NEURAL MECHANISMS OF ADDICTION

THE ROLE OF REWARD-RELATED LEARNING AND MEMORY

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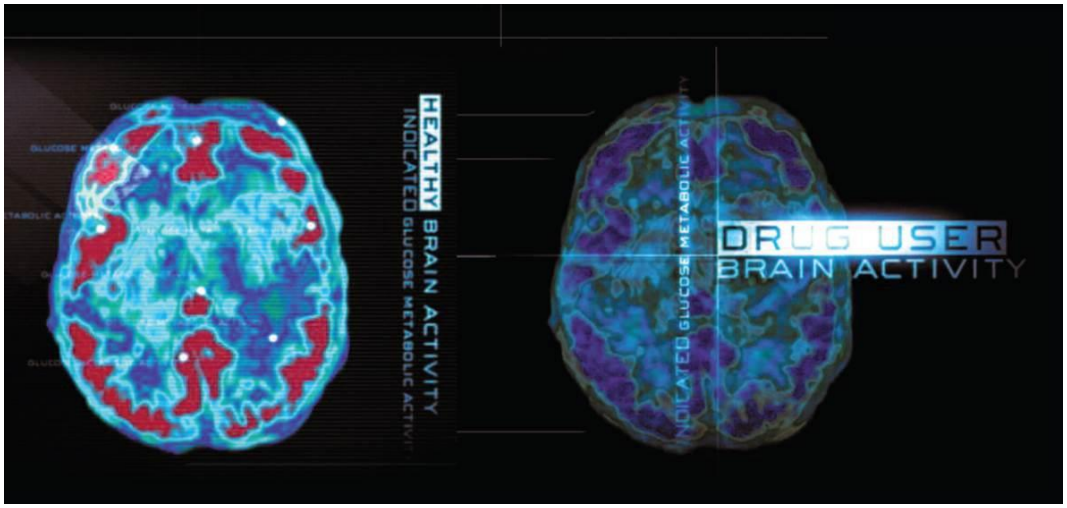
Addiction is a brain disease



- 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.).

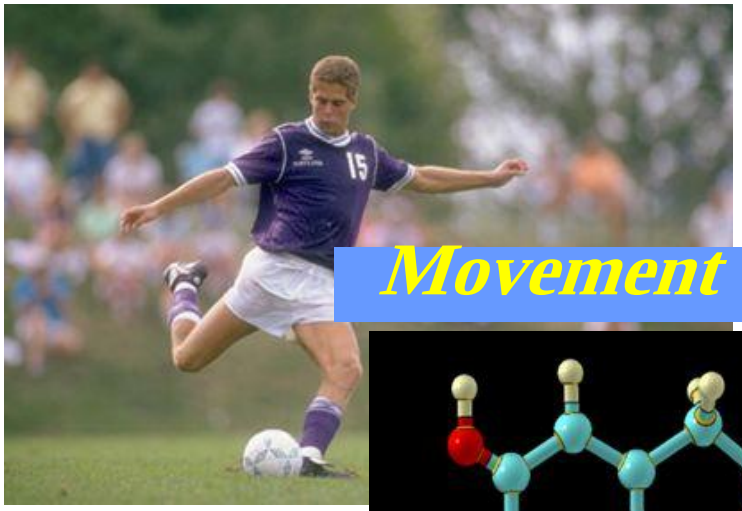
- **External cues** related to rewards (odor of food, etc.)

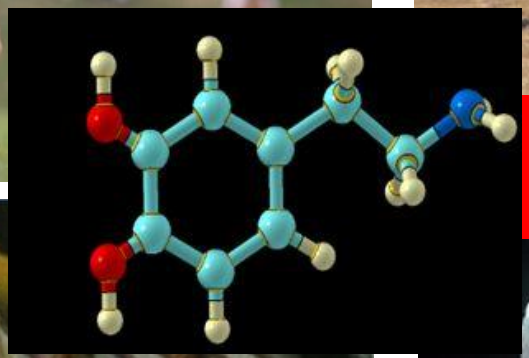
A hijacking of neural systems related to the pursuit of rewards

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

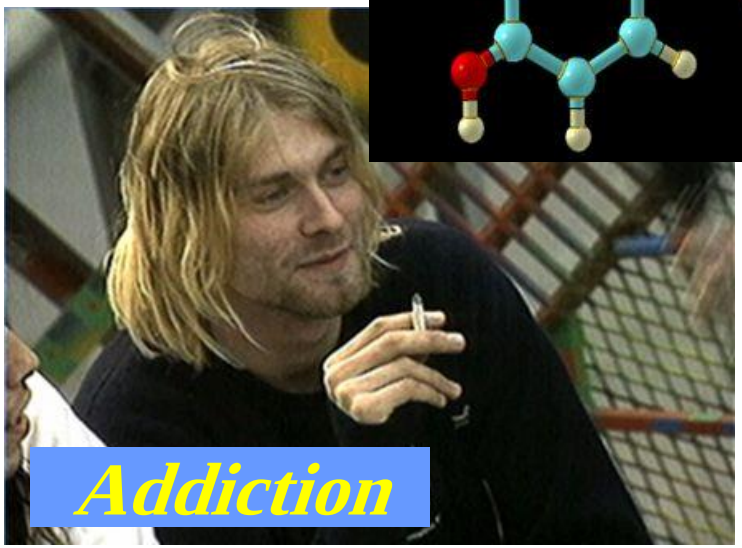
- **Addictive drugs** *elicit patterns of behavior reminiscent of those elicited by natural rewards*.

The dopamine hypothesis of addiction





Dopamine



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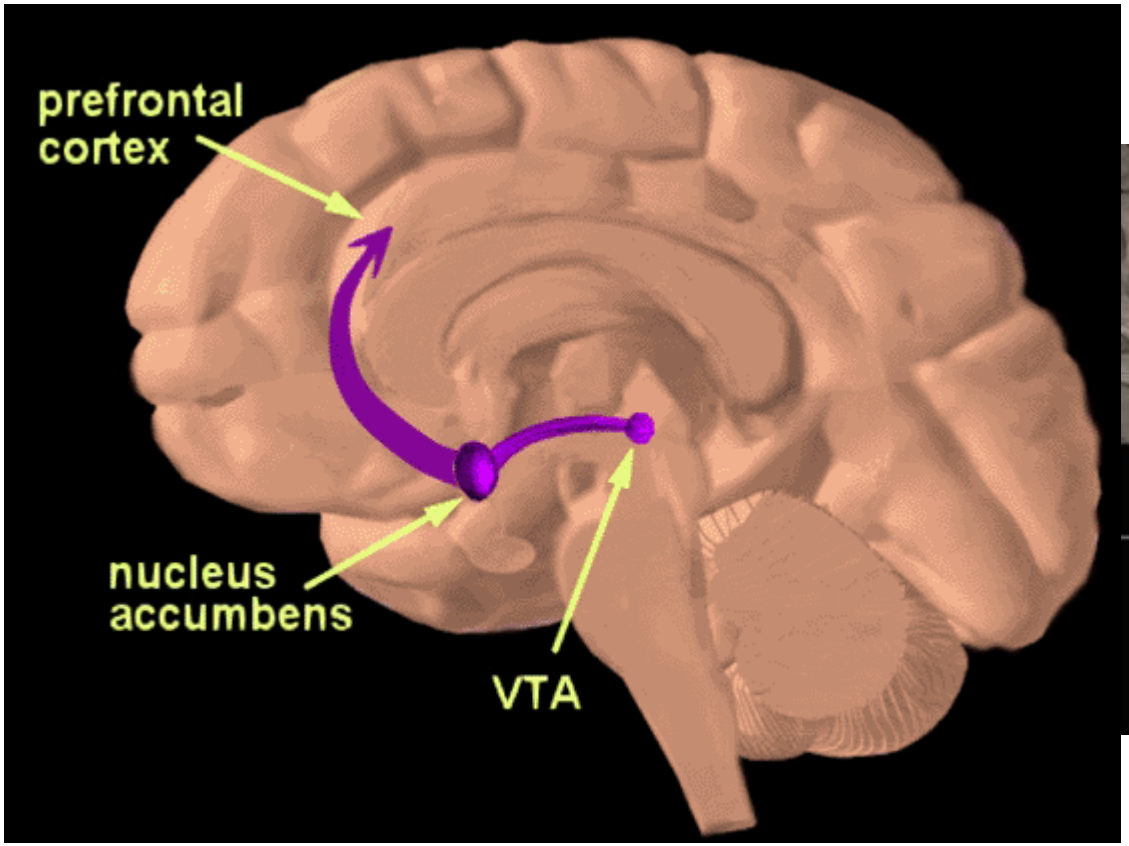

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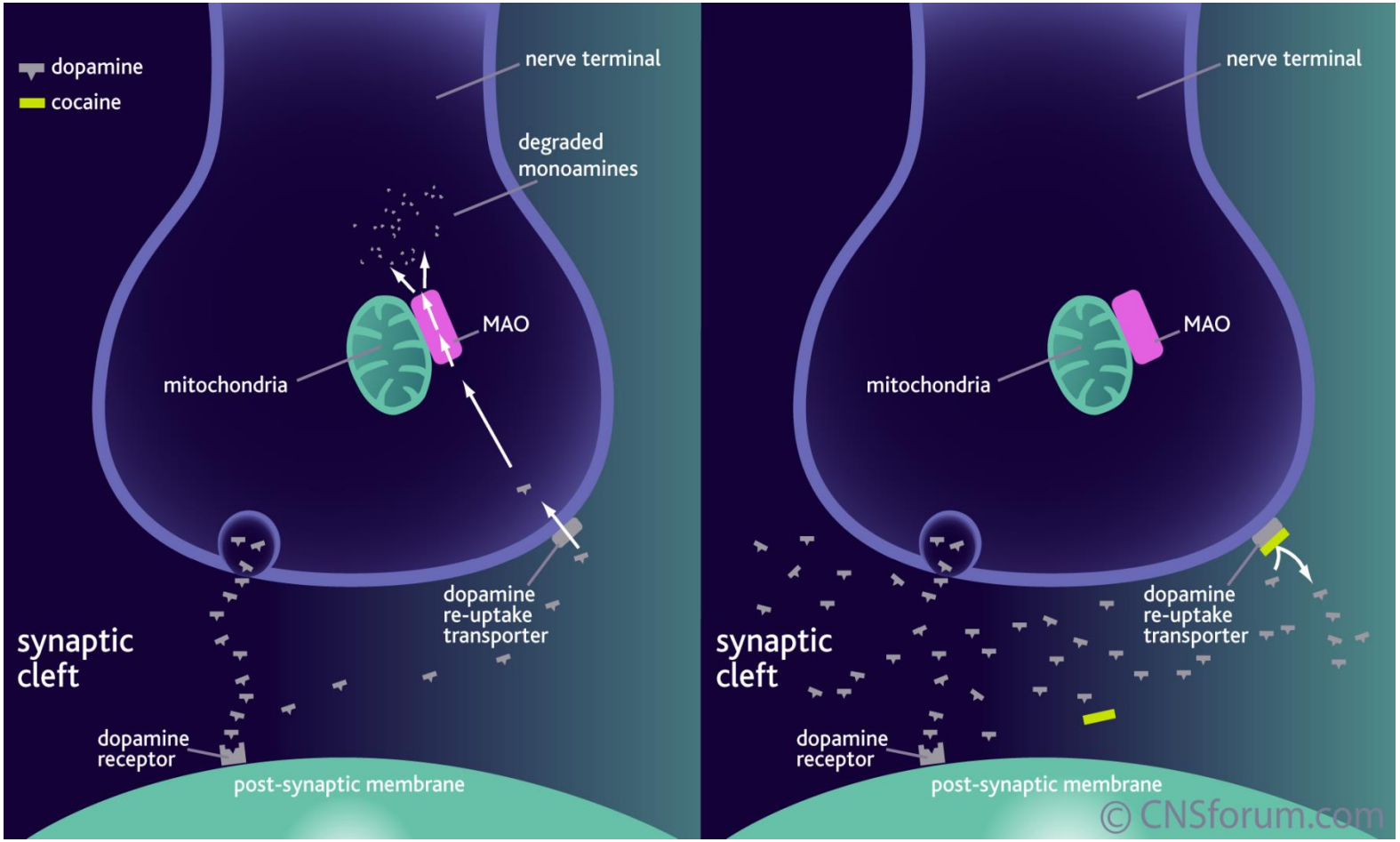
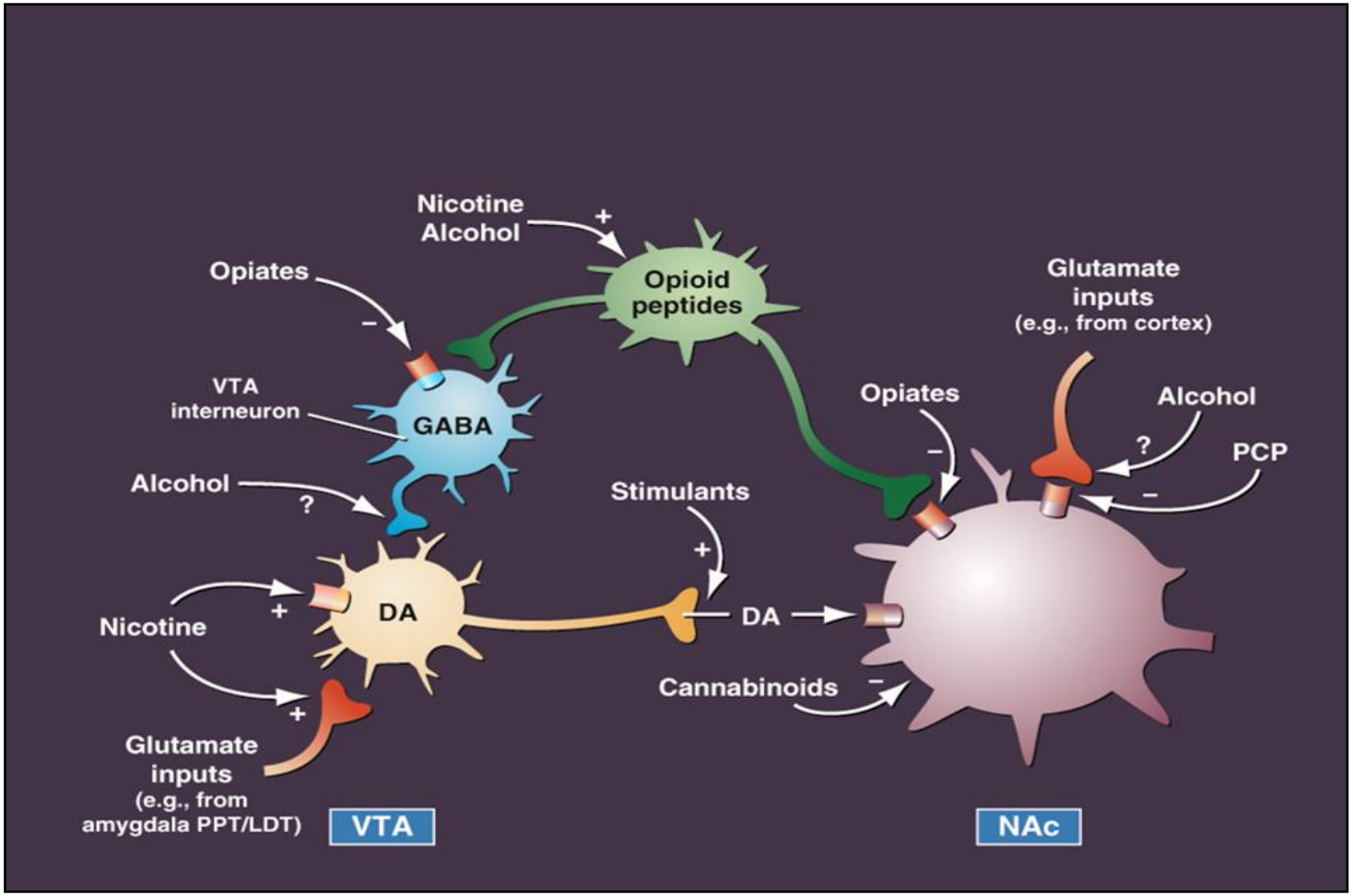


Drug action: indirect (via other receptors & neurotransmitters)



Drug action: indirect (via other receptors & neurotransmitters)

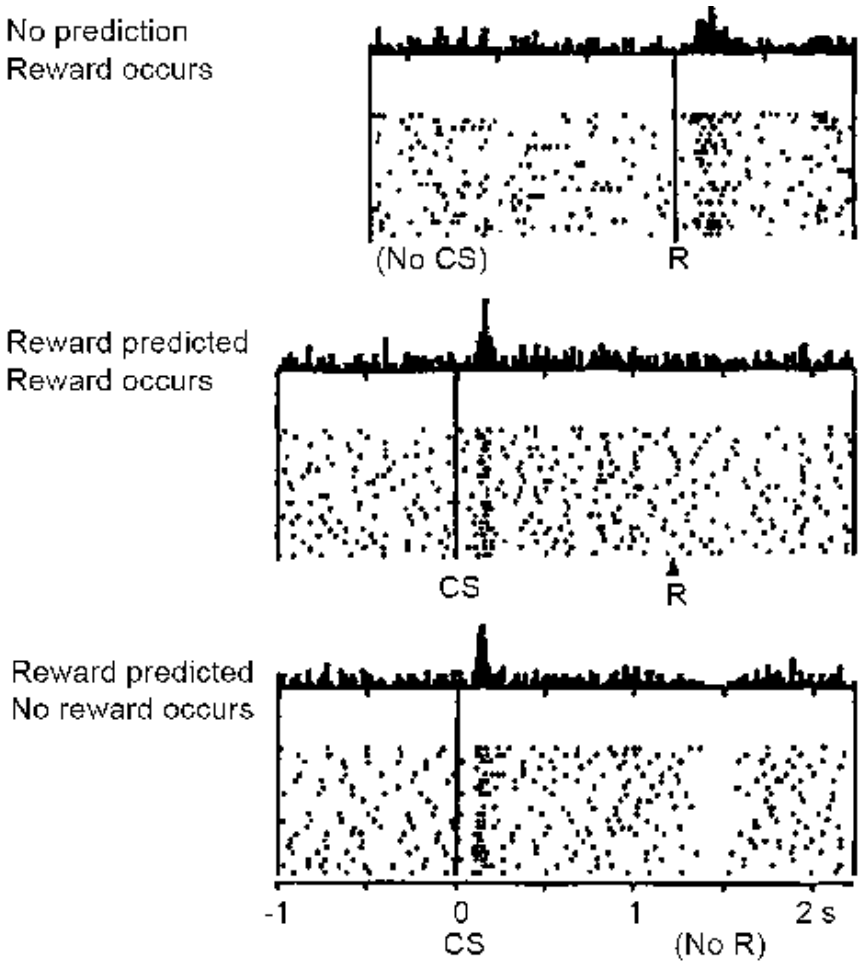
Alcohol Inhibit ***GABAergic neurons*** that project to dopaminergic neurons in the VTA	**Heroin** Binds to ***opioid receptors*** that inhibit GABAergic neurons that project to dopaminergic neurons in the VTA
Cocaine Blocks the function of ***DAT*** (by binding to the DAT and slowing transport)	**Nicotine** 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, ١٩٩٠s)

- 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*.

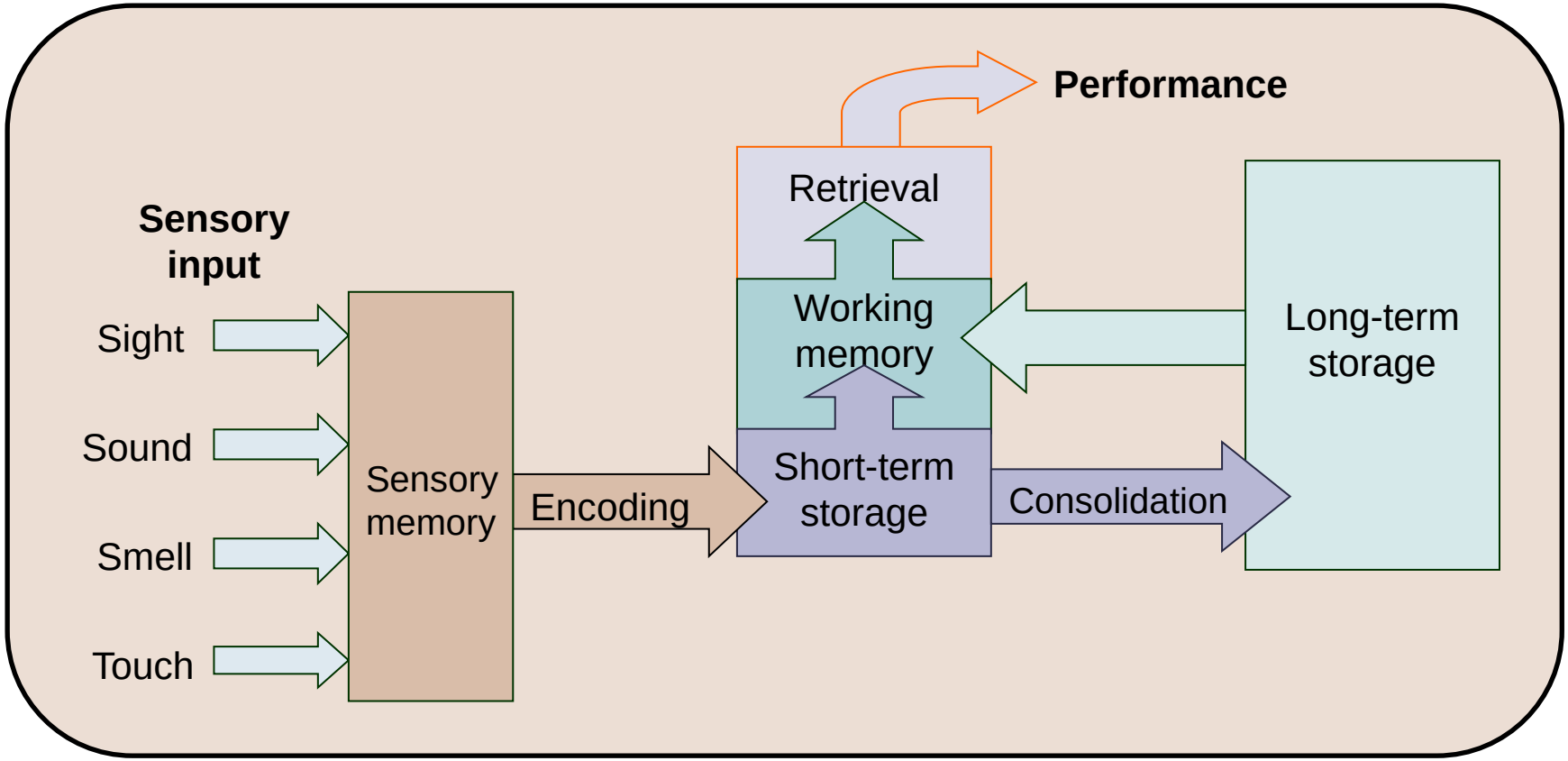
- A predicted **consequence** of these hypotheses would be *"**profound overlearning**" of the motivational significance of cues that predict the delivery of drugs*.

Learning & memory

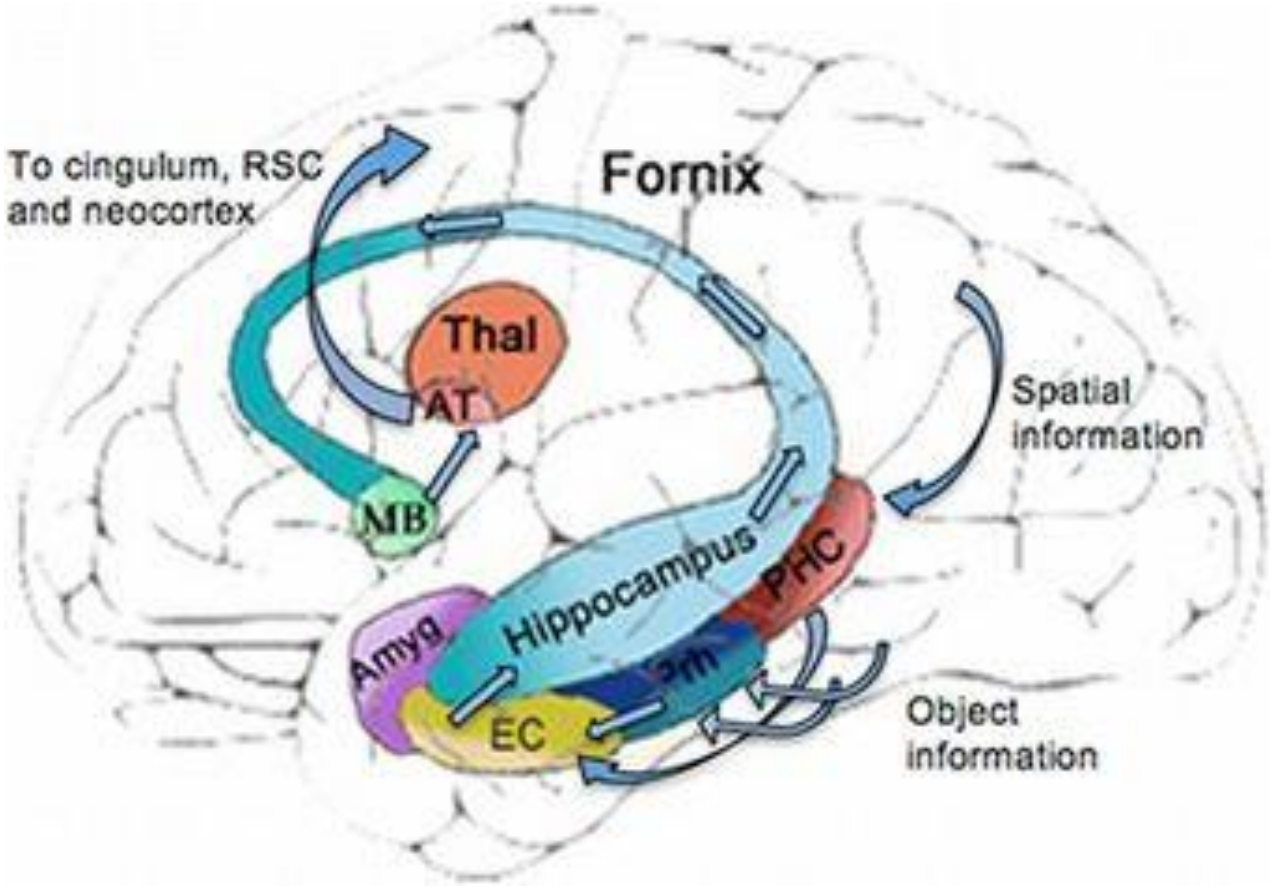
- **Learning** is the process by which we *acquire knowledge* about the world.

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

Information processing model of memory



Learning & memory



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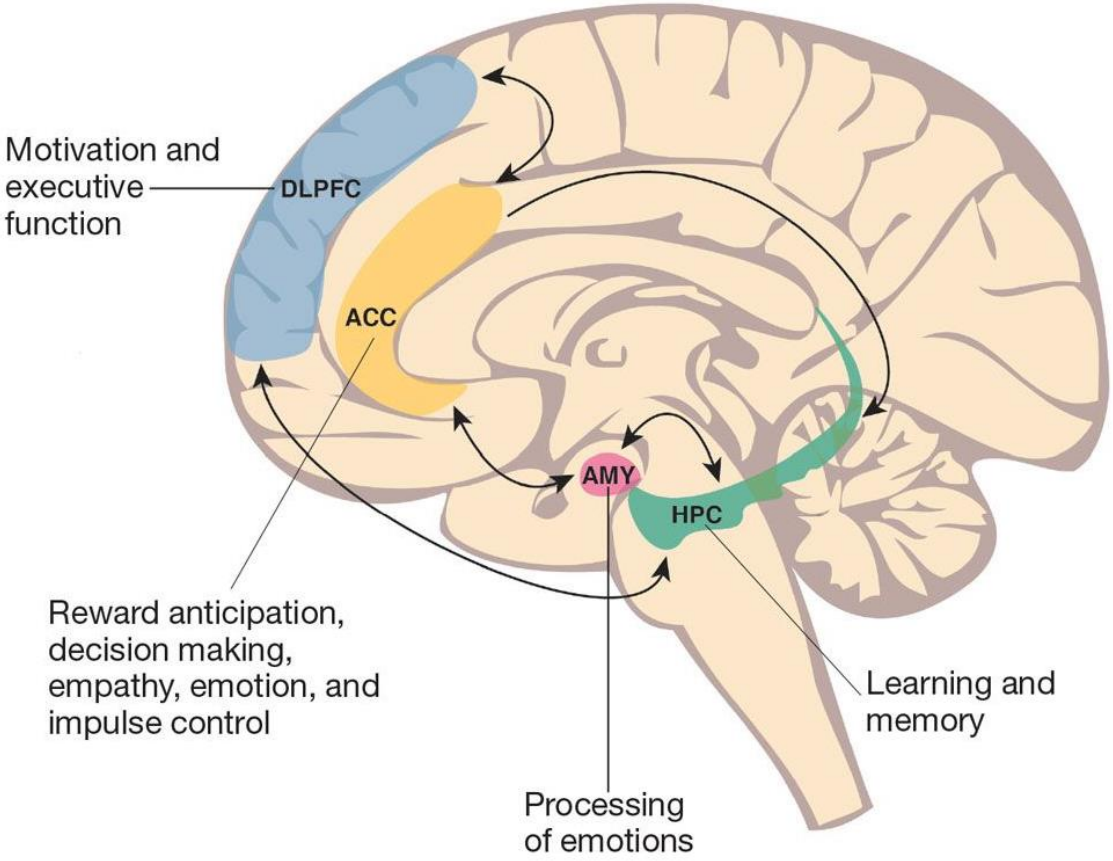
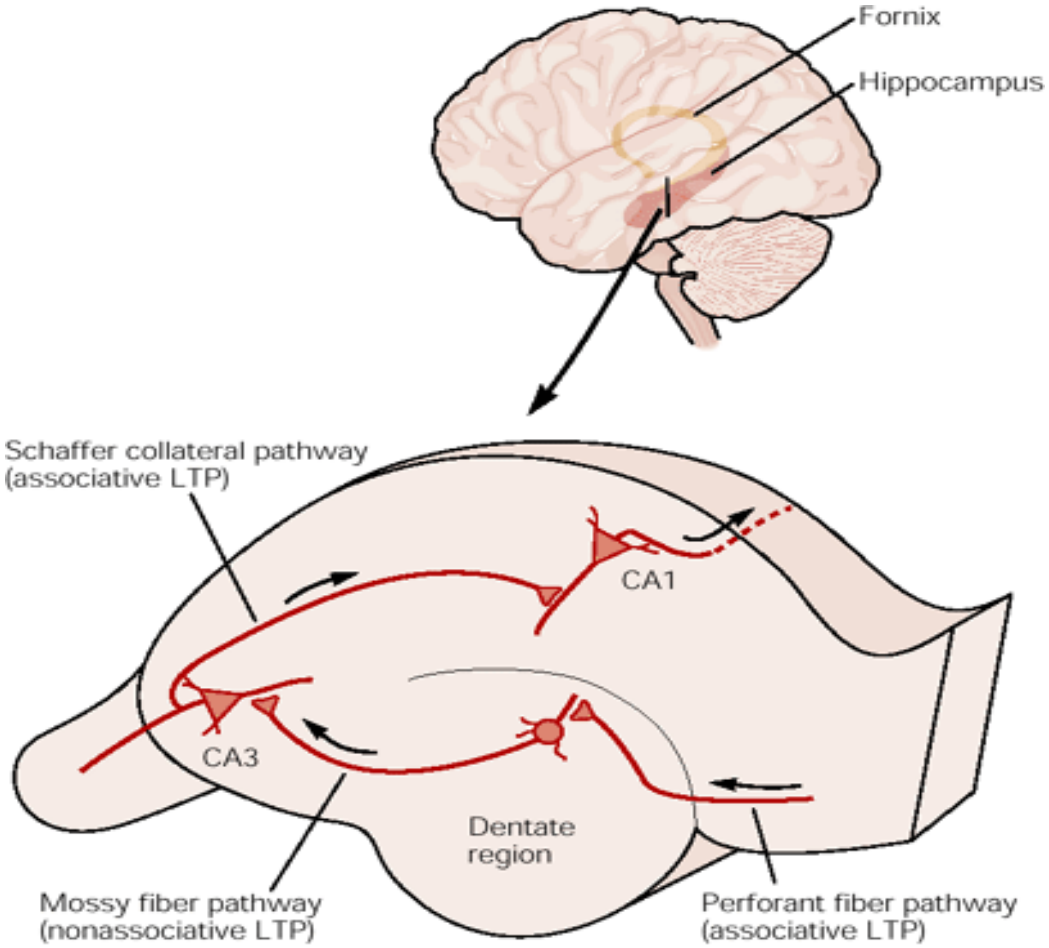
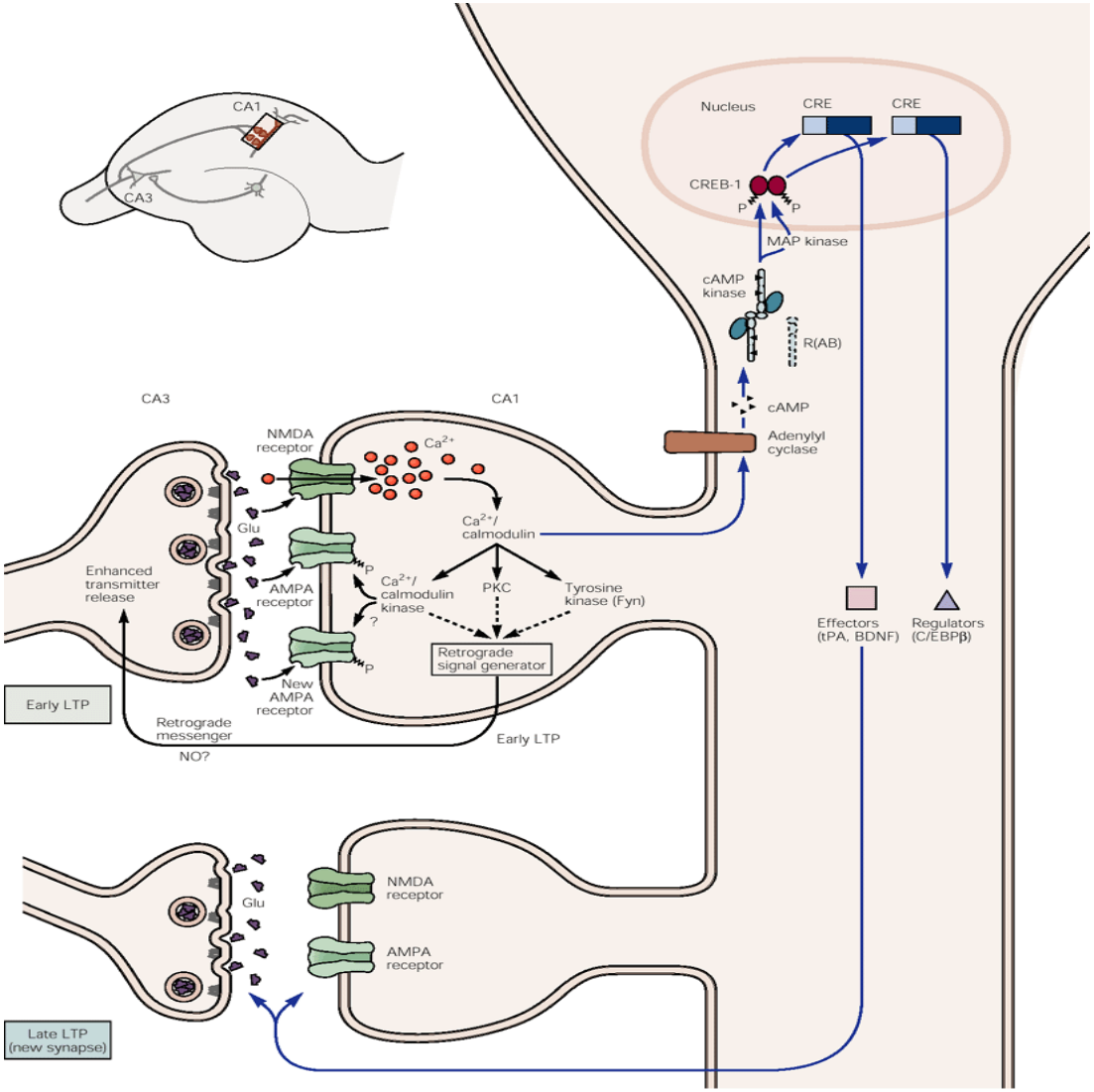


DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex; AMY, amygdala; HPC, hippocampus.

Learning & memory



Learning & memory: Long-term potentiation (LTP)

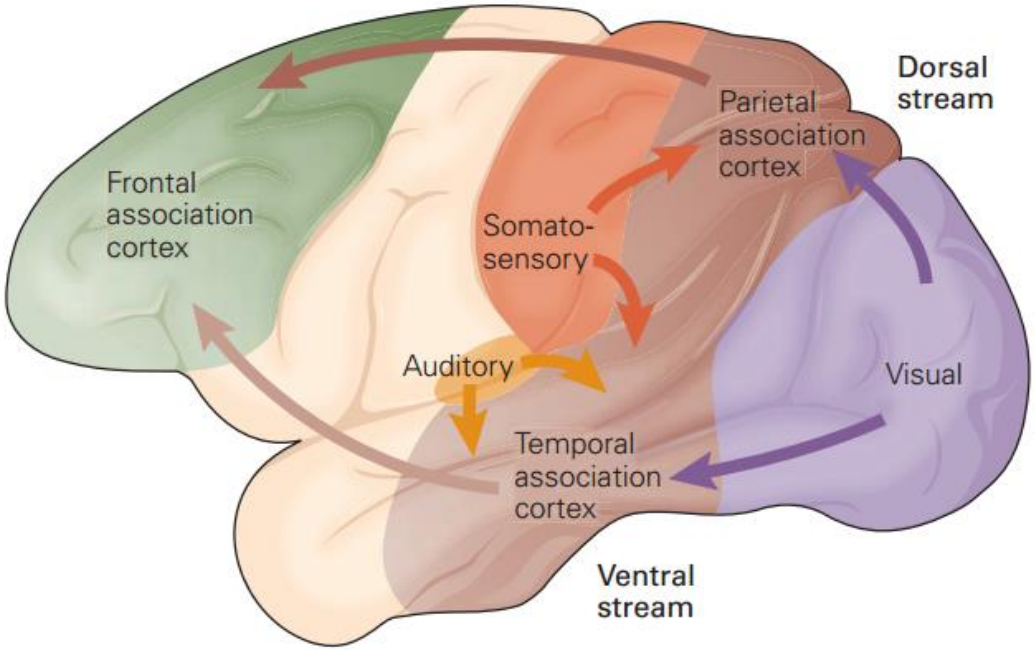


Addiction & long-term memory

- **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.

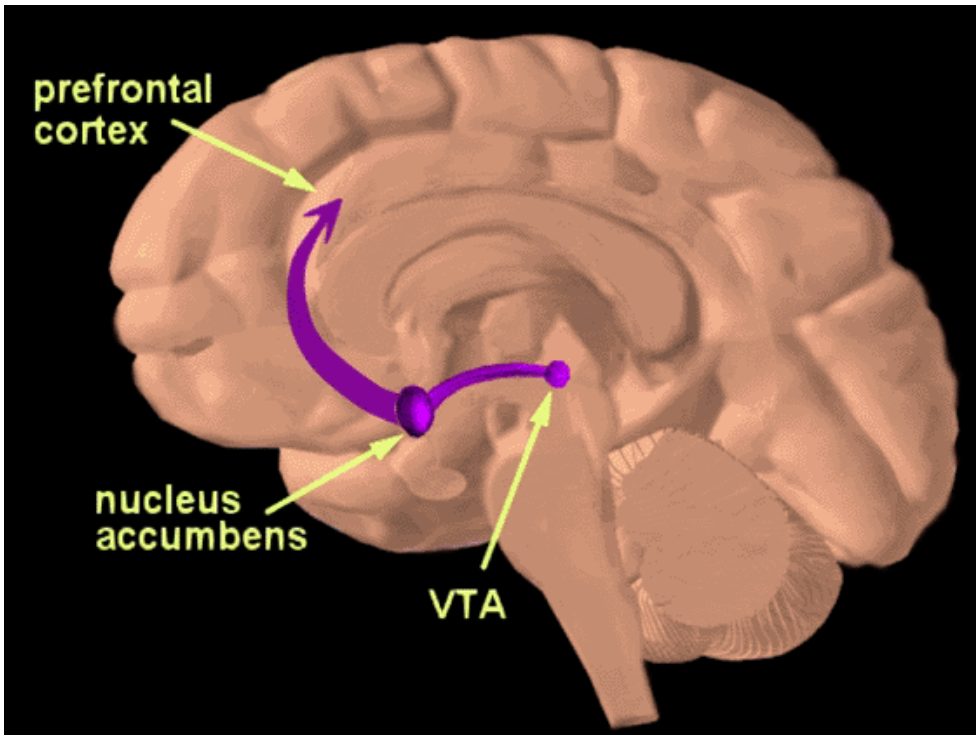
A role for the prefrontal cortex

- 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

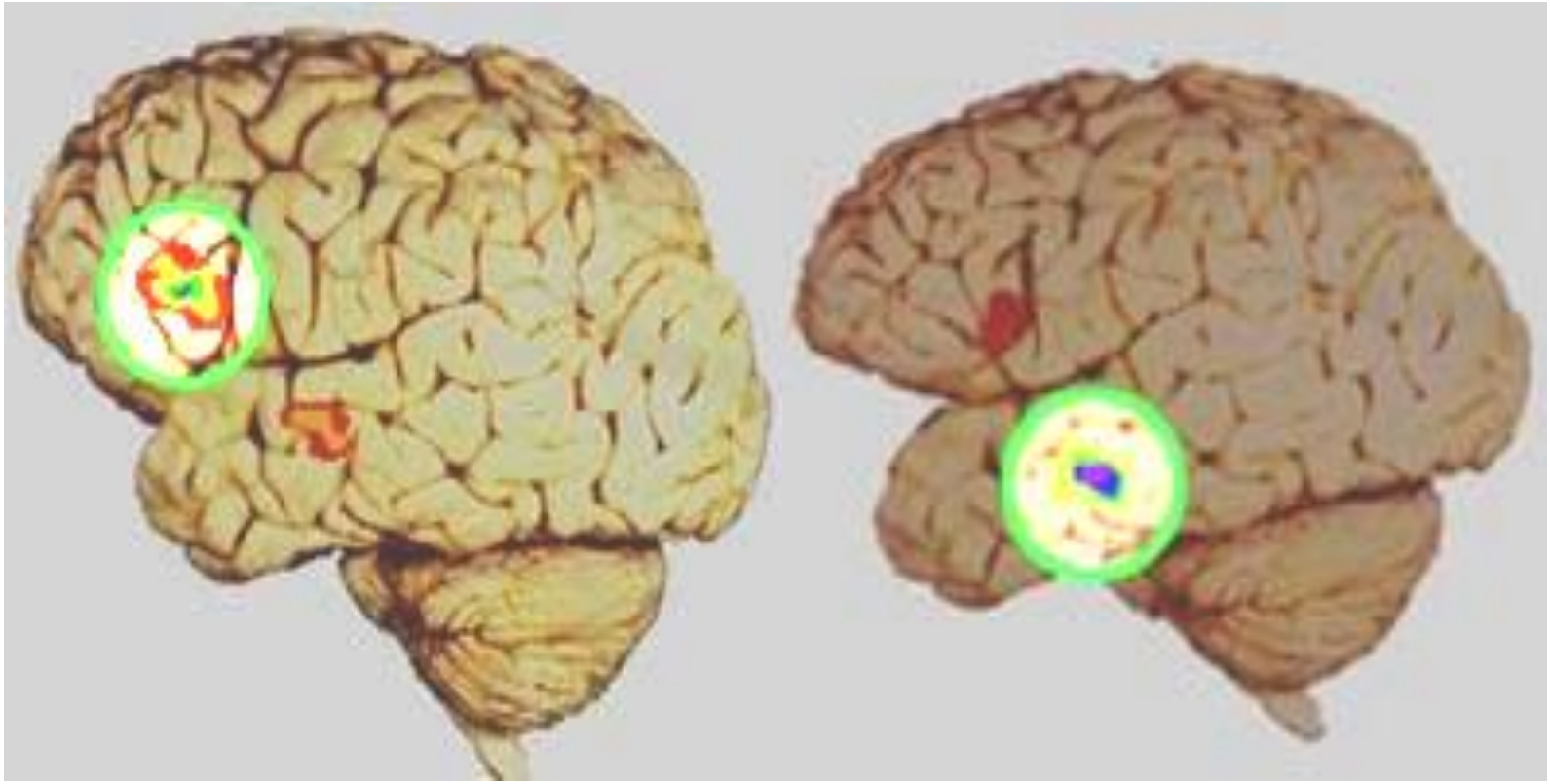
- **In an addicted person**, neural adaptations to repetitive, excessive dopaminergic bombardment might *decrease responses to natural rewards* or reward-related cues that elicit weaker dopamine stimulation, compared with drugs that directly cause dopamine release.

Why can’t addicts just quit?

- 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 *prefrontal cortex*, while **teens** rely more on the *amygdala*



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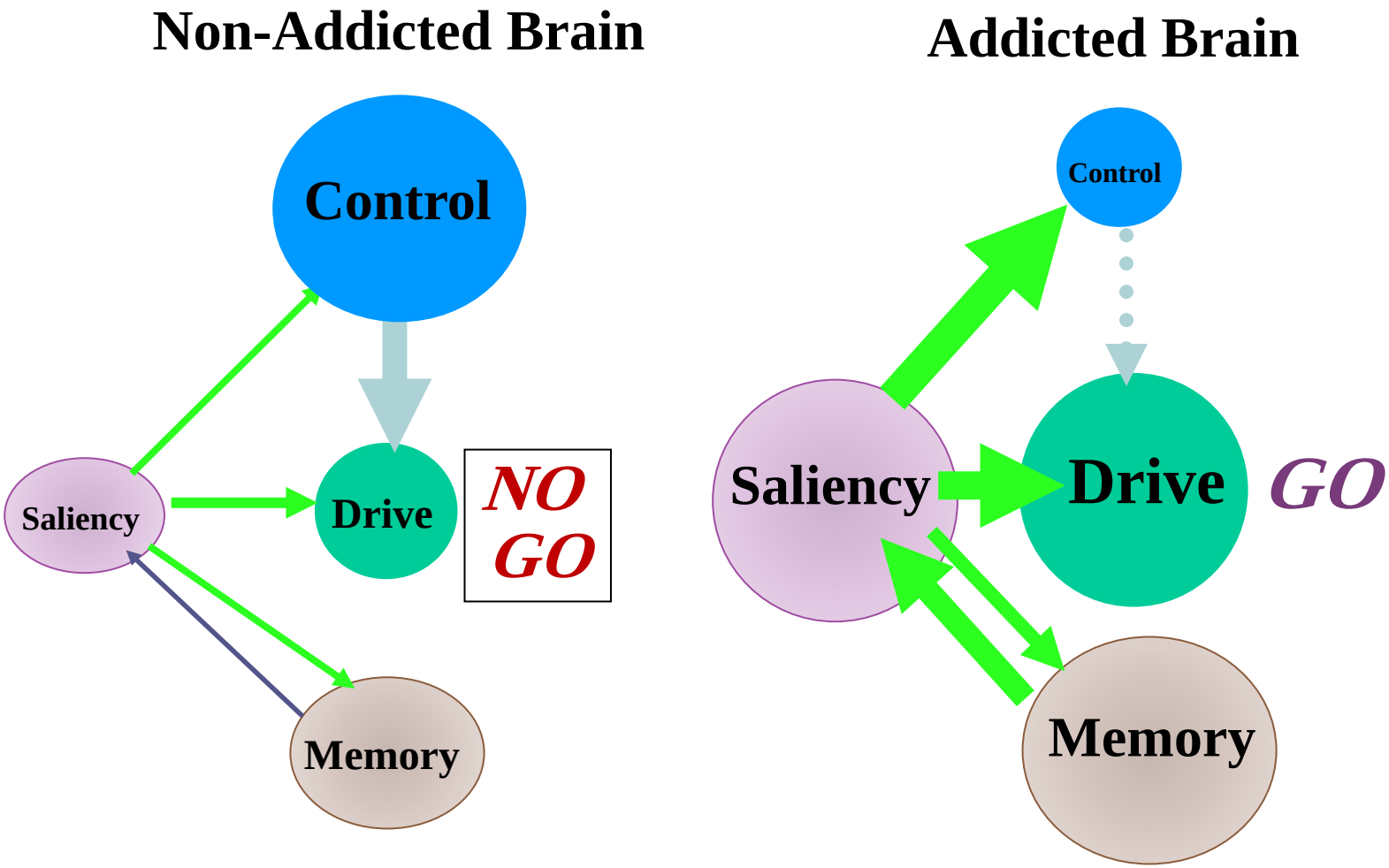

Because addiction changes brain circuits!

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