The Effect of Opioids on Brain Function, Pain, and Opioid Use Disorder

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Learning Objectives

- Describe the effects of opioids on brain function
- Define the effects of opioids on pain relief over time
- Identify brain opioid receptors and their function
- Differentiate between full and partial mu opioid receptor agonists and antagonists for opioid use disorder
- Identify the stages of addiction and associated neuroanatomy

General Opioid Receptor Function

Mu-Receptor Analgesia Respiration Sedation Euphoria	**Delta-Receptor** Analgesia Dysphoric affect Respiration GI Motility Hormone release
Kappa-Receptor Analgesia Dysphoric affect Sedation	**Sigma-Receptor** Respiration Dysphoric affect Hallucinogenic

Opioid Agonists

Endogenous Opioids

Mu receptor: beta-endorphin
endomorphin

Delta receptor: encephalins,
beta-endorphin

Kappa receptor: dynorphin

Exogenous Opioids

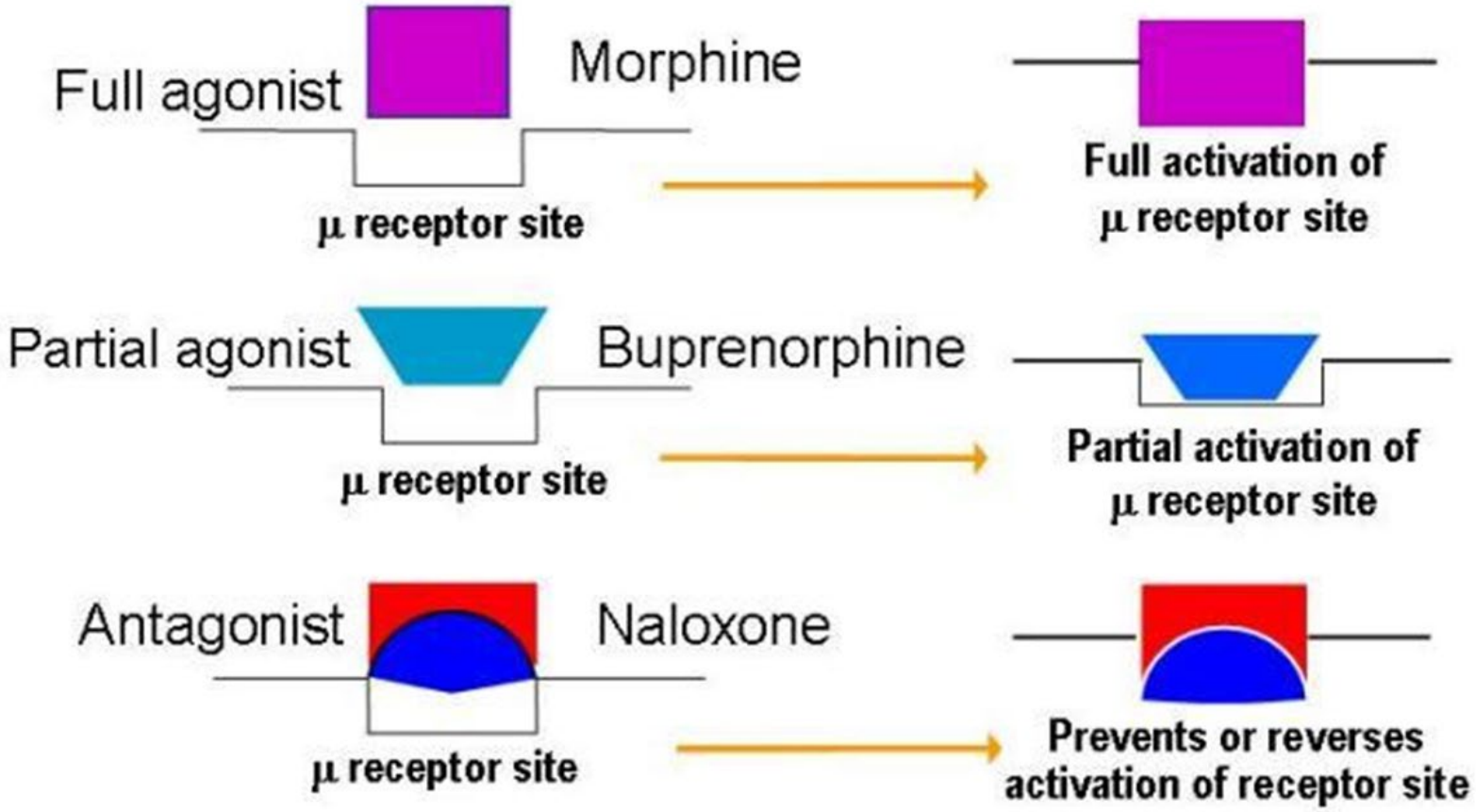
Mu receptor: morphine, fentanyl,
methadone, hydrocodone,
oxycodone, meperidine, tramadol

Delta receptor: morphine, fentanyl

Kappa receptor: morphine, fentanyl

Naloxone and naltrexone are mu, delta, and kappa receptor antagonists

Mu (μ) Receptor Activation



Cherny NI. Opioid Analgesics. Comparative Features and Prescribing Guidelines. *Drugs*. 1996;51:713-37.
Walsh SL, et al. *Clin Pharmacol Ther*. 1994;55:569-80.
Walsh SL, et al. *J Pharmacol Exp Ther*. 1995;274:361-72.

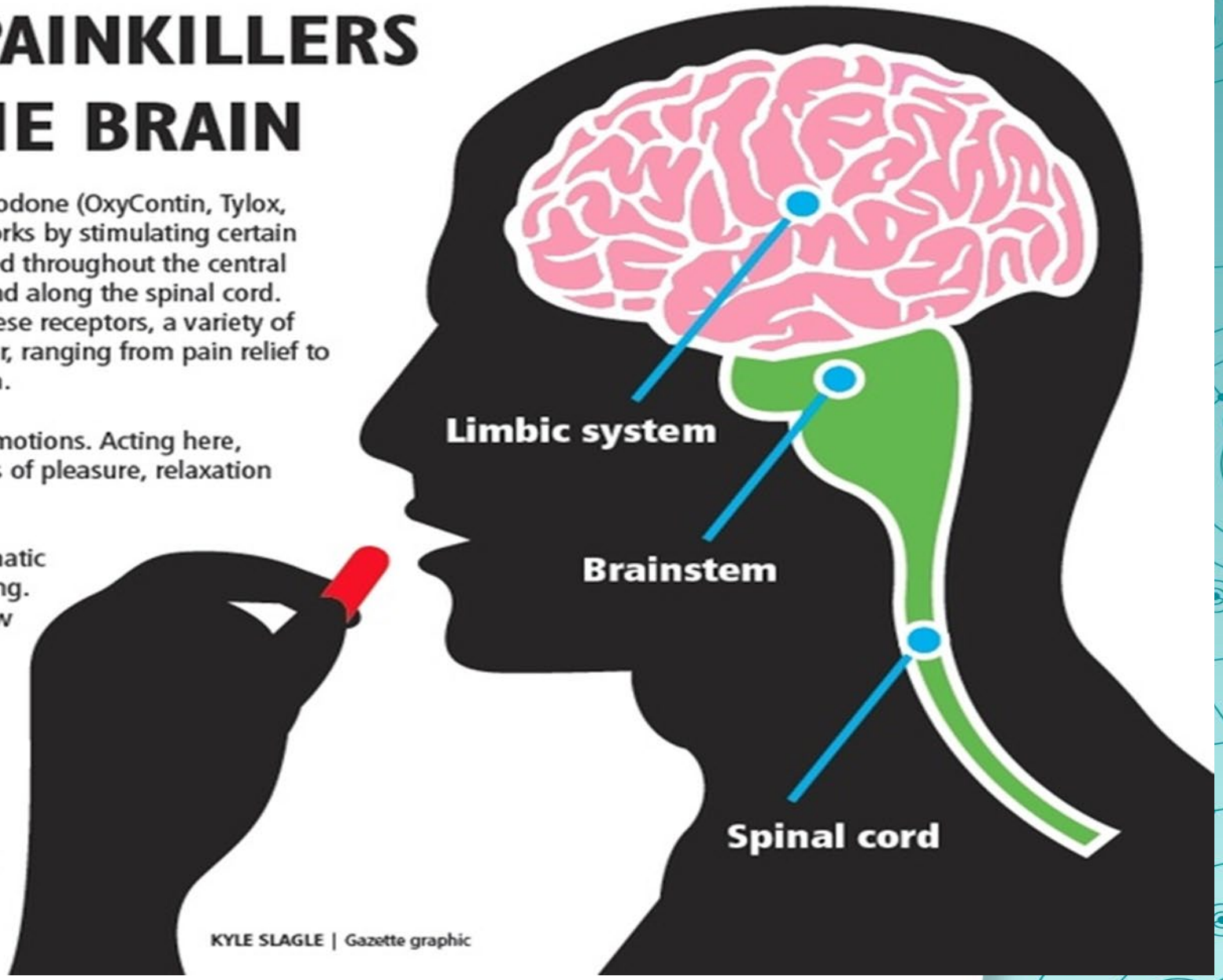
HOW Rx PAINKILLERS AFFECT THE BRAIN

When a painkiller such as oxycodone (OxyContin, Tylox, Percocet) enters the body, it works by stimulating certain opioid receptors that are located throughout the central nervous system, in the brain and along the spinal cord. When the chemical binds to these receptors, a variety of physiologic responses can occur, ranging from pain relief to slowed breathing and euphoria.

The **limbic system** controls emotions. Acting here, painkillers can produce feelings of pleasure, relaxation and contentment.

The **brainstem** controls automatic body functions such as breathing. Acting here, painkillers can slow breathing, stop coughing and lessen the intensity of pain.

The **spinal cord** transmits sensations from the body. Acting here, painkillers bond with the spinal cord to decrease the intensity of pain.



SOURCES: National Institute for Drug Abuse, Discovery Health, Drug Enforcement Agency

KYLE SLAGLE | Gazette graphic

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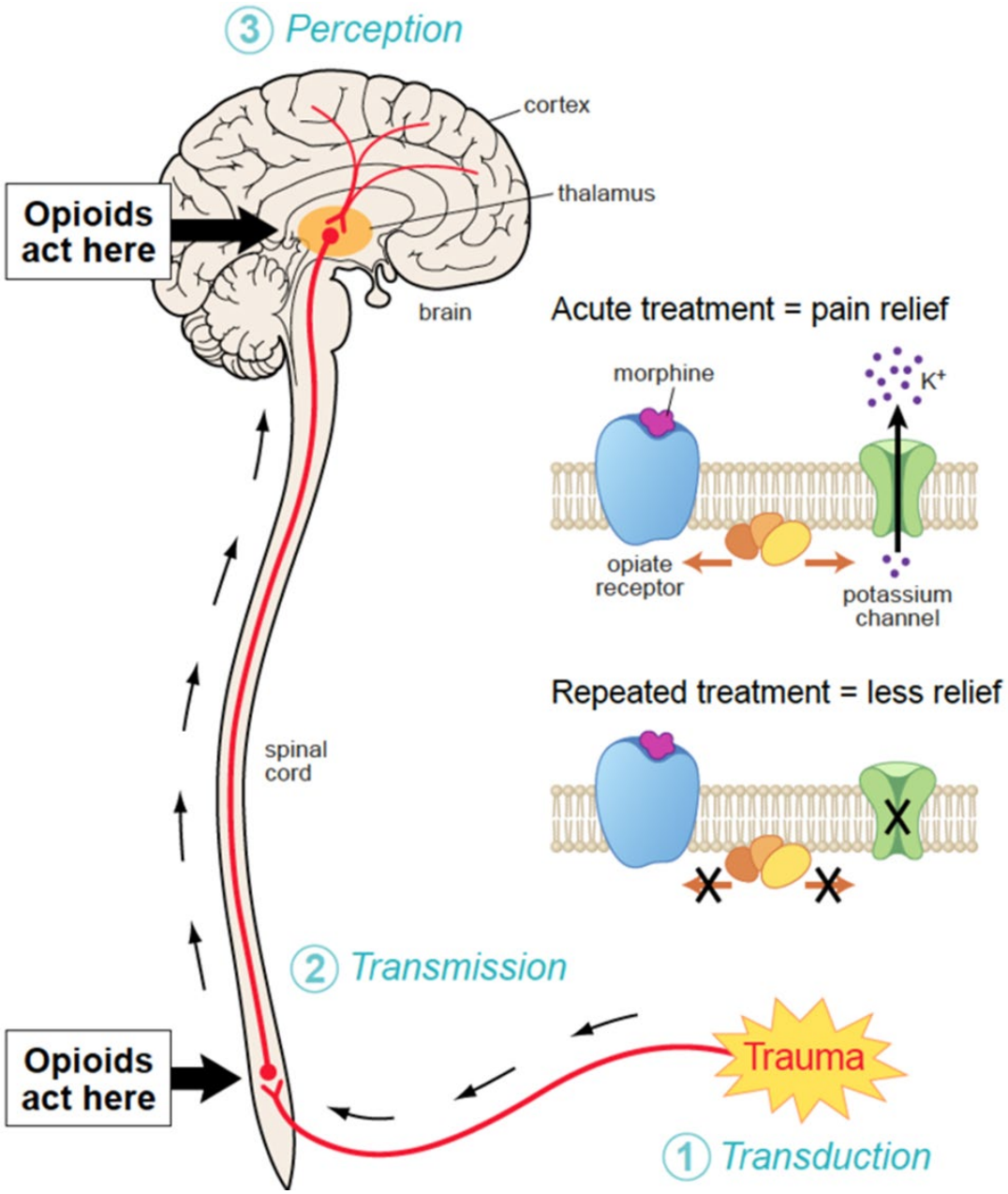
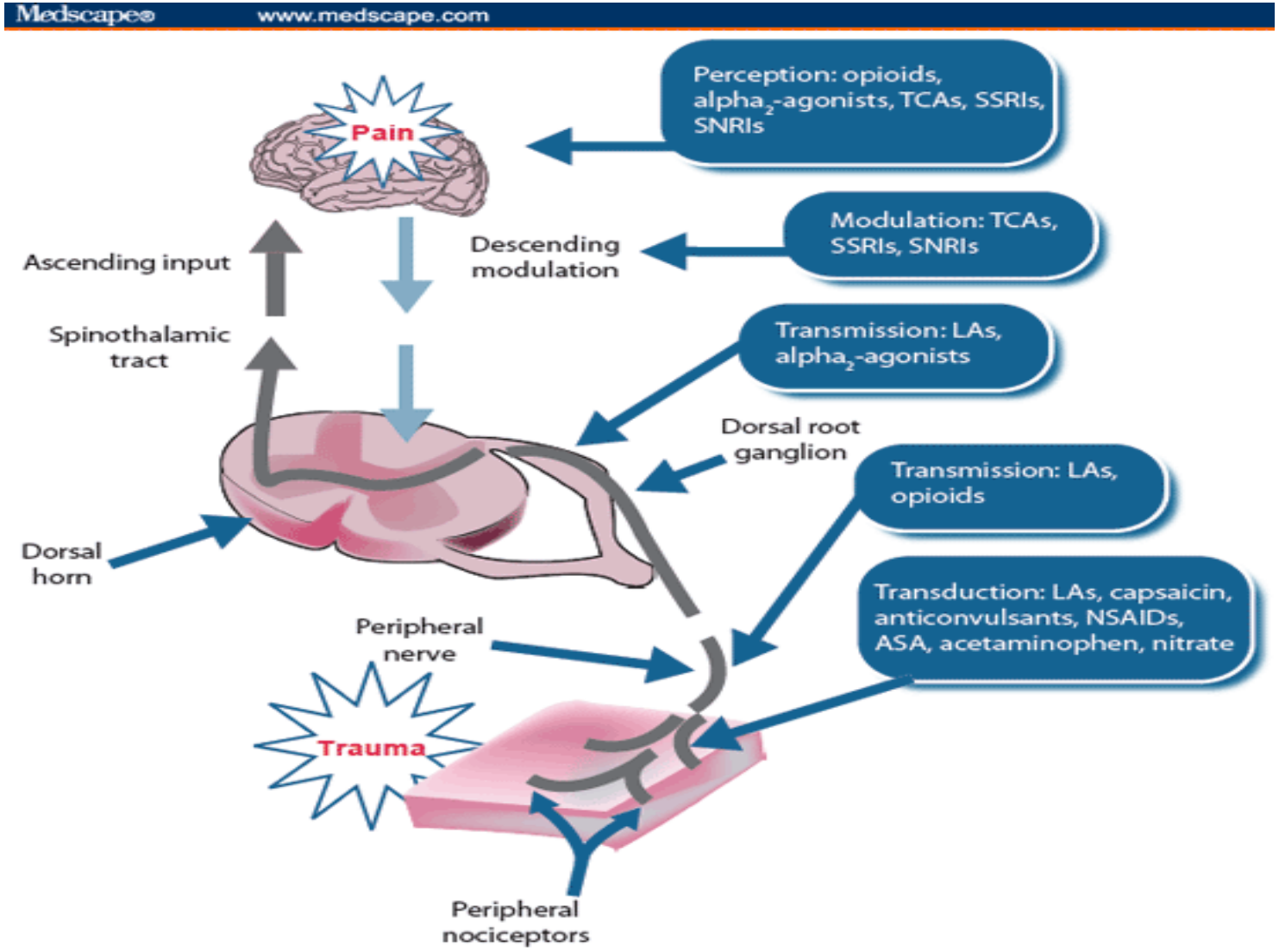
National Institute on Drug Abuse; Centers for Disease Control and Prevention

Effect of Opioids on Pain Relief Over Time



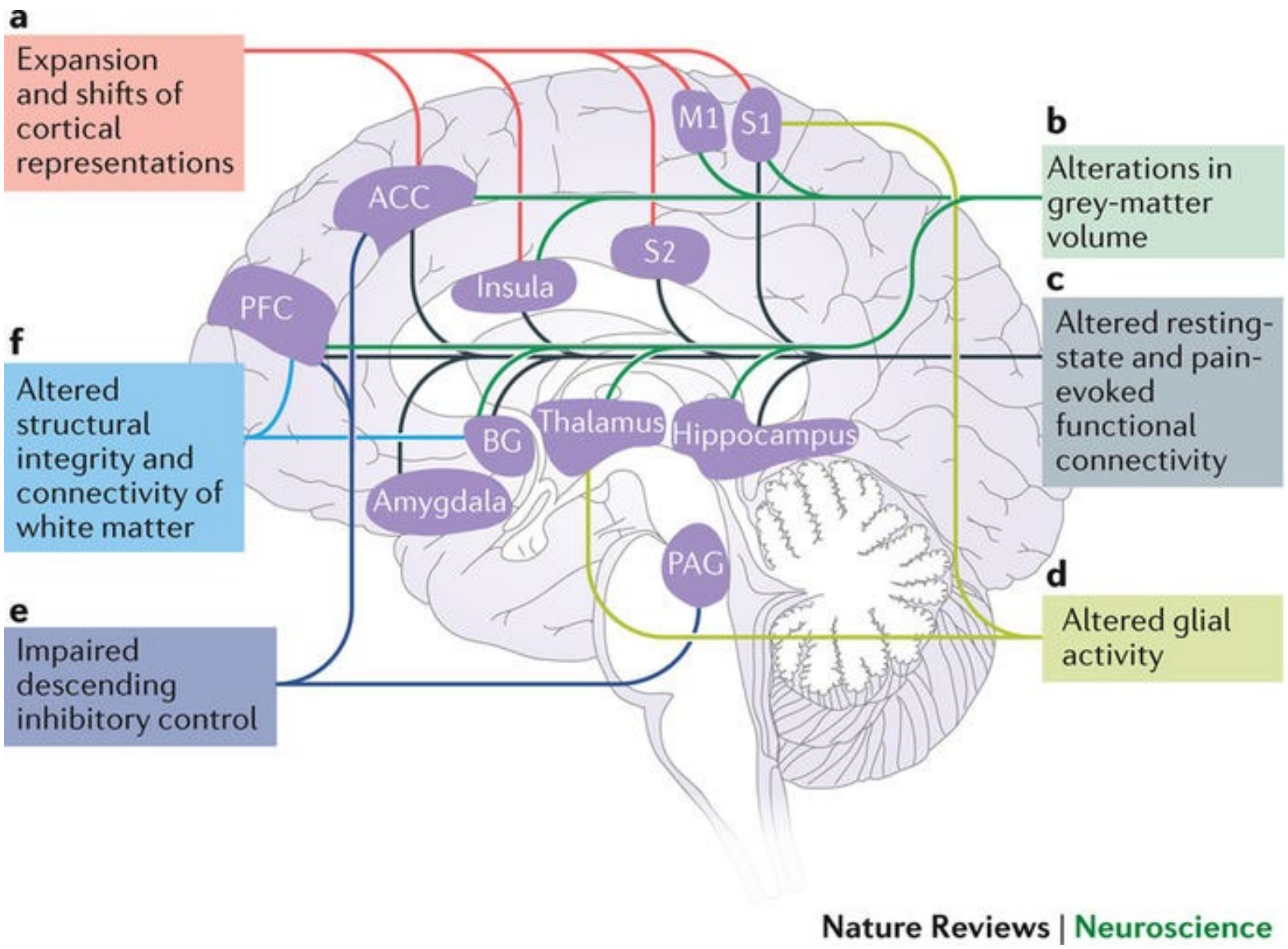
Opioids, Nociception (Pain), Anti-Nociception (Analgesia)

Multiple Learning and Memory Systems



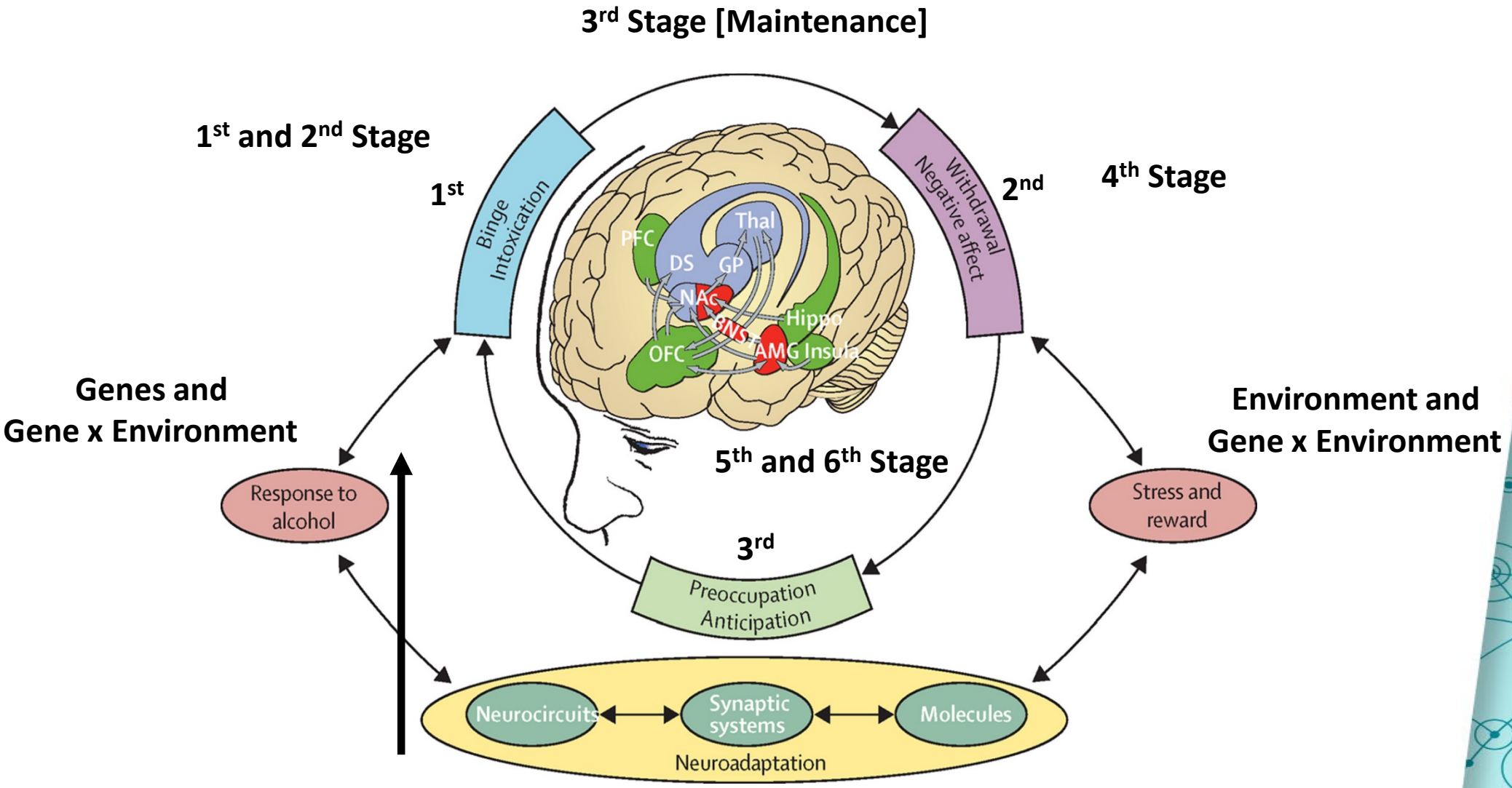
https://www.studyblue.com › ... › Pain Management, Analgesia

Alterations in Neurofunction Associated with Chronic Pain



Kuner and Flor, 2016

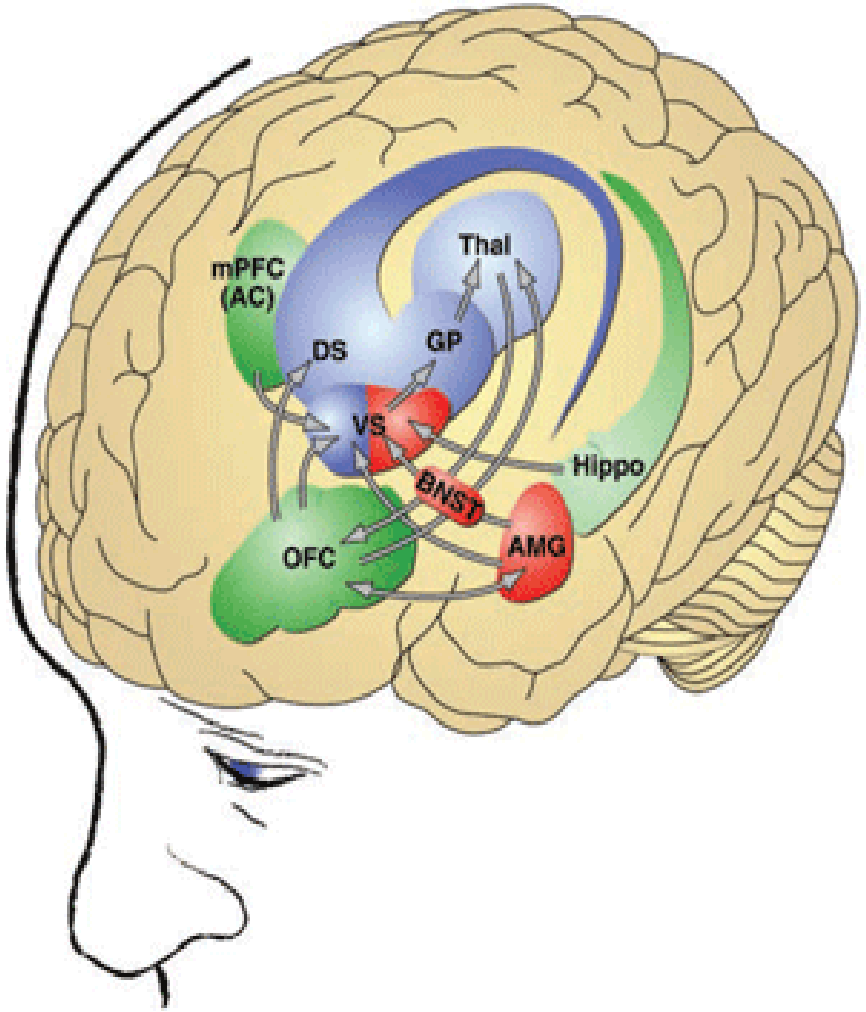
Stages of Addiction



This neurocircuitry is just as relevant for other drugs of abuse (i.e., opiates/opioids).

Koob et al., multiple publications

Stages of Addiction and Associated Neuroanatomy



Binge/intoxication — **1st and 2nd Stages**

- ventral striatum (VS), including nucleus accumbens
  euphoria, reward
- dorsal striatum (DS)
  habits, perseveration
- global pallidus (GP)
  habits, perseveration
- thalamus (Thal)
  habits, perseveration

Withdrawal/negative affect — **4th Stage**

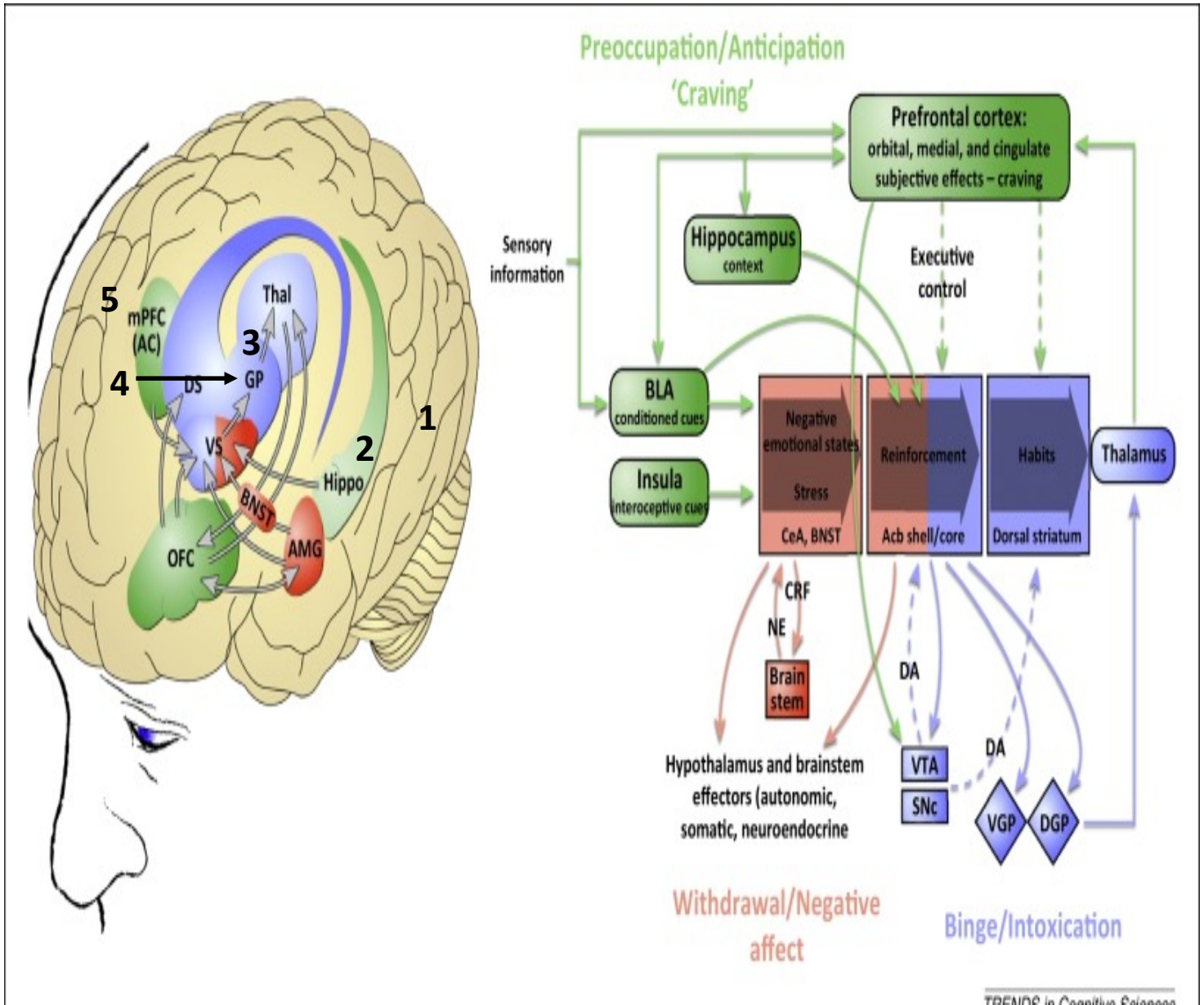
- amygdala (AMG), bed nucleus of the stria terminalis (BNST), together also known as the "extended amygdala"
  malaise, dysphoria, negative emotional states
- ventral striatum (VS)
  decreased reward

Preoccupation/anticipation — **5th and 6th Stages**

- anterior cingulate (AC)
- prefrontal cortex (mPFC), orbitofrontal cortex (OFC)
  subjective effects of craving, executive function
- basolateral nucleus of the amygdala
  conditioned cues
- hippocampus (Hippo)
  conditioned contextual cues

Koob et al., multiple publications

Addiction, Learning, and Memory



Multiple Memory Systems

1) Hippocampus mediates episodic/ autobiographic and spatial learning and memory

2) Amygdala mediates fear and anxiety conditioning/learning and memory Basal-Lateral-Amygdala (BLA), Medial-Amygdala (MeA) and Central-Amygdala (CeA)

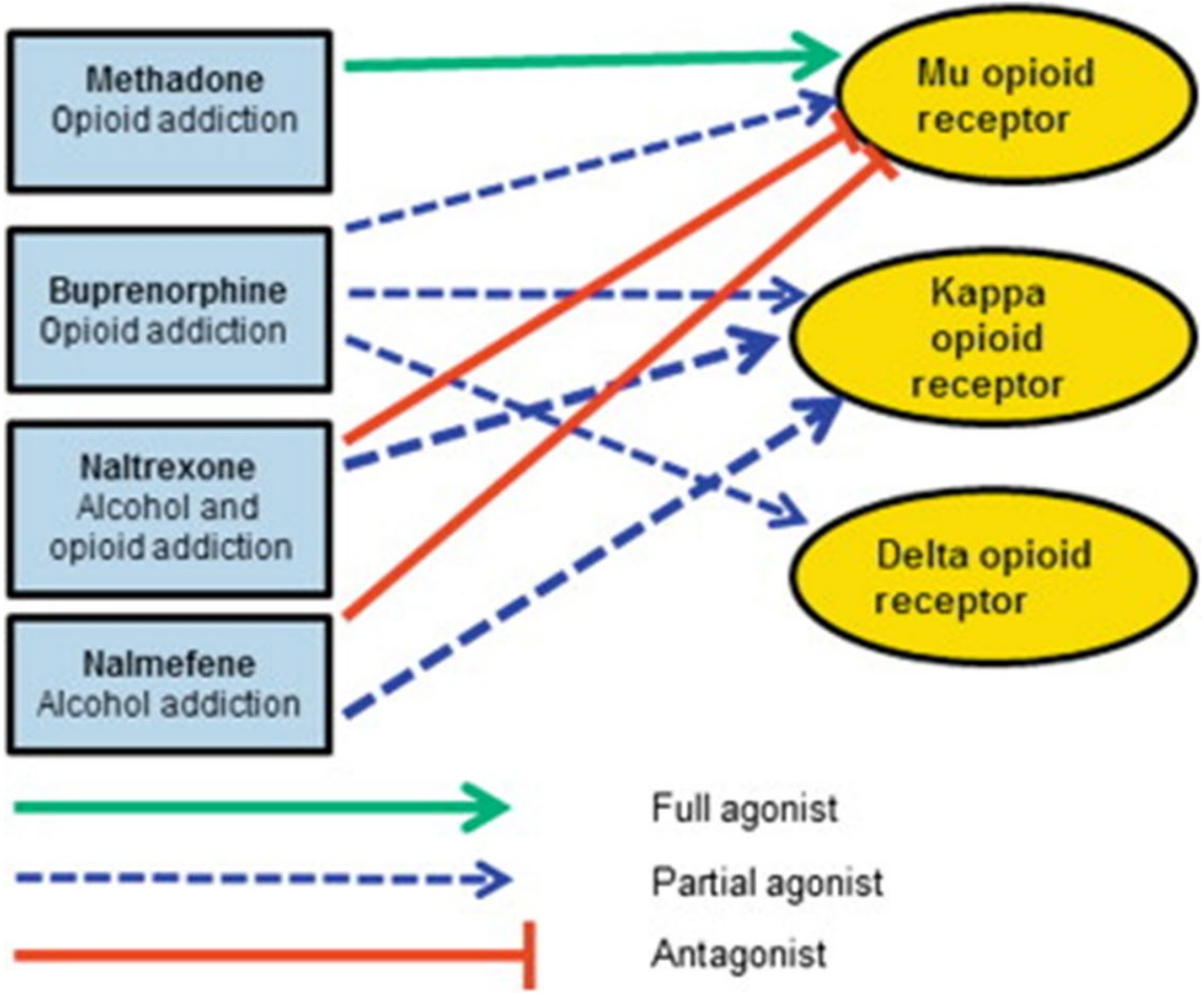
3) Caudate-putamen mediates stimulus-response/habit learning and memory *Dorsal Striatum*

4) Nucleus accumbens mediates reward conditioning/learning and memory (conditioned place preference)—*Ventral Striatum*

5) Dorsal-lateral-prefrontal-cortex (DLPFC) mediates 'working' learning and memory

Koob et al., multiple publications

Medications for Opioid Use Disorder



Summary

- The mu, delta, kappa, and sigma opioid receptors are involved in the actions of opioid drugs
- The limbic system, brainstem, and spinal cord are sites of action for the opioid drugs
- Pain relief from opioid doses decreases over time in chronic pain leading to the need for increasing doses
- Other types of medications can be useful in pain relief (TCAs, NSAIDs, SNRIs)
- Brain structures involved in the stages of addiction include the striatum, thalamus, amygdala, anterior cingulate, prefrontal cortex, and hippocampus