathic: Up-regulated spinal signal from a previous incident
  - Stabbing and burning, diffuse or localized
  - Chronic
  - Not compatible with release → impairs function to thrive

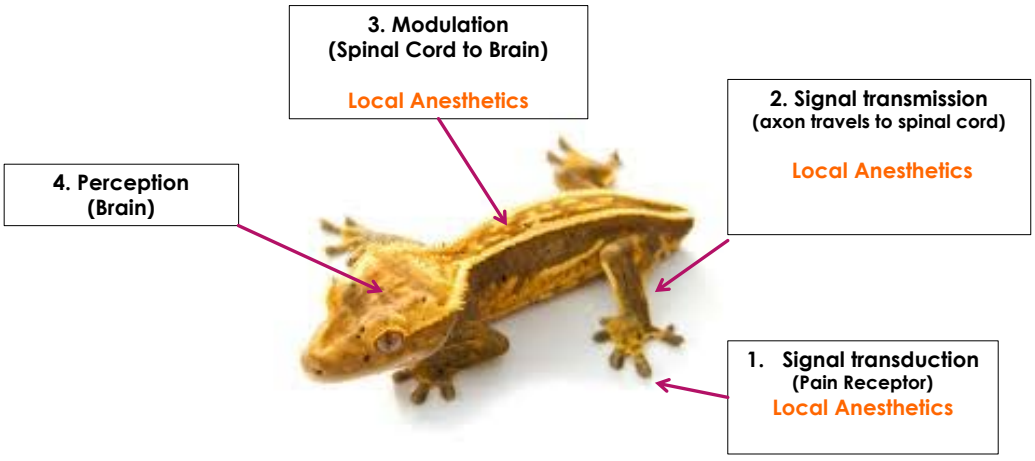
Common Analgesics for Wildlife

- Local Anesthetics
- NSAIDS
- Opioids
- Tramadol
- Ketamine
- Gabapentin

Local Anesthetics

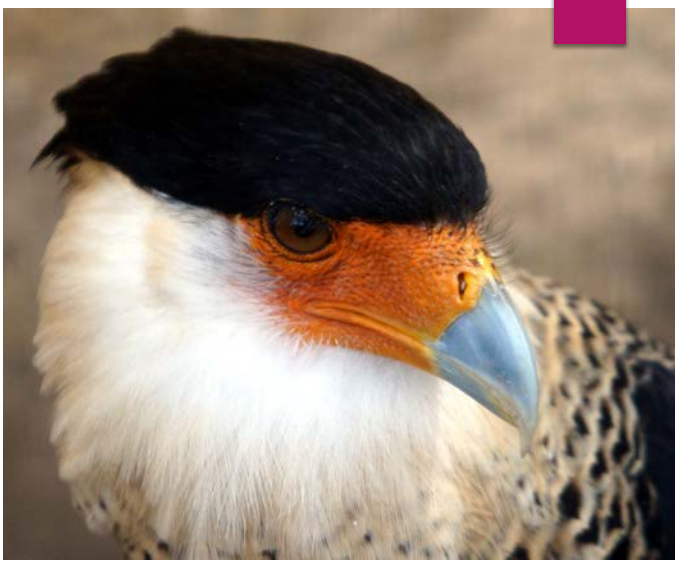
- Block pain transmission at the receptor level or in the spine
- Na-channel blockers (Lidocaine):
  - blocks Na influx into nerve cells, which prevents signal
- Bupivacaine
  - Na, K channels, NMDA antagonists?

Where Locals Work



"It's easier to prevent pain than to chase it."

Mader 2013



Local Anesthetics

- Clinical Pros:
  - Decrease morbidity before and after you handle tissue
  - Injectable and topical options
- Cons:
  - Short duration of action
  - Toxicity → intra-articular, cardiac administration, DEATH if given IV

Clinical Targets: NSAIDS

- Reduces inflammatory COX products
- "Protective/normal" PGs (Cox1 products)
- "Inflammatory" PGs (Cox2 products)
- Can inhibit ALL COX isoforms or preferably inhibit one COX pathway

NSAID Medications

Non Selective: Cox 1 & 2

- Flunixin Meglumine
- Ketoprofen
- Deracoxib
- Piroxicam

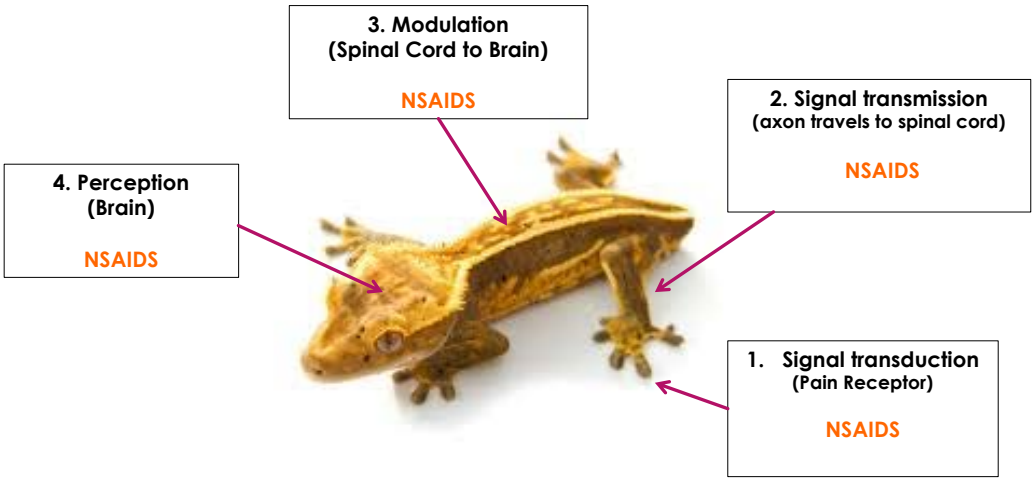
COX 2 >>1

- Carprofen
- Celecoxib
- Robenacoxib
- Meloxicam

NSAIDS

- Clinical Pros:
  - Decrease Acute & Chronic pain
  - Affects all pain machinery
- Clinical Cons:
  - Can cause gastric ulcers, kidney disease, clotting issues (Cox 1 suppression)
  - Dangerous to use in severely dehydrated animals

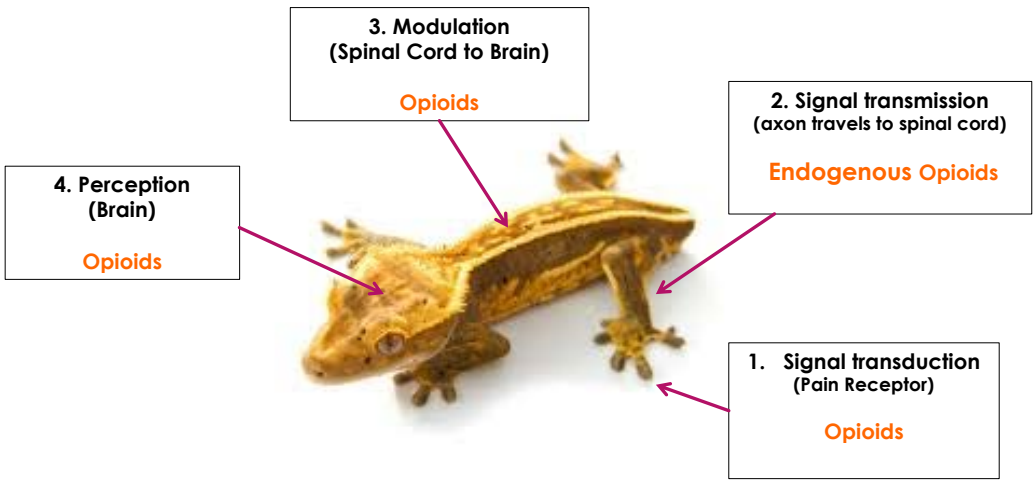
Where NSAIDs Work



Clinical Targets: Opioids

- Mu, kappa, delta receptors
- Mu-agonists : Internal pain relief mechanisms in the midbrain
  - Receptors in the thalamus and cortex and spinal cord
- Mu and delta agonists block excitatory AA release from primary afferents

Where Opioids Work



Opioids

- Clinical Pros:
  - Multiple targets to relieve pain
  - Can cause profound pain relief
- Clinical Cons:
  - Side effects: Respiratory depression, GI stasis, Sedation
  - Controlled substances

Evidence for Opioids: Mammals

- Rabbits: 0.05 mg/kg Buprenorphine decreases fecal motility
- Caution with hydromorphone, oxymorphone and fentanyl in rabbits
- Can alter mentation – challenges with monitoring

Evidence for Opioids: Birds

A lot of species variation and dose variation

Literature: Buprenorphine, Fentanyl, Butorphanol, Tramadol

Tramadol

- Parrots:
  - 15 mg/kg PO q8 (Geelen 2013)
- Columbiformes:
  - 7.5mg/kg PO q8-12h (Black 2010)
- Raptors:
  - Eagles: 5mg/kg PO q12 (Souza 2013)
  - Red Tailed hawks: 11 mg/kg PO q12-24h (Souza 2011)

Evidence for Opioids: Reptiles

- Turtles = mammal mu receptors
- Lizards – mixed bag
- Snakes- mu resistant/centrally unresponsive at low doses?

- Tramadol
  - **Turtles**: 5 mg/kg IV/SQ q24-48 (Baker 2011)
  - Lizards: 2.5-5 mg/kg q12-24h

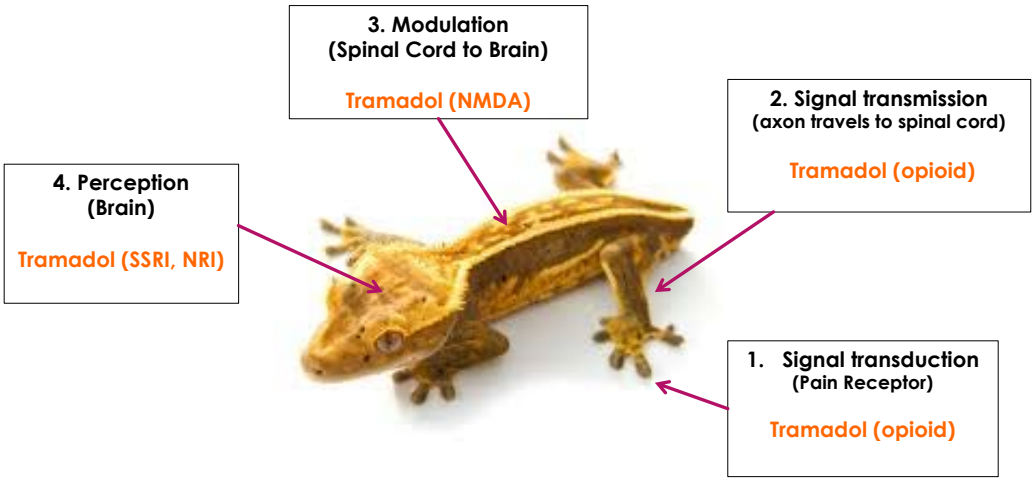
- Hydromorphone 0.5 mg/kg- monitor respiration (Mans 2012)

- Fentanyl Patches:
  - Snakes: 12.5 mcg q7d in snakes <1.5kg (Darrow 2010, Sladky 2017)
    - > 2kg: 25 mcg patch
  - Lizards: 12.5 mcg patch <2 kgs (Gamble 2008)
    - >2 kgs: 25 mcg patch

Clinical Targets: Tramadol

- Synthetic analog of codeine with activity at mu, kappa, and delta opioid receptors, SRI/ NRI
- M1: O-desmethyltramadol metabolite
  - Affinity to mu: 200 times greater than tramadol alone
  - Affinitity to mu: 6000 times less than morphine
- Decreased the opioid side effect profile!!

Where Tramadol Works



Clinical Targets: NMDA antagonists

- Inhibits Na^+ and K^+ channels and serotonin, dopamine re-uptake in the spinal cord
- "Decrease wind-up". Reduces the hyper-excitability of neurons in the dorsal horn of the spinal cord
- Repetitive pain receptor firing = slow, cumulative, continual pain

Clinical Targets: Gabapentin

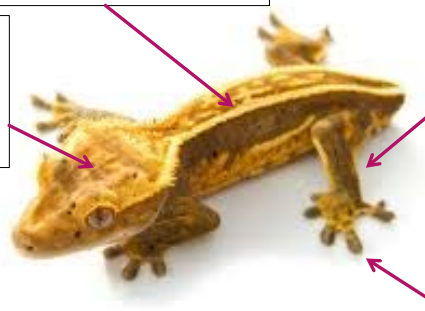
- Binds subunit on voltage gated Ca channels o minimize trafficking of chronic pain signal in CNS
- Treats neuropathic pain
- Anti-epileptic

Where Everything Works

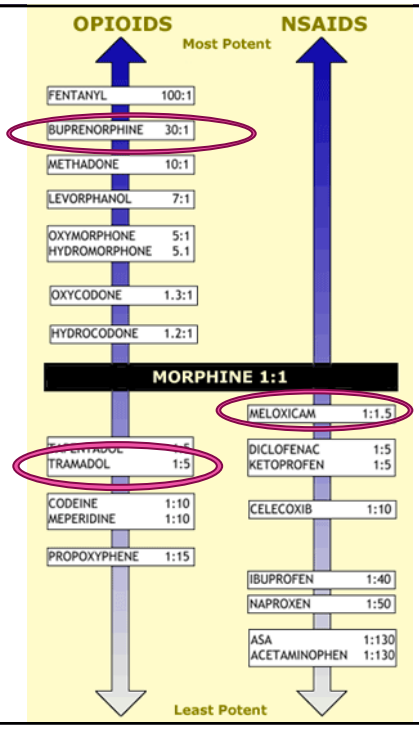
3. Modulation
(Spinal Cord to Brain)
Opioids
Locals anesthetics
Ketamine
NSAIDS
Tramadol
Gabapentin

2. Signal transmission
(axon travels to spinal cord)
Local anesthetics
NSAIDS
Endogenous Opioids
Tramadol

4. Perception
(Brain)
Opioids
NSAIDS
Tramadol
Gabapentin



1. Signal transduction
(Pain Receptor)
NSAIDs
Opioids
Local Anesthetics
NSAIDS
Tramadol



How Do They Compare?

Doses: NWRA Wildlife Formulary 4th ed, 2017


SHUT YOUR BEAK....I'VE HEARD ENOUGH