



The Center for Compulsive
Behavior and Addiction

EDUCATION FOR PREVENTION
RESEARCH FOR RECOVERY

Neurobiology of Pain and Addiction

Focus on Opioids

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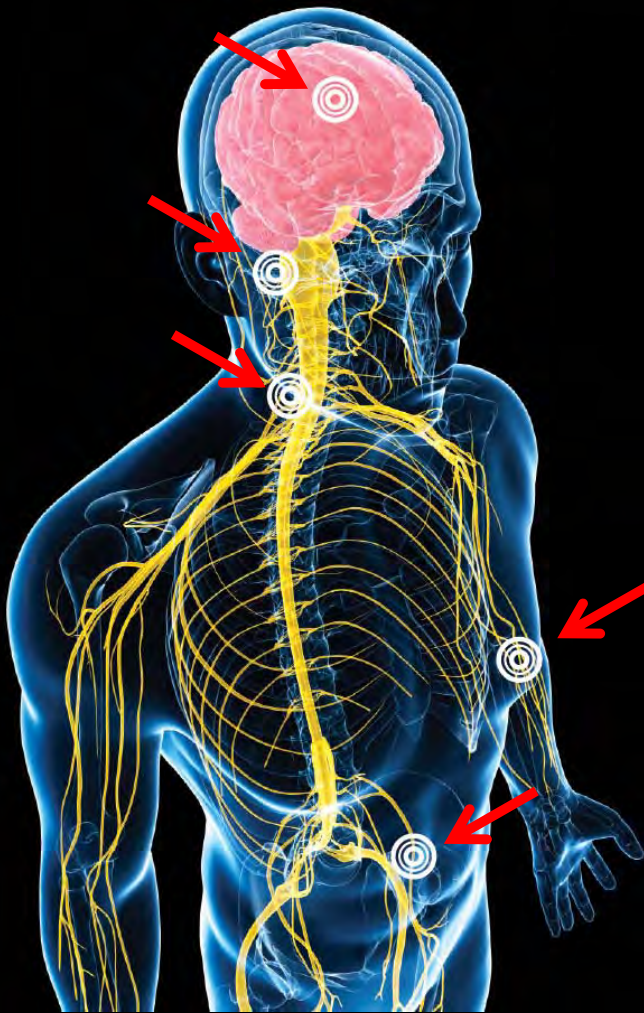
Disclosures

- In the past three years, I have received funding support from the National Institutes of Health and Acadia Pharmaceuticals, Inc. for biomedical research. I have received honoraria for speaking at academic medical centers and universities, and scientific societies. None of this support relates to the topics covered in the current presentation.
- In the past three years, I have served on/am serving as a scientific advisor/board member for the National Center for Responsible Gaming, Beverly, MA; Robert Crown Center for Health Education, Hinsdale IL; the Epworth Village Foundation, York, NB, the Ponce Research Institute, Ponce, PR; the Brain Research Foundation, Chicago, IL; and the Society for NeuroImmune Pharmacology.

Common pathophysiology of addiction and pain

- Temporal and Spatial features
- Allostatic neuro-adaptations
- Assumptions/features for pain to mirror addiction
 - Centralization of the pain experience
 - Reward deficiency theory (within dopamine system)
 - Anti-Reward theory (across systems)

OPIOID FUNCTIONS IN THE BODY



**brain: pain perception,
emotion, reward**

**brainstem: respiratory
suppression**

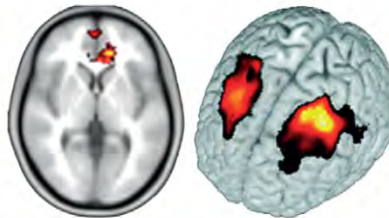
**spinal cord: dampening of pain
signals**

**peripheral neurons: curbs pain
sensation**

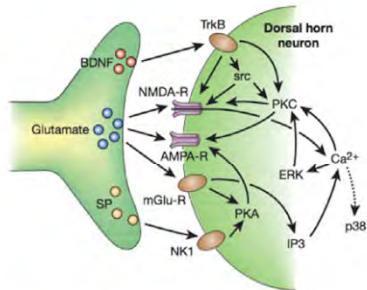
**intestine: inhibition of
peristalsis**

Descartes, 1644

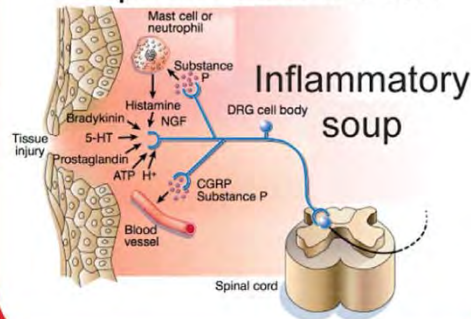
Cortical reorganization



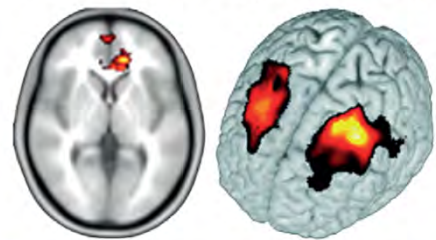
Central sensitization

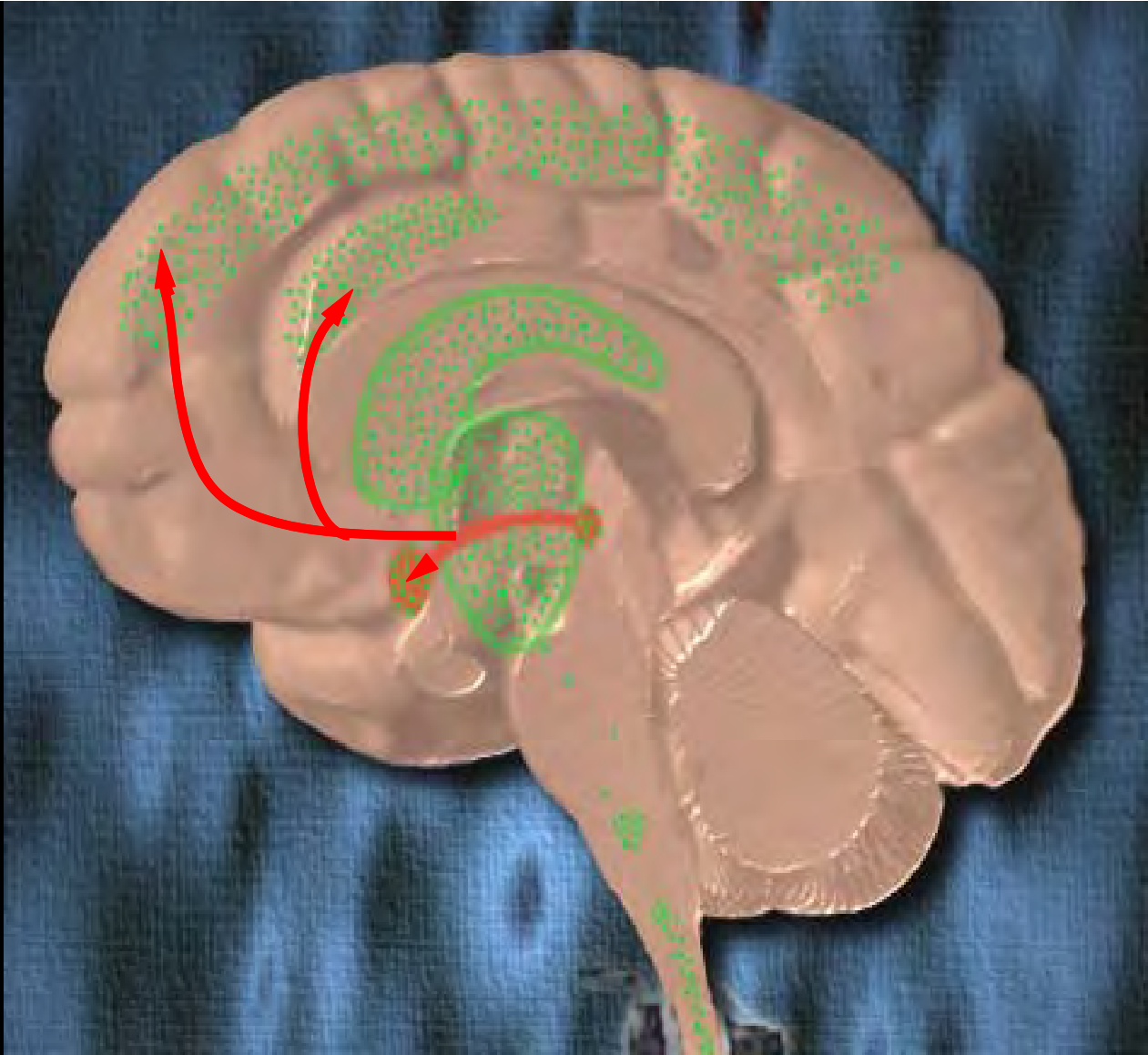


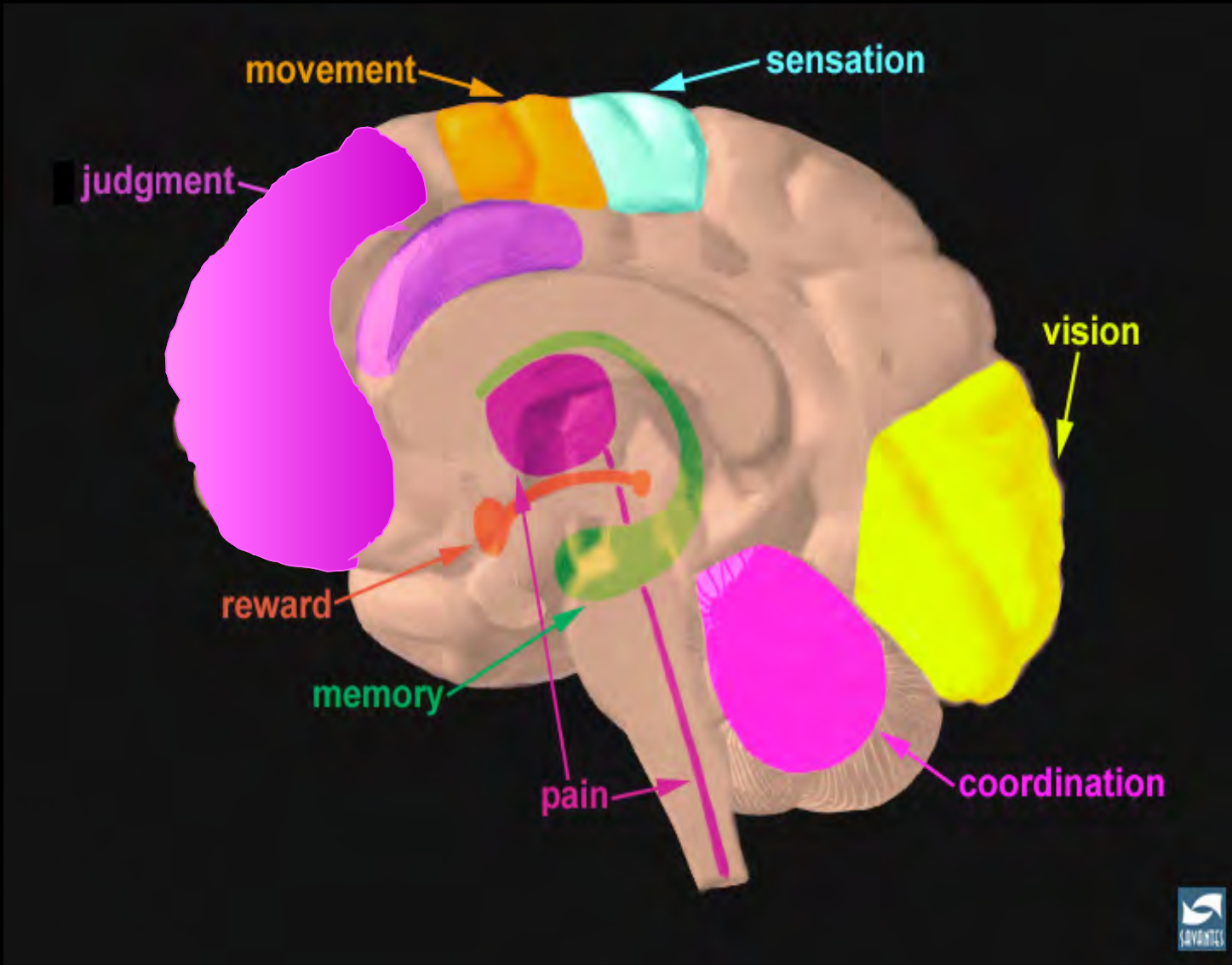
Peripheral sensitization



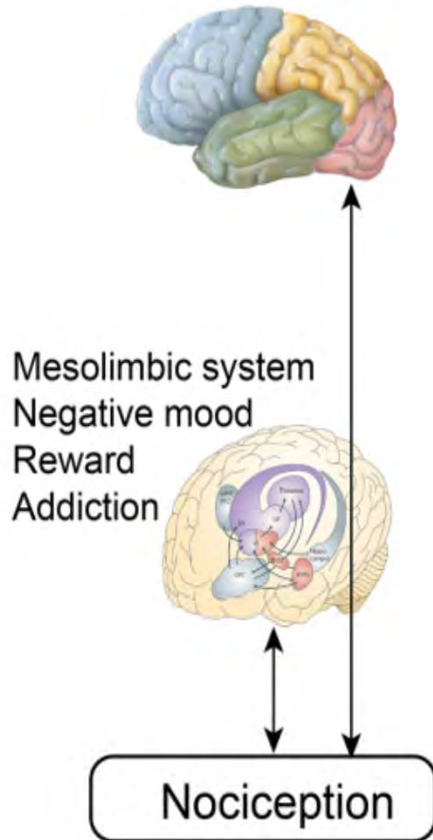
Cortical reorganization



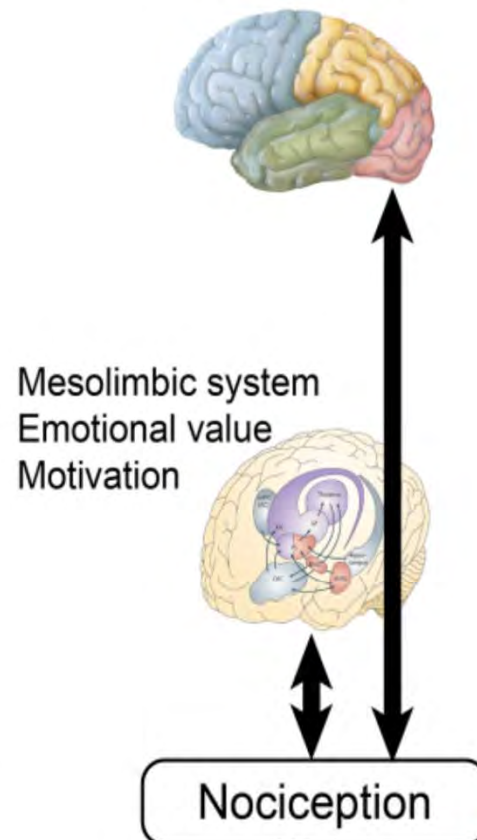




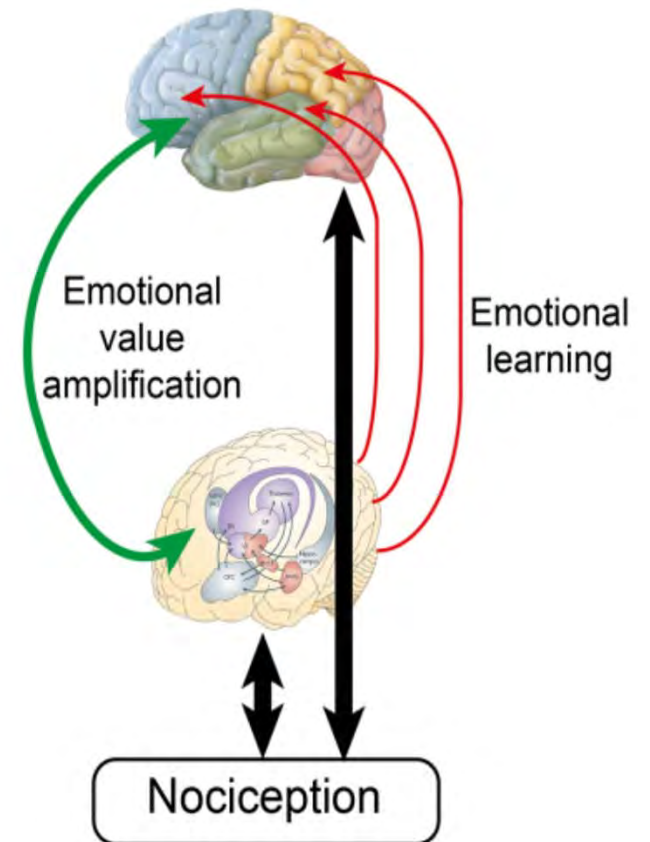
Cortical control of emotional learning



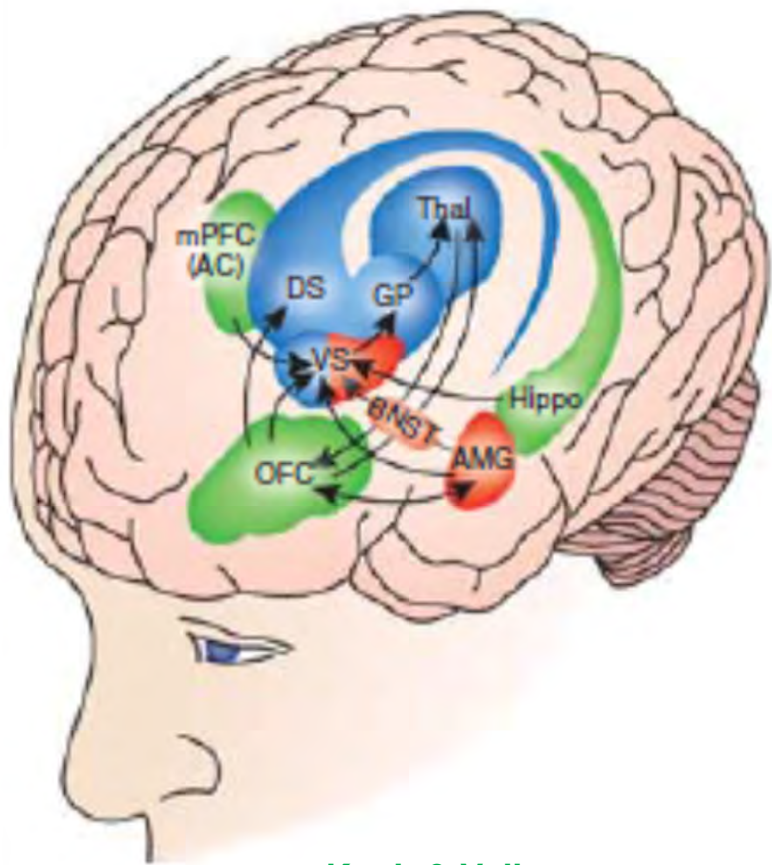
Acute pain



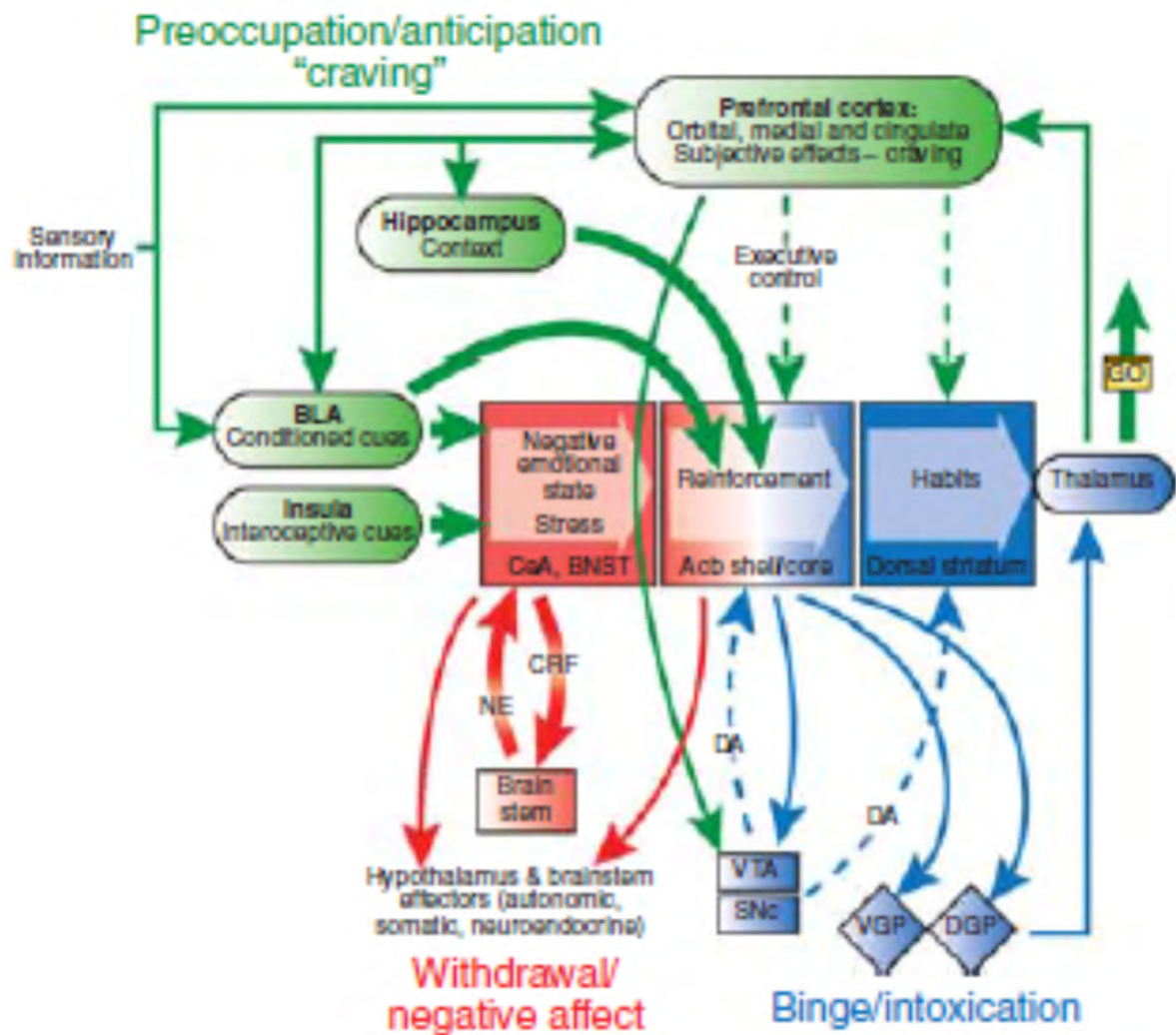
Pain persistence

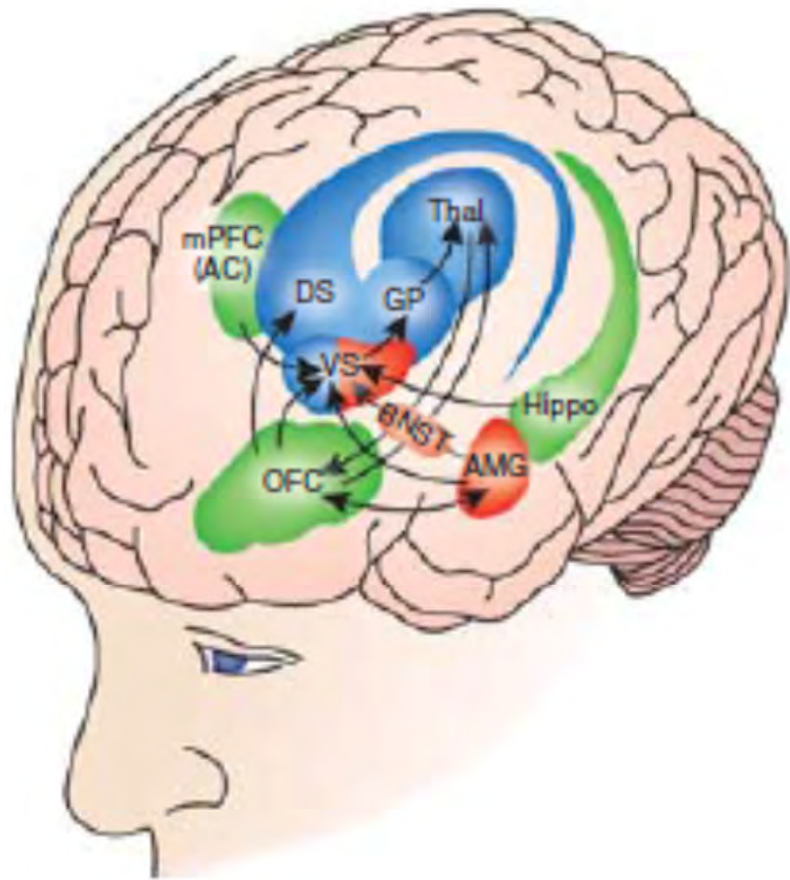


Vachon-Preseau et al.,
Critical Rev in Oral Bio & Med, 2016

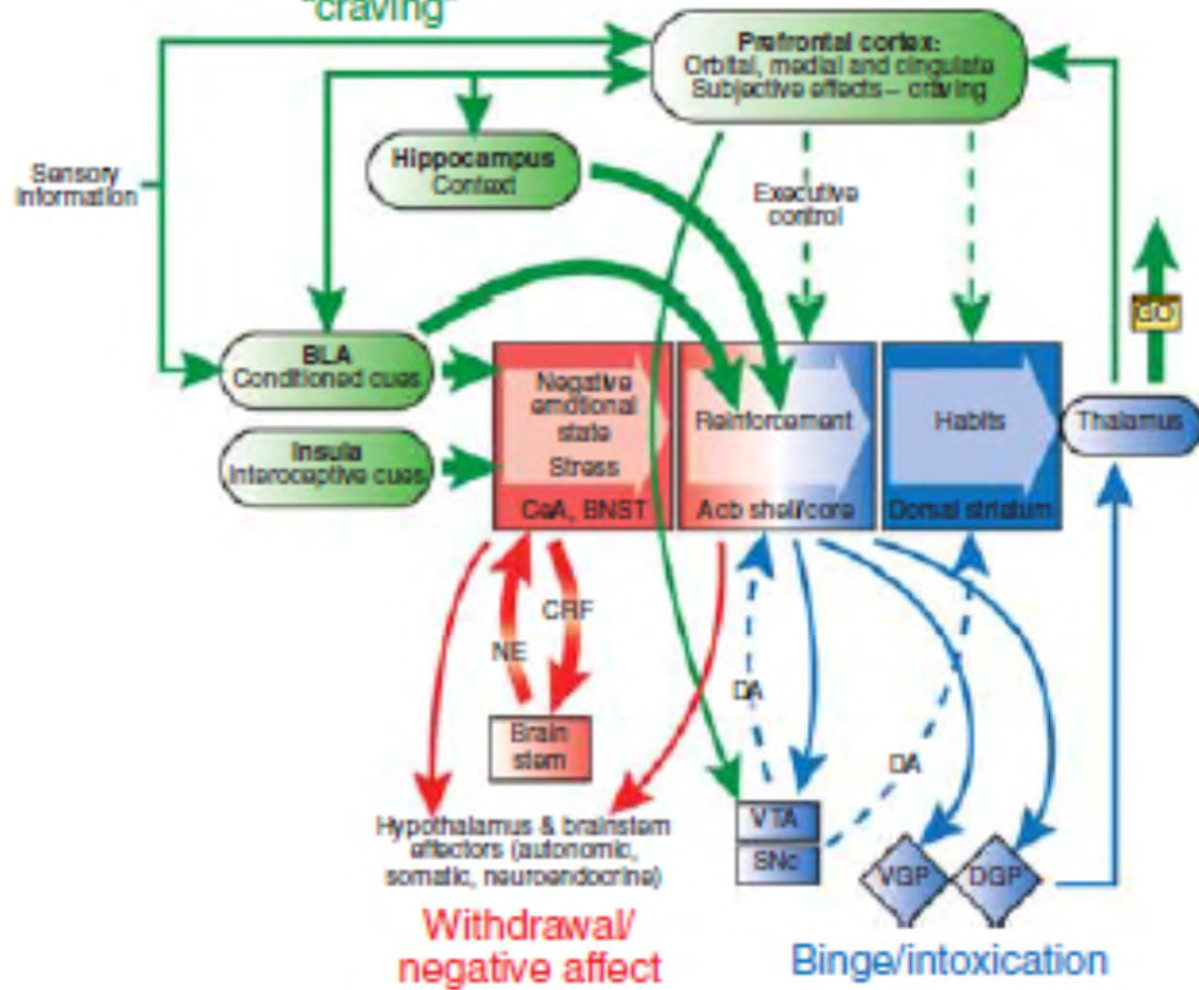


Koob & Volkow, Neuropsychopharm 2010.





Preoccupation/anticipation "craving"



Applicability of Prevailing Addiction Theories to Understanding of Pain

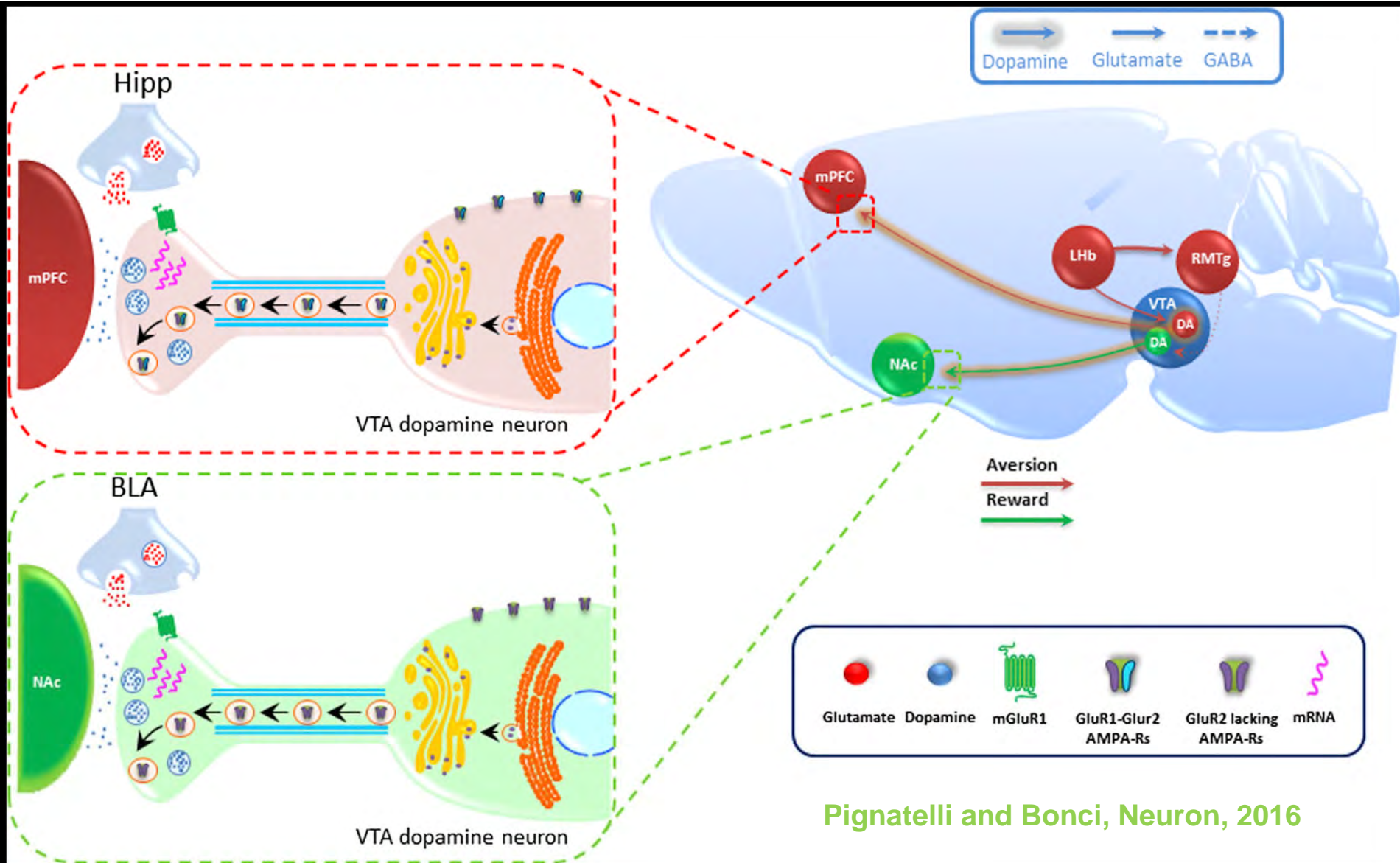
Elman and Borsook,
“Common Brain Mechanisms of Chronic Pain and Addiction”
Neuron 89:11-36, 2016

Neuro-adaptation	Mechanism	Manifestation	Role in Pain

Characteristic	Reward deficiency	Anti-reward
Type of neuroadaptation	Within system	Between systems
Neuroanatomy	Mesolimbic dopaminergic circuitry, including dopamine terminal fields (e.g., the striatum, amygdala, and Prefrontal Cortex (PFC))	Extended amygdala (basolateral amygdala, bed nucleus of the stria terminalis & lateral tegmentum), hippocampus & habenula
Neurochemistry	<p>↓ dopamine receptors, ↑ dopamine transporters &</p> <p>↓ dopamine synthesis</p> <p>↑ cAMP Response Element Binding (CREB) protein,</p> <p>↓ tonic dopamine & ↑ long-term depression</p>	<p>↑ in dynorphin, norepinephrine, corticotropin-releasing factor & glutamate</p>
Reciprocal interactions	↑ stress as it is not buffered by reward	Dynorphin contributes to reward deficiency
Clinical significance	↓ in positive reinforcement of addictive drugs	Avoidance of potentially harmful situations (e.g., pain, fear & losses)
Clinical manifestation	Anhedonia	Hyperkatifeia, craving & compulsivity

Applicability of the Prevailing Addiction Theories to Understanding of Pain

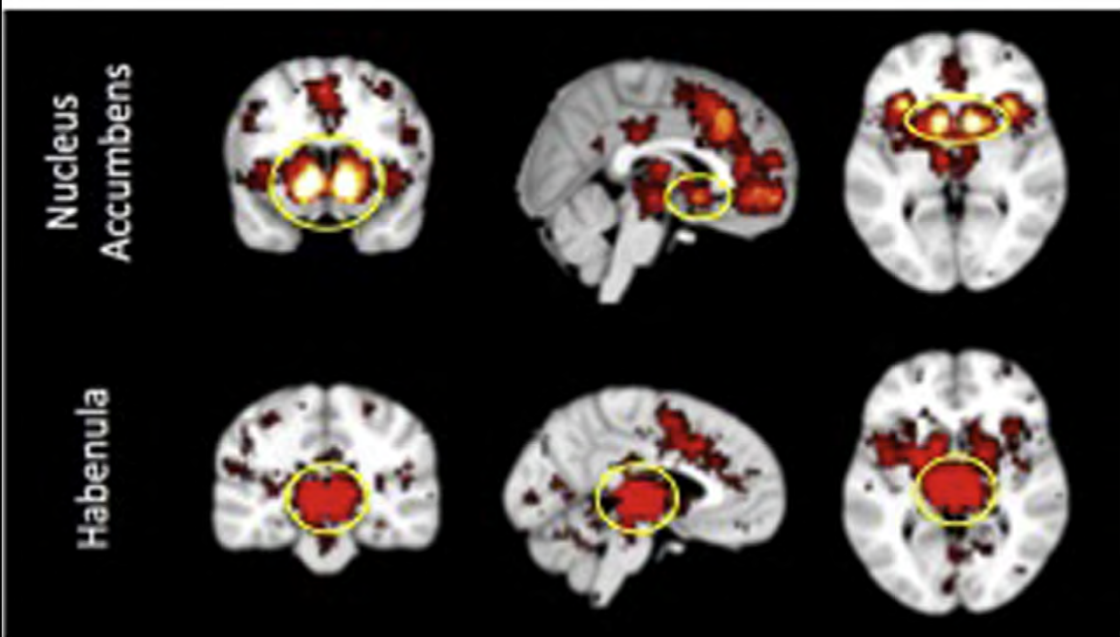
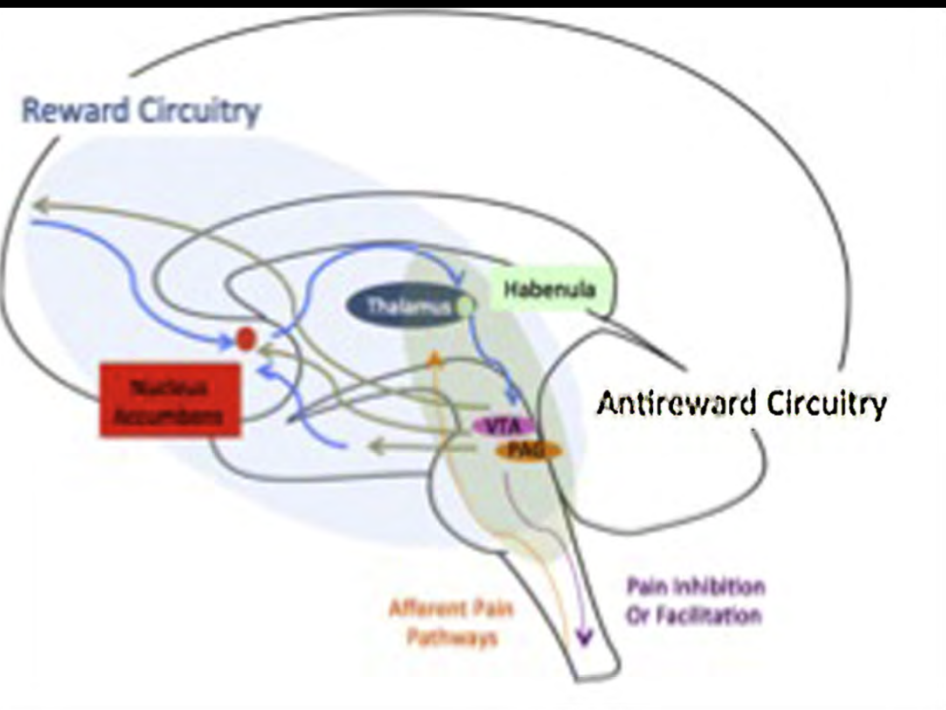
Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Reward Deficiency	<ul style="list-style-type: none"> - Prolonged periods of pain - ↓ DA NAc & PFC 	<ul style="list-style-type: none"> - Emotional numbing - Anhedonia - ↓ responses to natural reward 	<ul style="list-style-type: none"> - ↓ control of drug urges, seeking, & consumption - ↑ pain (reward buffers pain) - ↓ placebo - ↑ nocebo



Pignatelli and Bonci, Neuron, 2016

Applicability of the Prevailing Addiction Theories to Understanding of Pain

Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Anti-Reward	Repeated artificial ↑ DA by pain: ↑ NE, CRF, ↑ VP, SubP	<ul style="list-style-type: none"> - Aversive emotional state - Anhedonia - ↑ social isolation & withdrawal 	↓ reward, ↑ pain ↓ placebo, ↑ nocebo



Borsook et al., Neurosci Biobeh Rev, 2016

Applicability of the Prevailing Addiction Theories to Understanding of Pain

Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Opponent Process	Pain vs Reward	Exhilaration and euphoria with discontinuation of pain	Pain becoming a motivational target

Applicability of the Prevailing Addiction Theories to Understanding of Pain

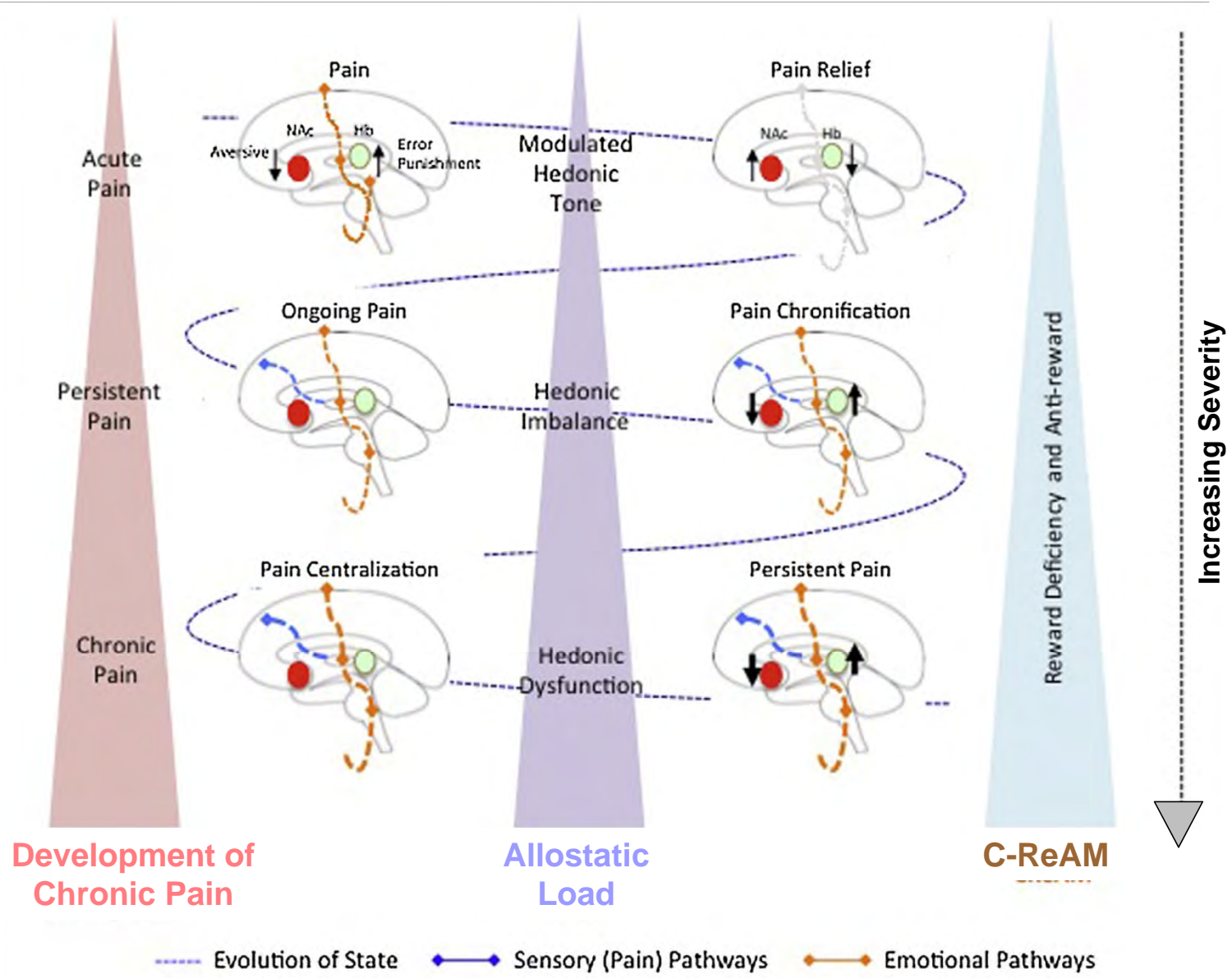
Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Incentive sensitization	Pain- and analgesia-induced changes in limbic DA (NAc, Amg, PFC)	Pain and analgesia become sensitized motivational targets	<ul style="list-style-type: none">- Chronic pain in the absence of nociceptive input- Therapeutic dependence- Catastrophizing- Stress-induced pain episodes

Applicability of the Prevailing Addiction Theories to Understanding of Pain

Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Impaired Inhibitory Control	<ul style="list-style-type: none">- Prolonged periods of pain- ↓ DA NAc & PFC	<ul style="list-style-type: none">- Emotional numbing- Anhedonia- ↓ responses to natural reward	↓ control of drug urges, seeking, & consumption

Applicability of the Prevailing Addiction Theories to Understanding of Pain

Neuro-adaptation	Mechanism	Manifestation	Role in Pain
Aberrant learning	<ul style="list-style-type: none">- Adaptations to excessive DA-response to pain and analgesics- Epigenetics- LTP and LTD associated with overlearning- Ventral-to-dorsal striatal shift of behavioral control	Enhanced significance of cues that predict delivery of analgesics (exaggerated prediction error)	Positive reinforcement qualities of acute pain in the context of chronic pain



Borsook et al.,
 Neurosci Biobehav
 Rev 2016

Neurobiology of Pain and Addiction

***Impact on Opioid Use and
Abuse Therapy***

