# Neuroplasticity in Opioid Addiction

JAKE BARNES
WITH DR. MARGRET FLANIGAN AND DR. BILL FLYNN

# Introduction

- Opioid: class of prescription drug used for pain diarrhea, cough suppression, recreational used for euphoric high (ex. heroin)
  - High abuse potential and addiction rate
  - Desensitization and withdraw occur with chronic use

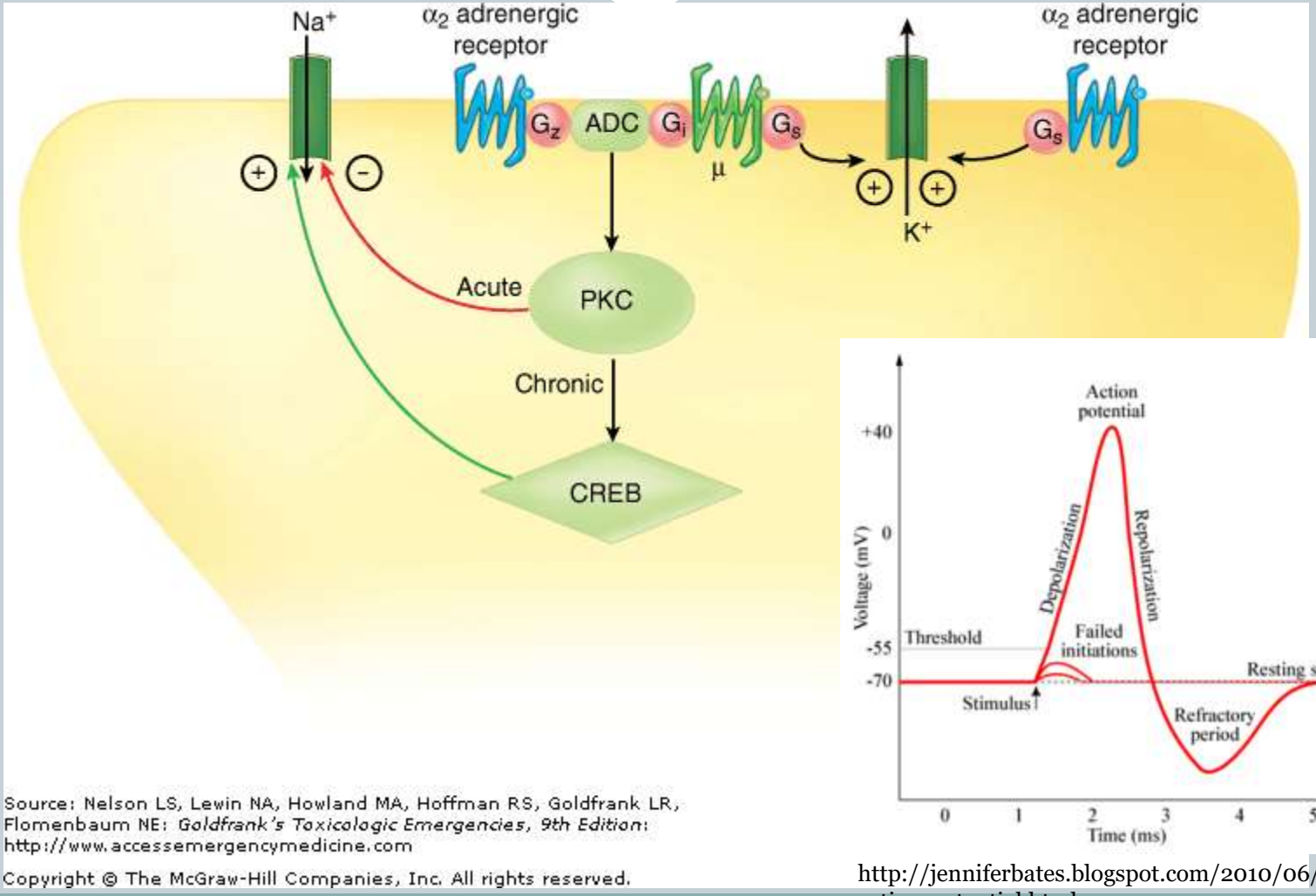
# Outline

- Endogenous Opioid System (EOS)
- Opioid Receptors
- Neural Changes

# EOS

- Endogenous opioids bind to opioid receptors to inhibit the release of neurotransmitter
- Receptors usually on GABA neurons, so they stop inhibition
- Generally results in the release of dopamine for pain modulation, euphoric feelings

# Mechanism of Action for Opioid Receptors



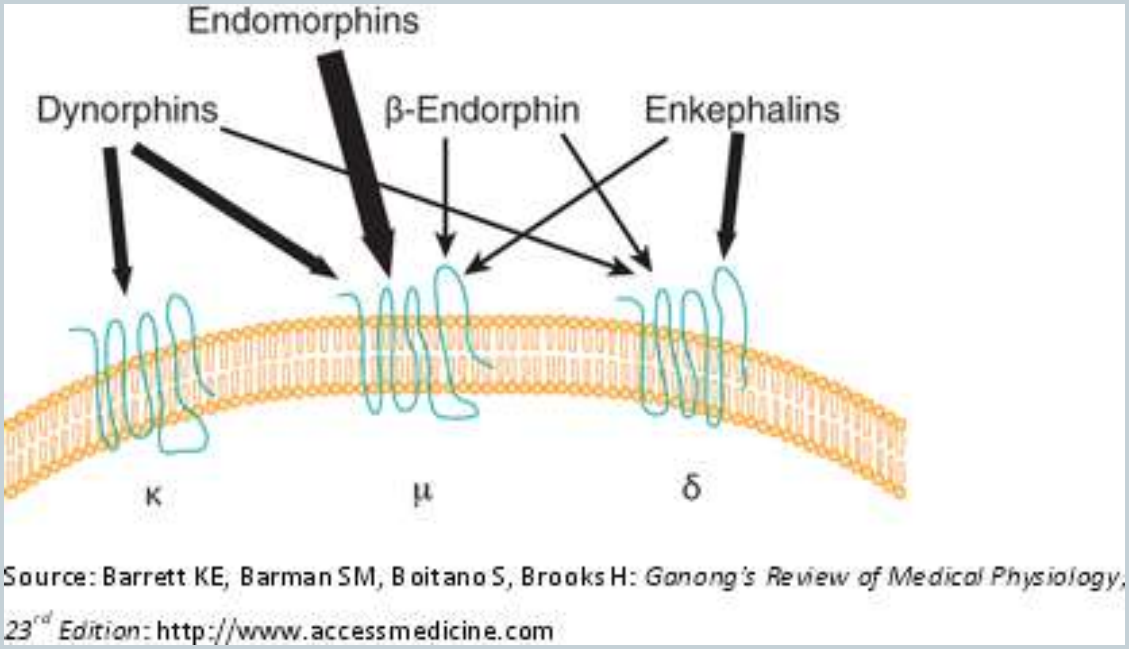

Source: Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE: *Goldfrank's Toxicologic Emergencies, 9th Edition*: http://www.accessemergencymedicine.com






http://jenniferbates.blogspot.com/2010/06/like-action-potential.html

# Endogenous opioid affinities for opioid receptors




Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology*, 23rd Edition: http://www.accessmedicine.com

Thicker arrows indicate higher affinities for receptors

# Opioid Recepors

- Mu:
  - most important receptor
  - Target of nearly all drugs
  - Internalization with chronic exogenous opioids (Bailey and Connor, 2005)
- Kappa
  - Some role in pain modulation
  - Can cause dysphoria, ↑ with cocaine withdraw
- Delta
  - Some supraspinal analgesia
  - May colocalize with CRF peptides (Williams and Milner, 2011)
    - Implications for stress in withdraw
  - Competitive inhibition of mu receptors and heterodimerization with mu receptors: desensitization

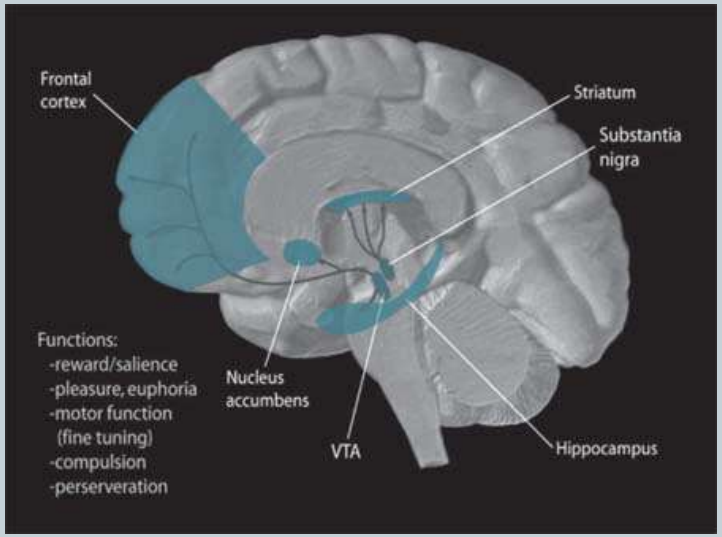
# Physiological effects of opioid receptor types

| Receptor | Effect |
|---|---|
| Mu | Analgesia (medial thalamus) |
| | Euphoria |
| | Sedation |
| | Respiratory Depression (medulla) |
| | Constipation (GI tract) |
| | Meosis (substantia negra) |
| Kappa | Analgesia (medial thalamus) |
| | Sedation |
| | Meosis (substantia negra) |
| | Diuresis |
| Delta | Supraspinal analgesia (medial thalamus) |

Barrett et al., 2011

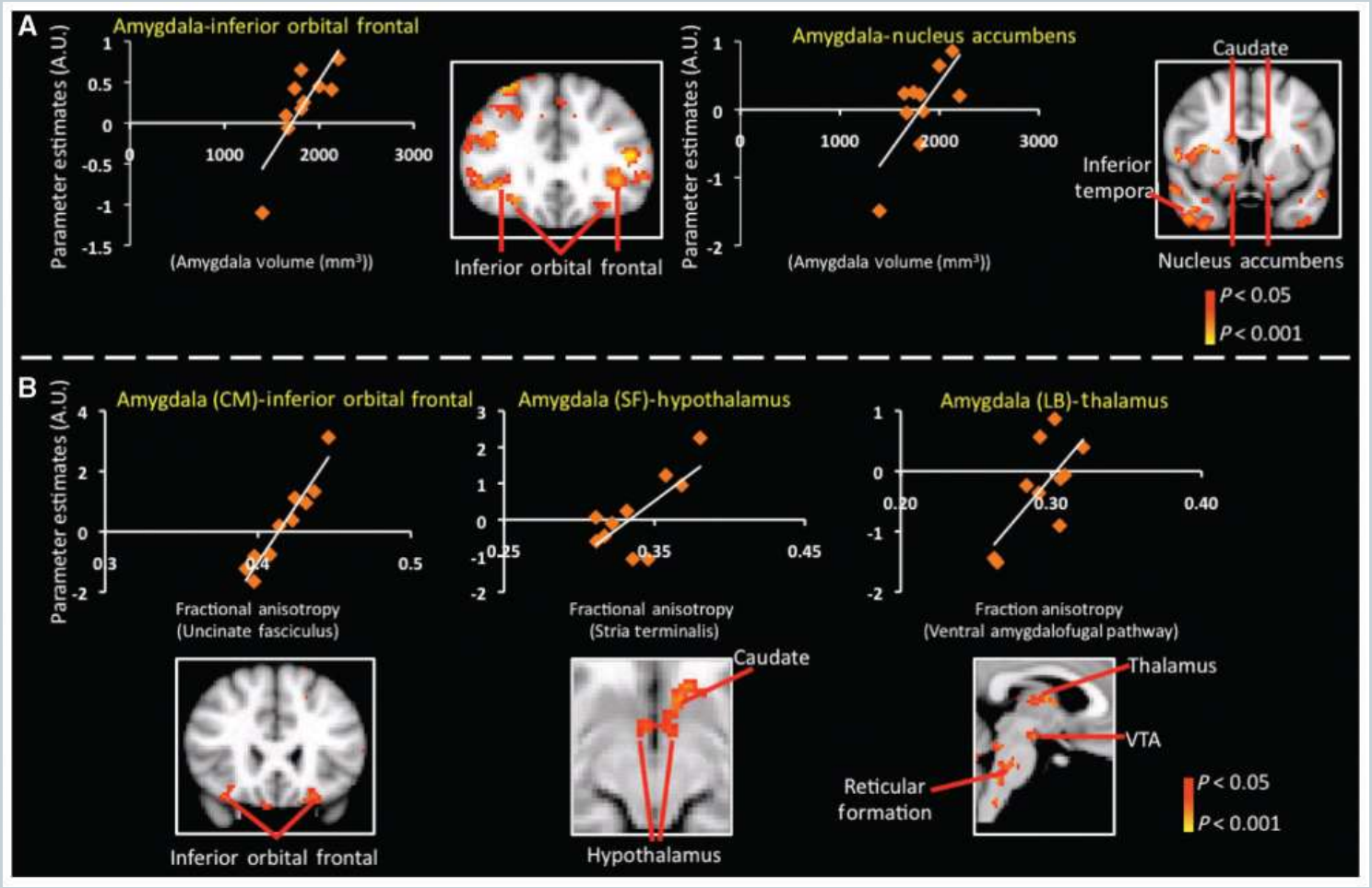
# Changes In Functional Connections

- Amygdala
  - ↓functional connectivity with:
    - Insular cortex (emotions)
    - Nucleus accumbens (addiction)
- Nucleus Accumbens-
  - ↓ functional connectivity with:
    - Frontal lobe (decision making)
    - Hippocampus(emotional memories)
    - Amygdala (emotional memories)
    - Periaqueductal gray (brainstem activity)
- VTA
  - Increase in delta receptors, decrease in mu receptors




http://en.wikipedia.org/wiki/File:Dopamine_Pathways.png

# Structural and functional connectivity changes from chronic use of Rx opioids




Upadhyay et al., 2010

# Conclusions

- Opioid receptor expression is varied with opioid use:
  - ↓ number of mu receptors
    - Via internalization
  - ↑ number of delta receptors and heterodimerization
- Mesolimbic reward system brain areas: VTA, hippocampus, nucleus accumbens, and amygdala change their connectivity with opioids

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