Addiction: A Disease of Learning and Memory

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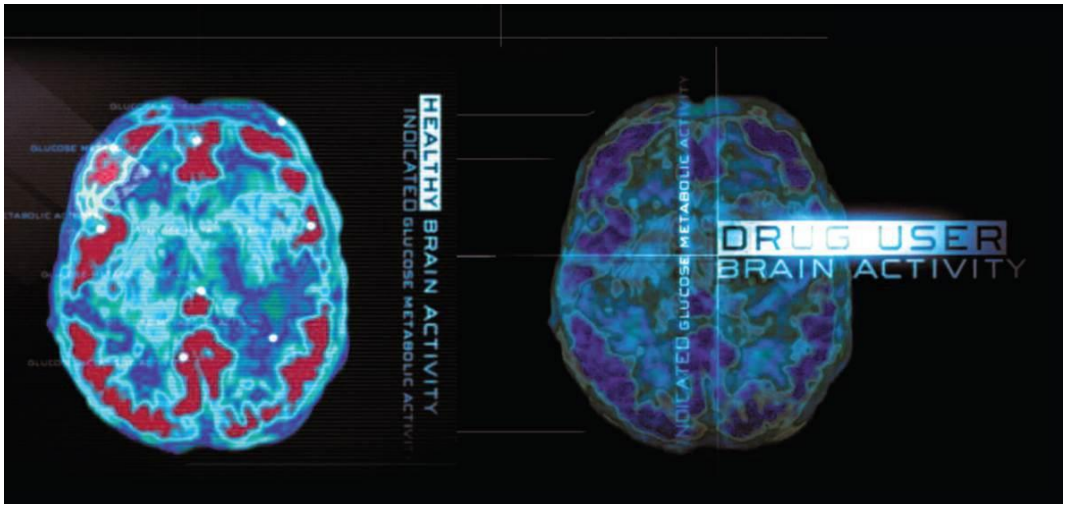
Addiction is A Brain Disease



- Characterized by:
  - Compulsive Behavior.
  - Continued abuse of drugs despite negative consequences.
  - Persistent changes in the brain's structure and function.

Addiction

- The **central problem** in the treatment of addiction: the risk of relapse, often precipitated by drug-associated cues.

- **Dependence** and **withdrawal** do not explain addiction.

A Hijacking of Neural Systems Related to the Pursuit of Rewards

- Drugs of abuse engage motivation and pleasure pathways of the brain

- **Survival-relevant natural goals act as rewards:**
  Produce desired outcomes → Make things better

A Hijacking of Neural Systems Related to the Pursuit of Rewards

- **Internal motivational states** (hunger, thirst, sexual arousal, etc.).

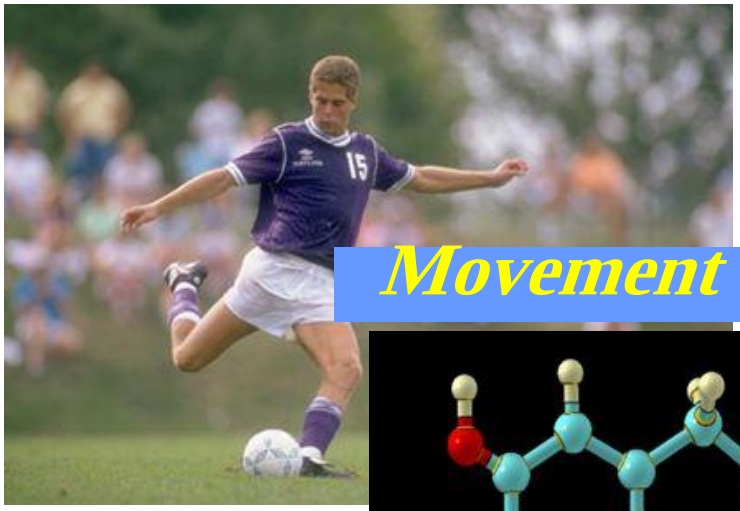
- **External cues** related to rewards (odor of food , etc.)

A Hijacking of Neural Systems Related to the Pursuit of Rewards

- The **behavioral sequences** involved in obtaining desired rewards become overlearned.

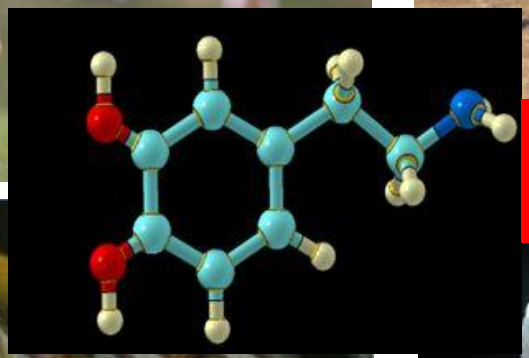
- **Addictive drugs** elicit patterns of behavior reminiscent of those elicited by natural rewards.

The Dopamine Hypothesis of Addiction

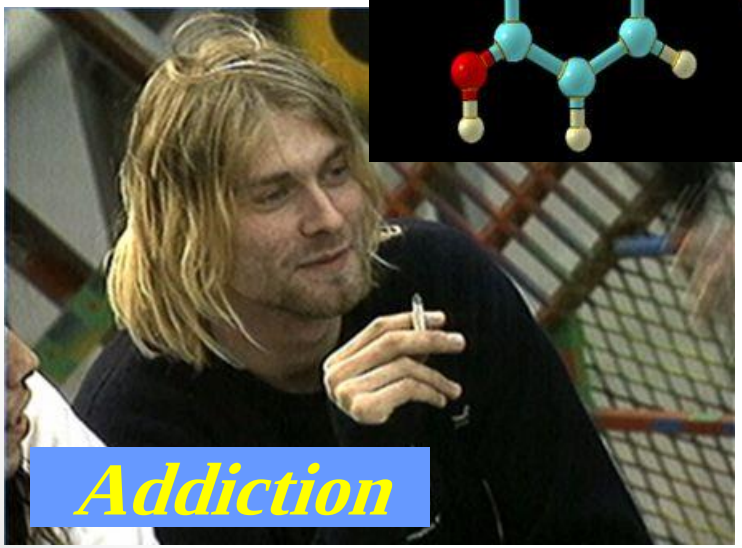


Movement

Motivation



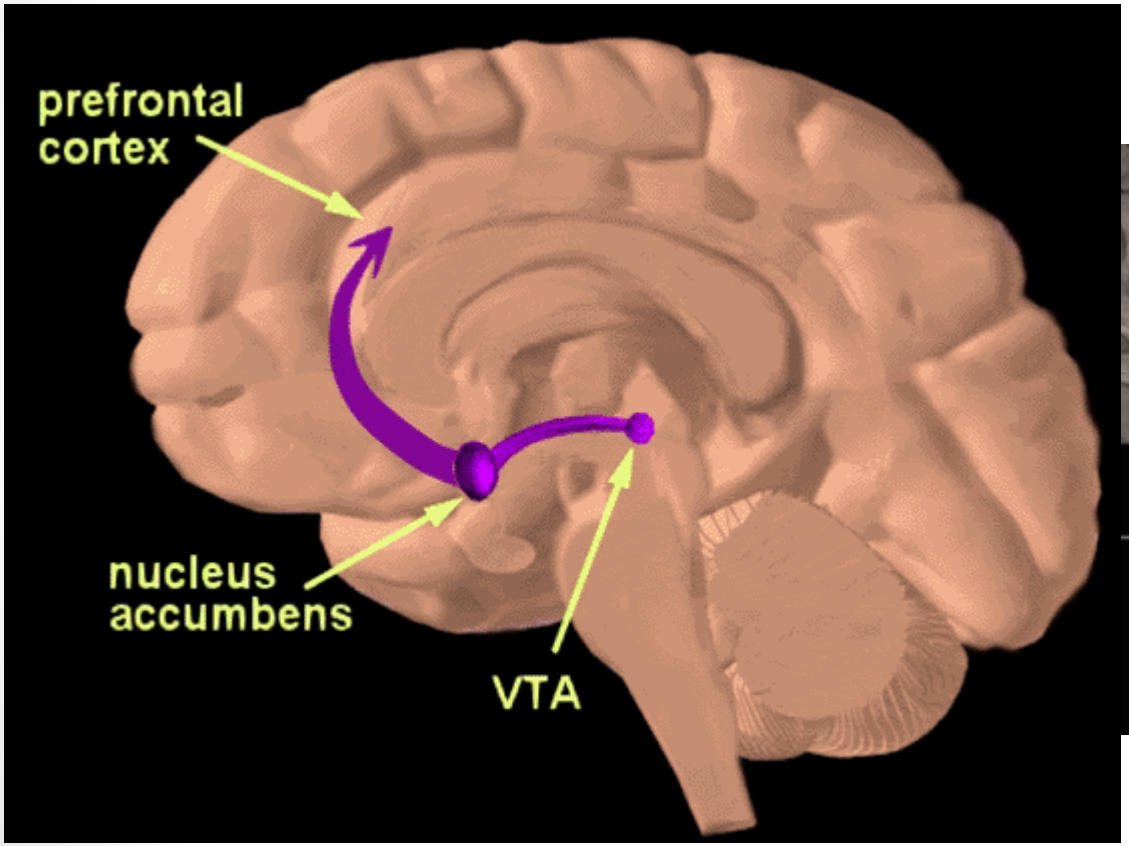
Dopamine



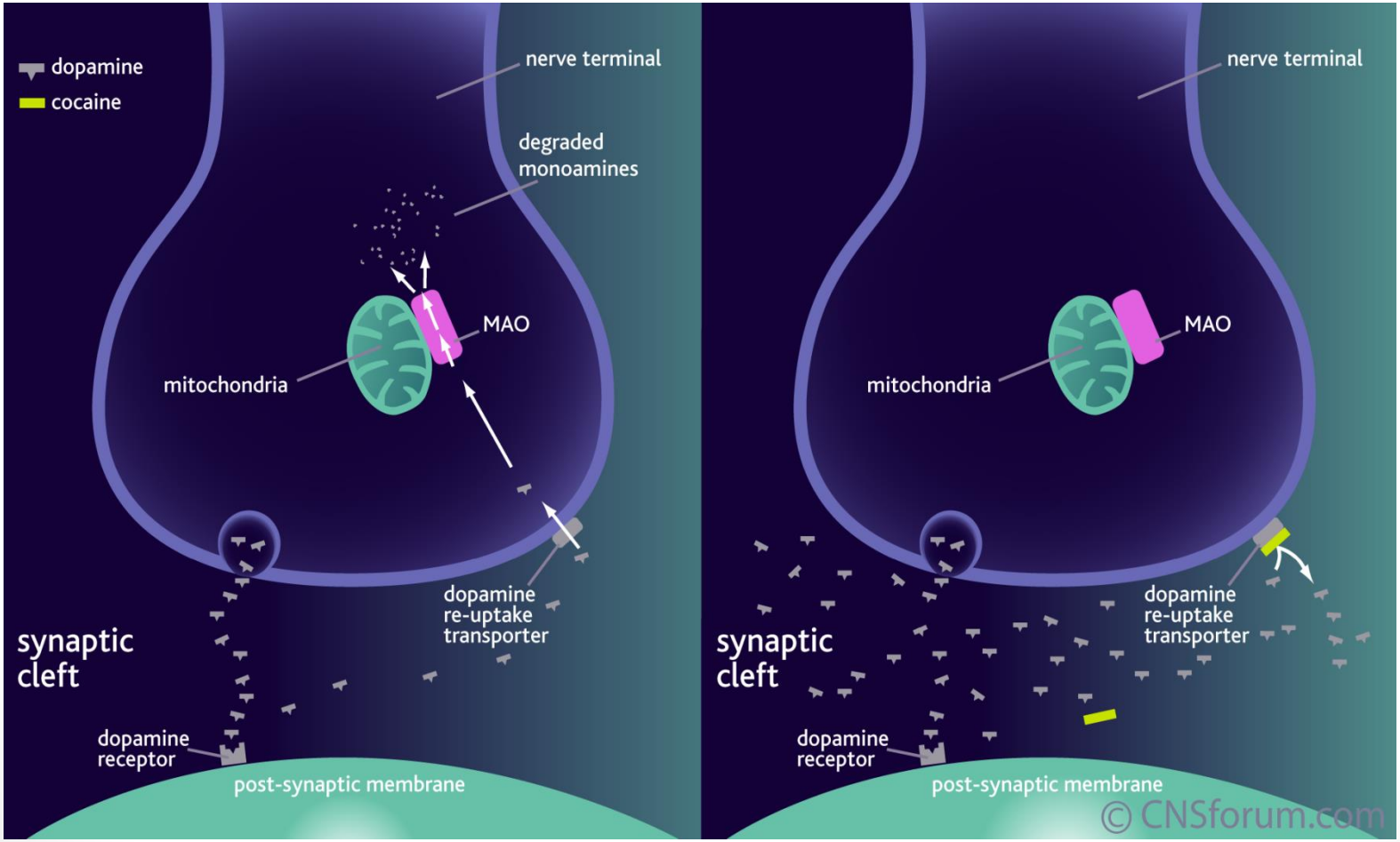
Addiction

Reward & well-

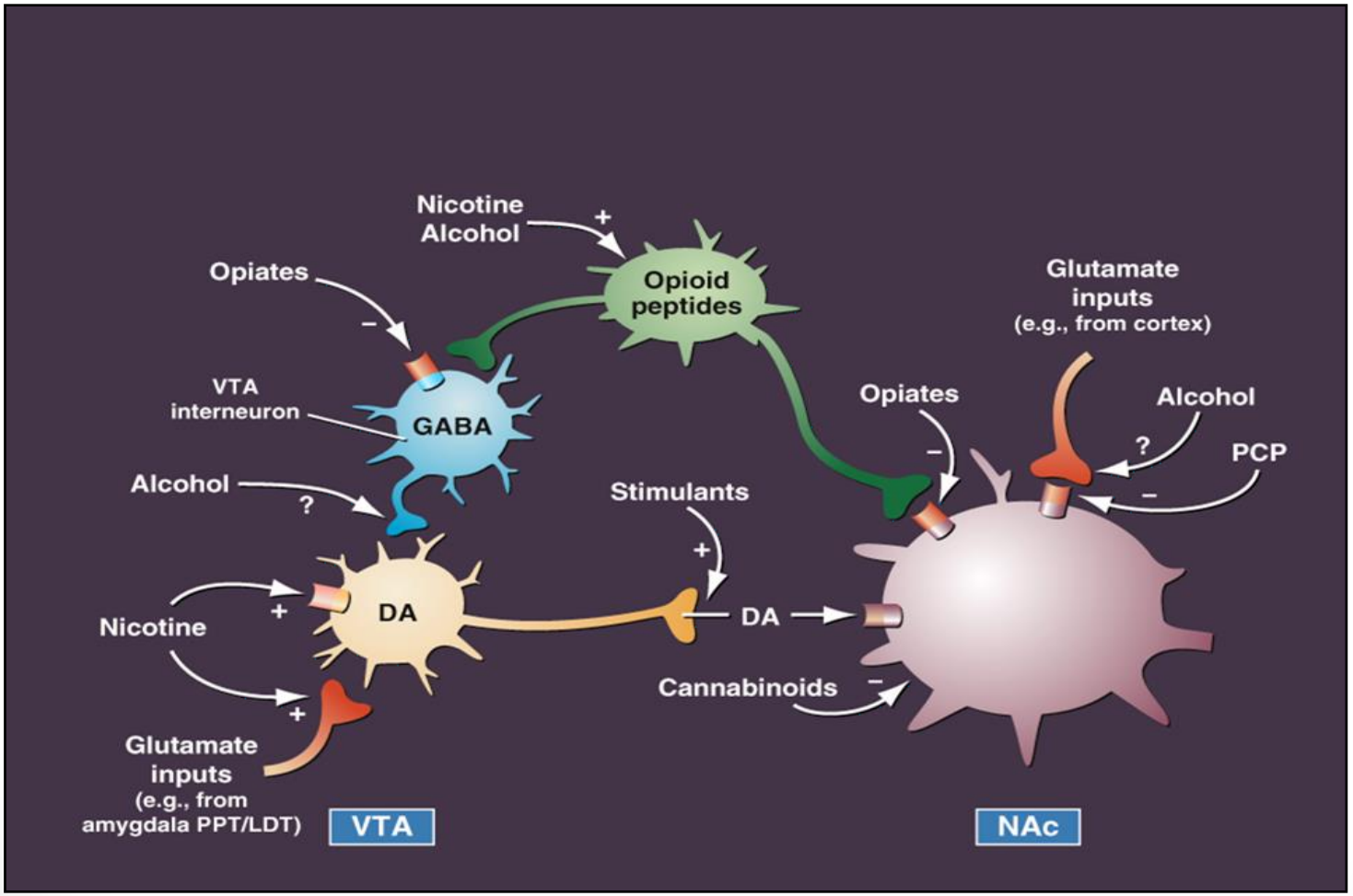
The Dopamine Hypothesis of Addiction



The Dopamine Hypothesis of Addiction



Drug Action: Indirect (Via Other Receptors & Neurotransmitters)



Drug Action: Indirect (Via Other Receptors & Neurotransmitters)

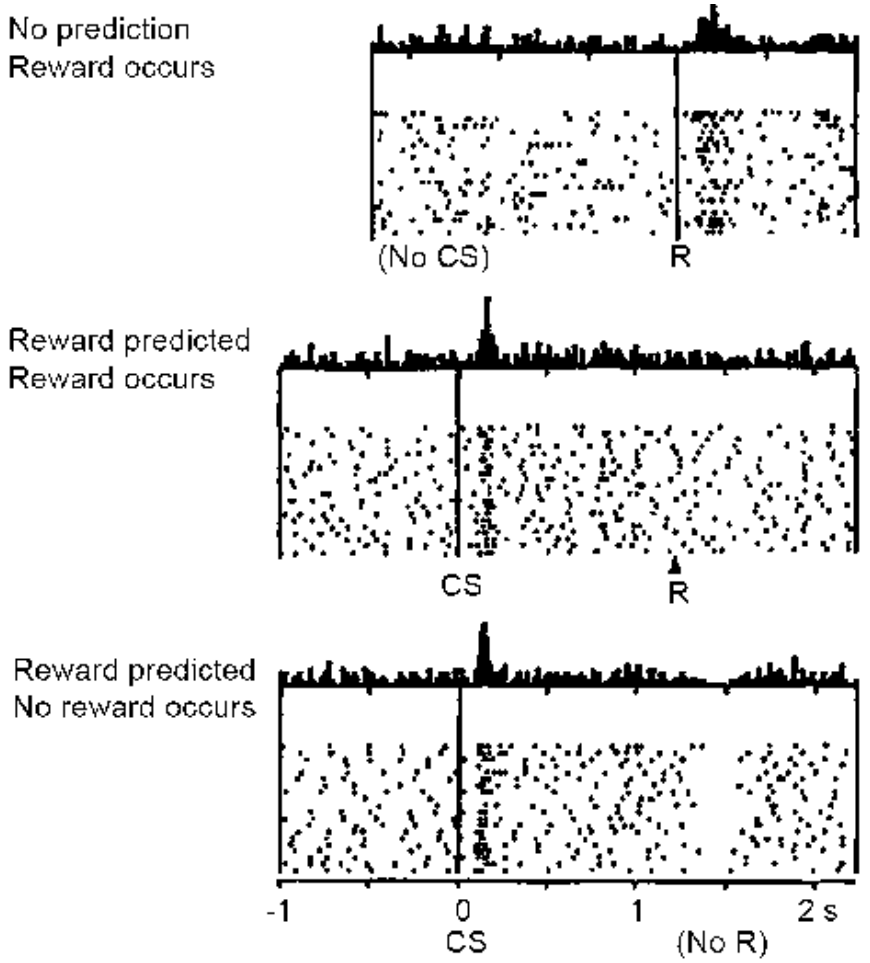
Alcohol • Inhibit GABAergic neurons that project to dopaminergic neurons in the VTA	Heroin • Binds to opioid receptors that inhibit GABAergic neurons that project to dopaminergic neurons in the VTA
Cocaine • Blocks the function of DAT (by binding to the DAT and slowing transport)	Nicotine • Activates cholinergic neurons that project to dopaminergic neurons of the VTA

Dopamine Action

- **What information is encoded by dopamine release?**
- An **early view** of dopamine function was that it acted as a hedonic signal (signaling pleasure).
- Instead of acting as a hedonic signal, dopamine appears to promote reward-related learning and reward-related behavior.

Dopamine Action (Schultz et al, ۱۹۹۰s)

- Monkeys classically-conditioned to associate light with food
- After learning, VTA neurons increase firing to light instead of food
- Decreased firing if light-cued food doesn't appear
- Baseline DA = expected reward
- Increased firing = better than expected
- Reduced firing = worse than expected



Dopamine Action

- **Addictive drugs exceed natural stimuli** in the reliability, quantity, and persistence of increased synaptic dopamine levels.

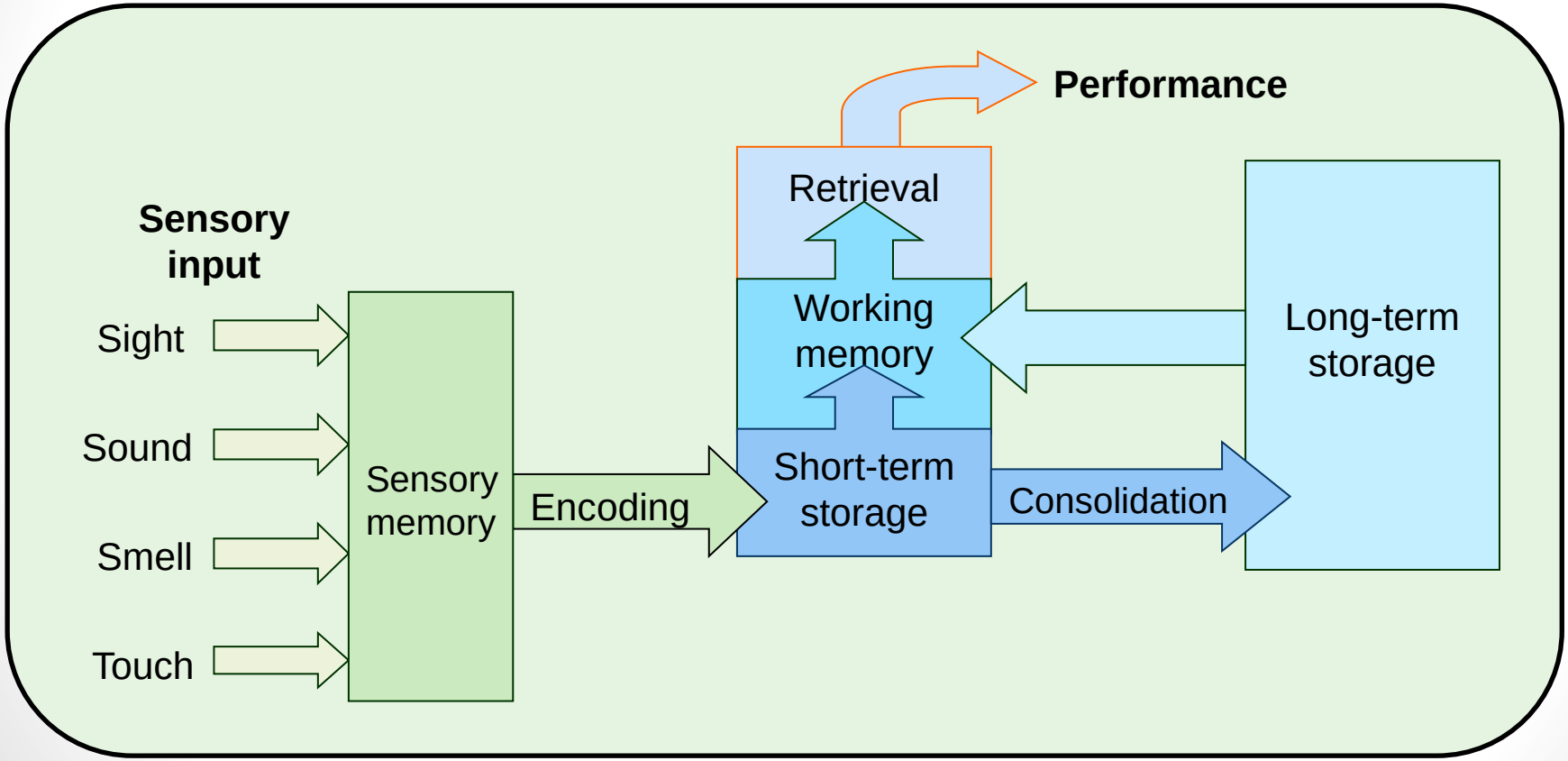
- A predicted **consequence** of these hypotheses would be "profound overlearning" of the motivational significance of cues that predict the delivery of drugs.

Learning & Memory

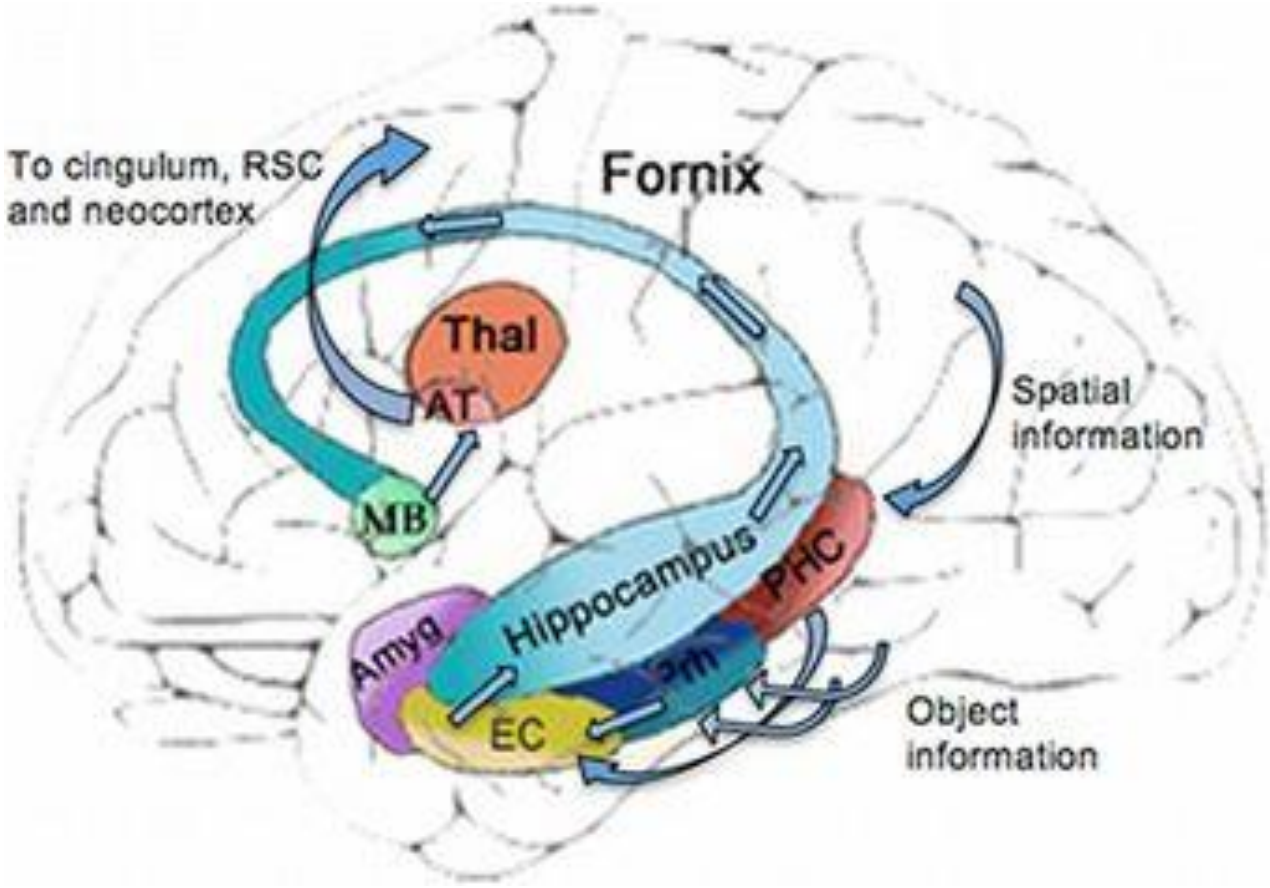
- **Learning** is the process by which we acquire knowledge about the world

- **Memory** is the process by which that knowledge is encoded, stored, and later retrieved

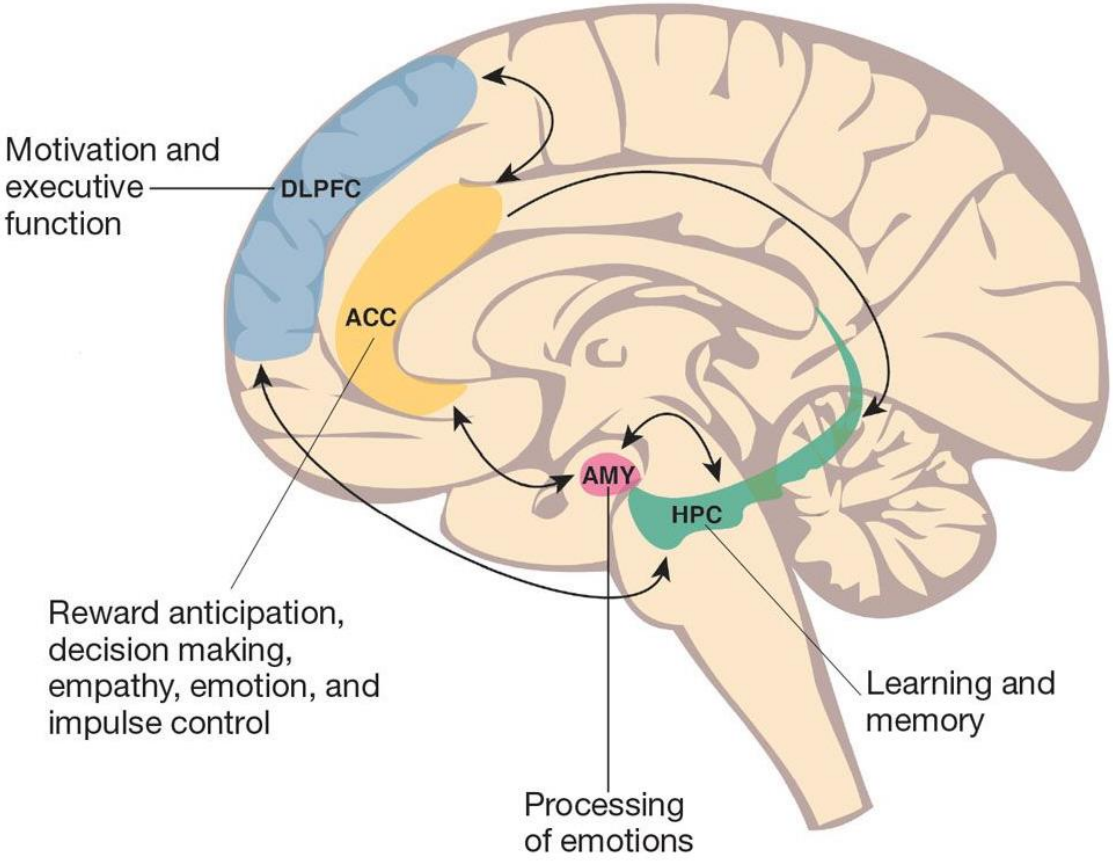
Information Processing Model of Memory



Learning & Memory

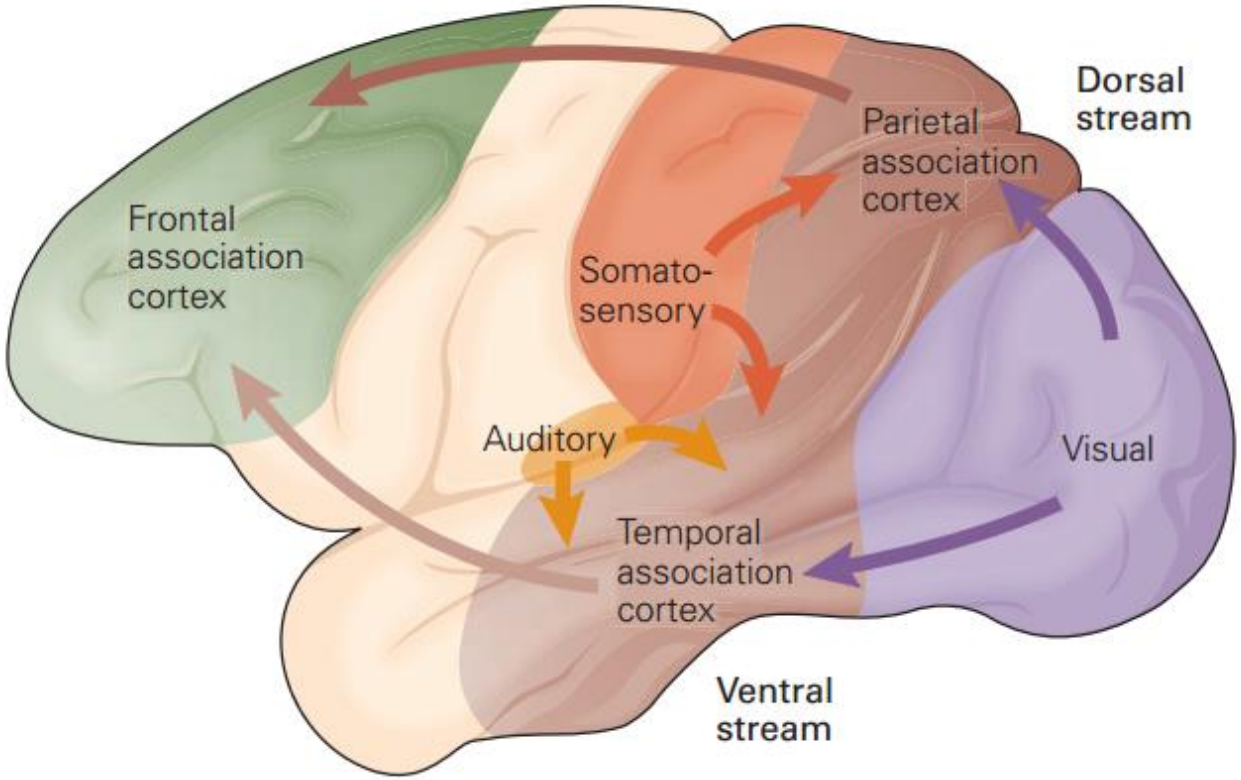


Learning & Memory

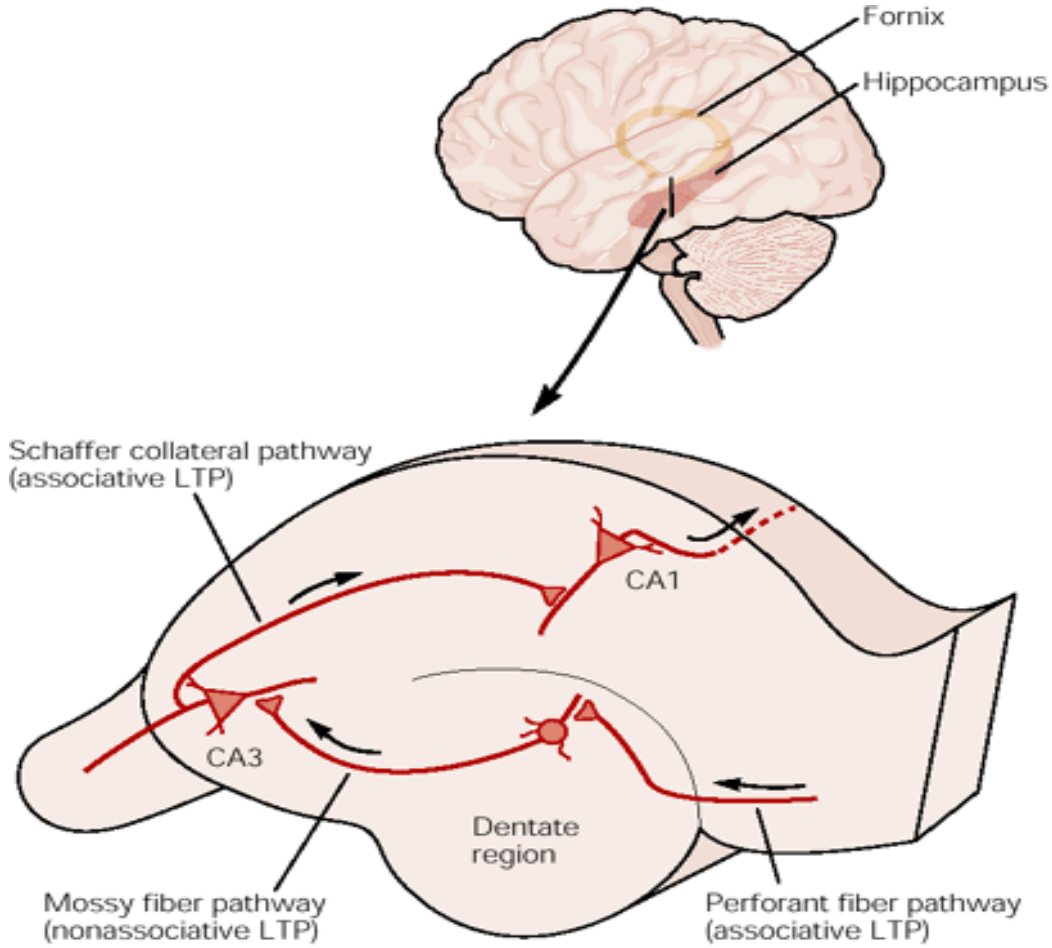


DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex; AMY, amygdala; HPC, hippocampus.

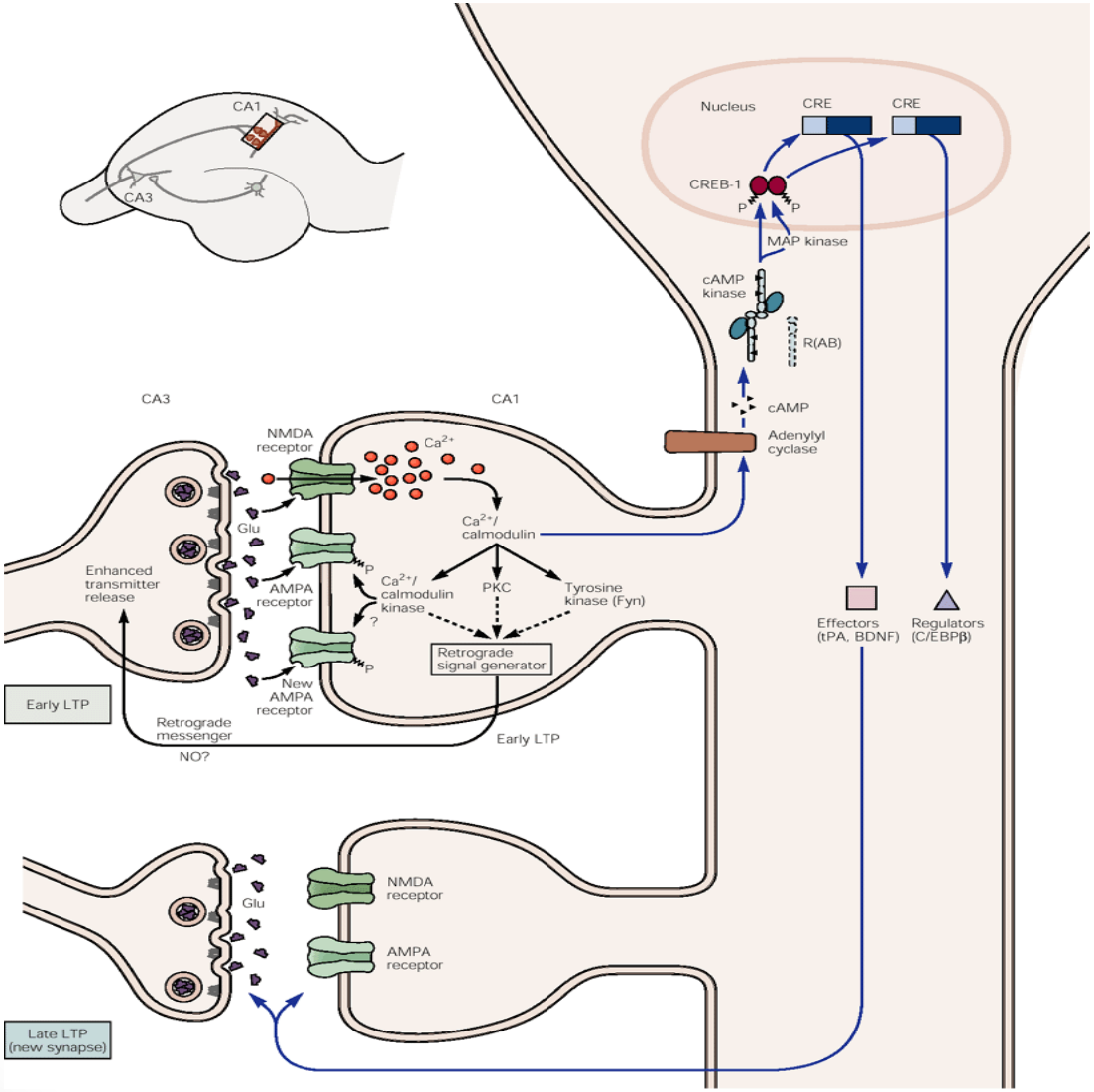
Learning & Memory



Learning & Memory



Learning & Memory: Long-Term Potentiation (LTP)



Addiction & Long-Term Memory

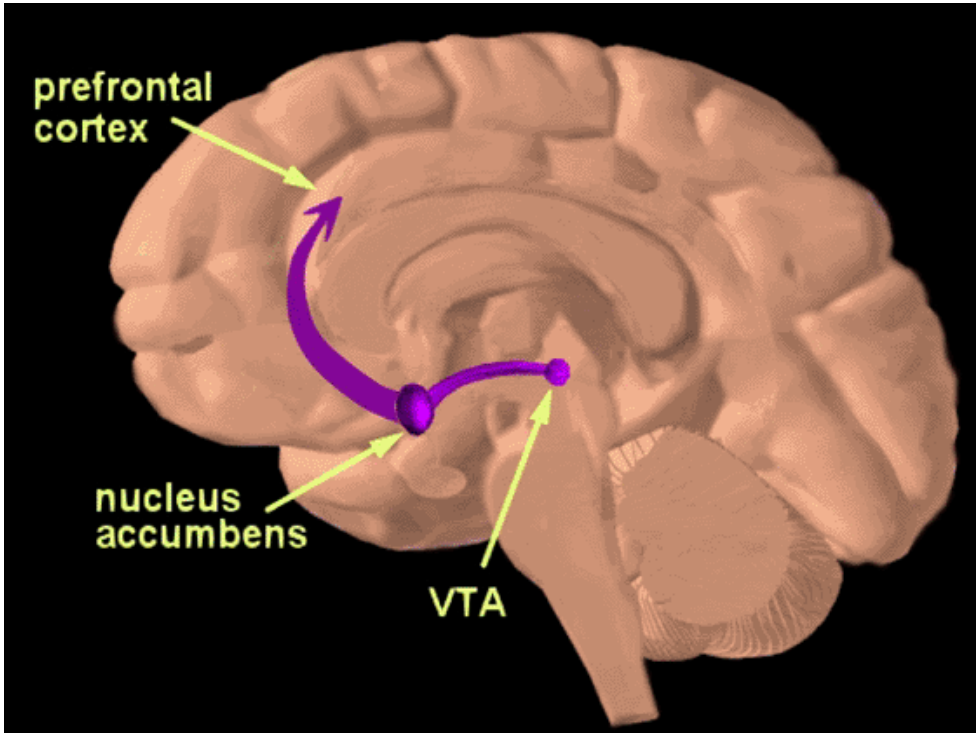
- **What happens if the brain remembers too much or too powerfully records?**
- **Dopamine**, reward-related learning & pathological learning.
- **Addiction** represents a pathological usurpation of the neural mechanisms of learning and memory.

A Role for the Prefrontal Cortex

- The representation of goals
- Assignment of value to them
- Selection of actions

A Role for the Prefrontal Cortex

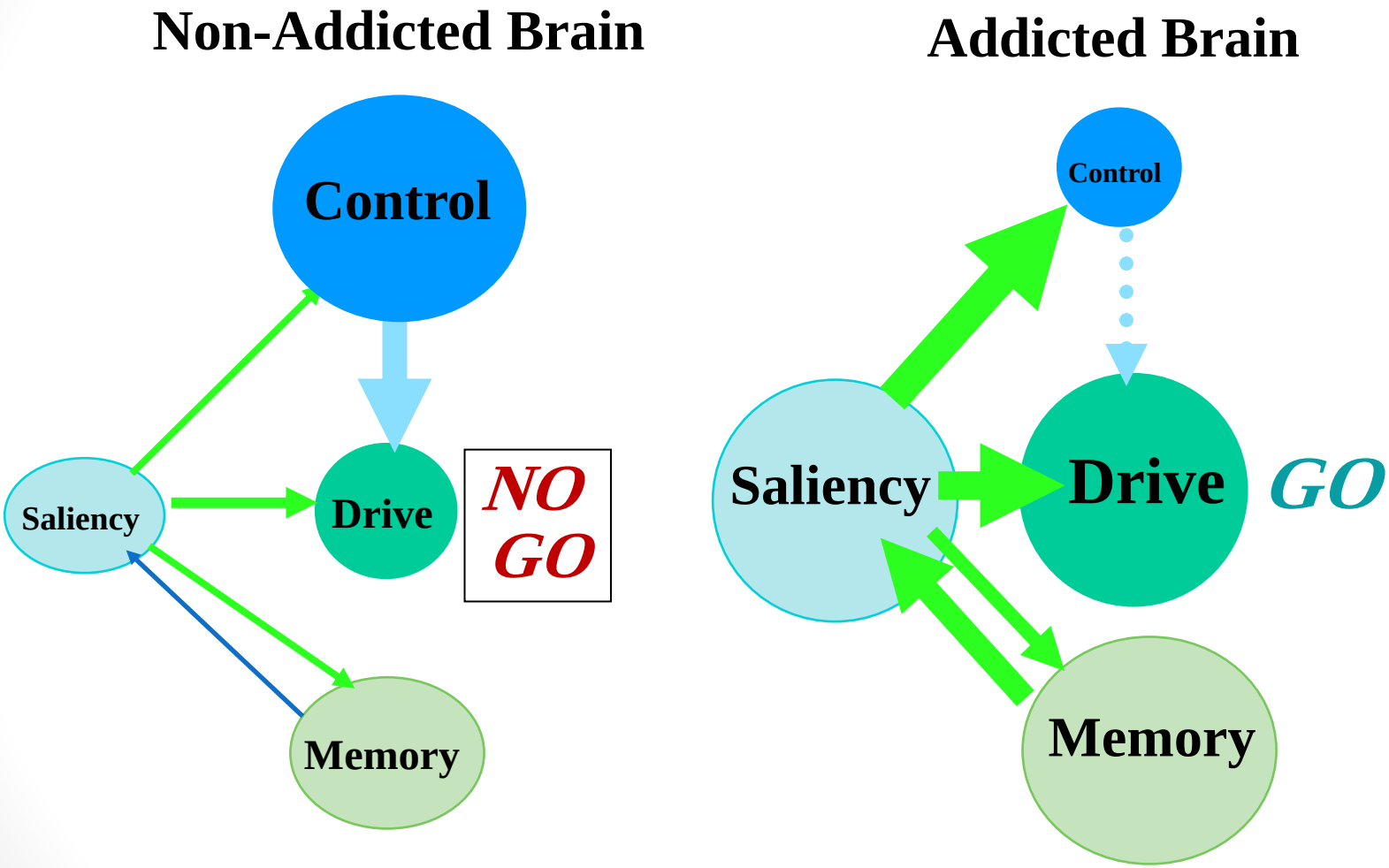
- The ability to **update information within the prefrontal cortex** such that new goals can be selected and perseveration avoided is gated by phasic dopamine release.



A Role for the Prefrontal Cortex

- **In an addicted person**, neural adaptations to repetitive, excessive dopaminergic bombardment might decrease responses to natural rewards or reward-related cues that elicit weaker dopamine stimulation, compared with drugs that directly cause dopamine release.

Why Can't Addicts Just Quit?

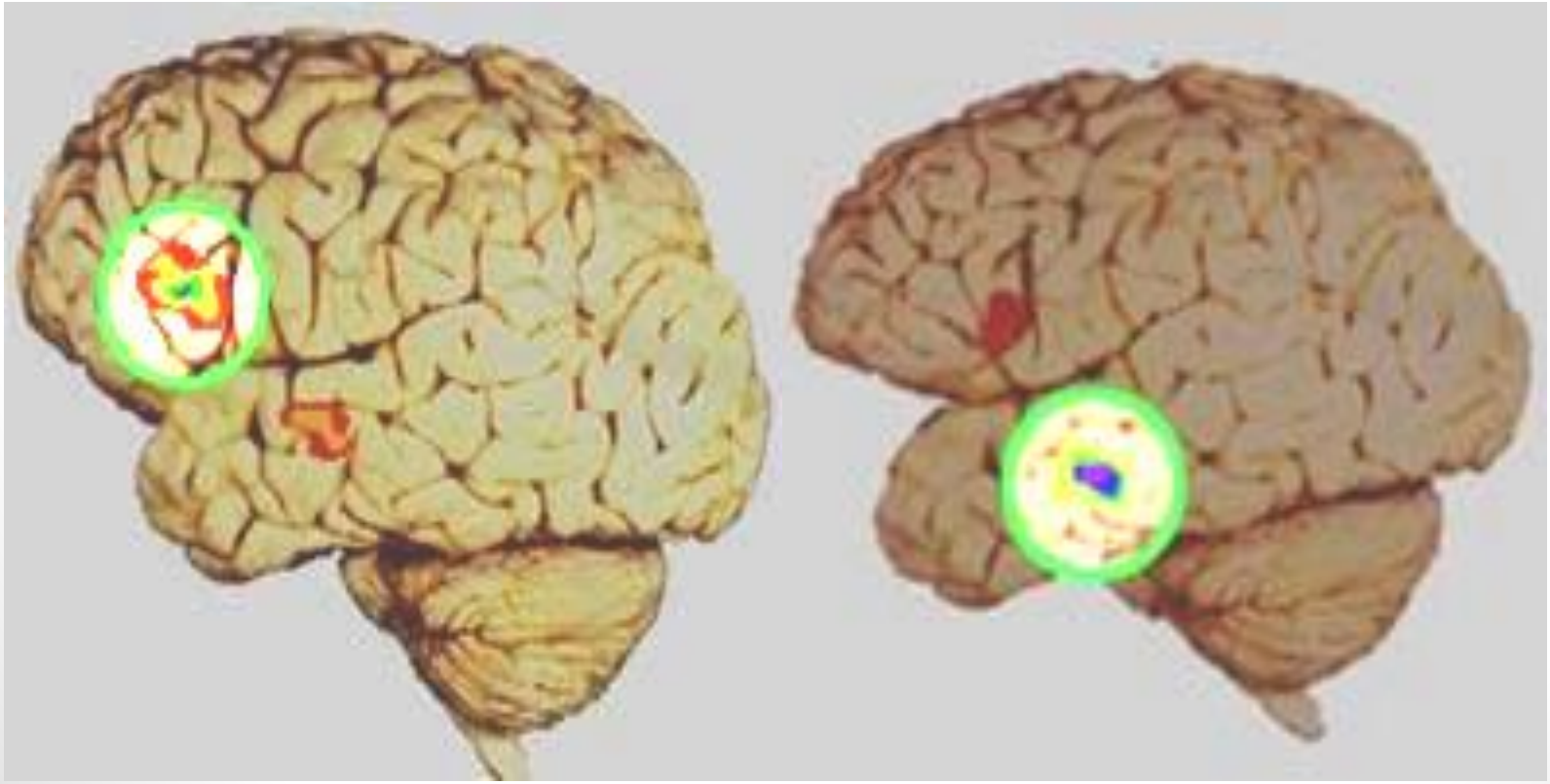


Because addiction changes brain circuits!

A Role for the Prefrontal Cortex

- The upshot of such a scenario would be a ***biased*** representation of the world, powerfully overweighted toward drug-related cues and away from other choices, thus contributing to the loss of control over drug use that **characterizes addiction**.

When Reading Emotion… Adults Rely More on the Frontal Cortex While Teens Rely More on the Amygdala



Take Home Message

- **Addiction** represents a pathological usurpation of the neural mechanisms of learning and memory that under normal circumstances serve to shape survival behaviors related to the pursuit of rewards and the cues that predict them.

- The neural mechanisms of learning and memory might be a target to manage drug-related memory and risk of relapse.

THANK YOU