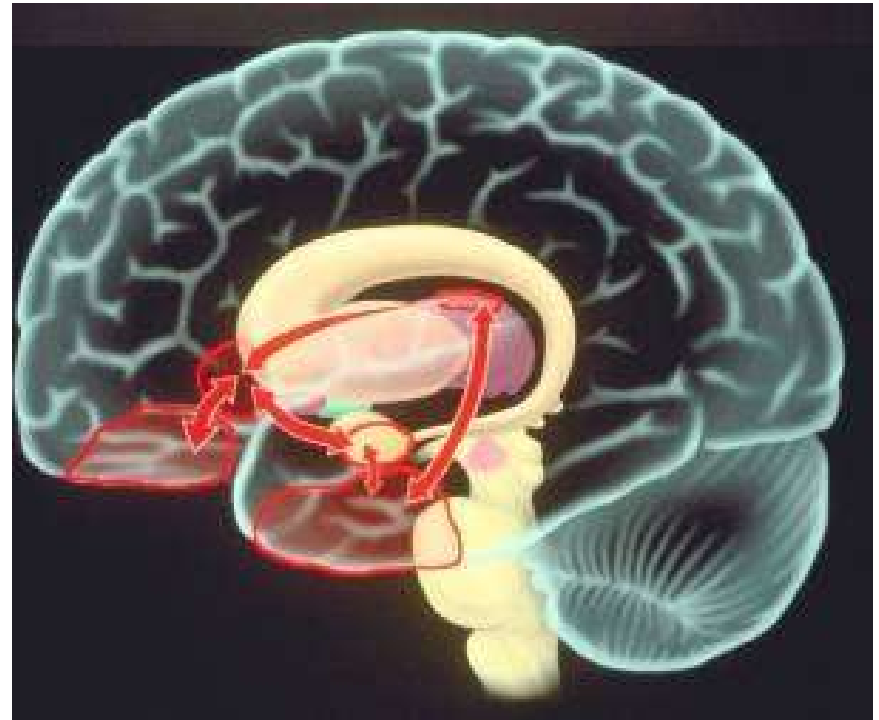


# Adolescent Brain Development, Substance Use and Gambling Involvement

**Ken Winters, Ph.D.**  
**Department of Psychiatry**  
**University of Minnesota**  
**winte001@umn.edu**

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Problem Gambling  
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- **Adolescence is a period of profound brain maturation.**
  - It was believed that brain development was complete during childhood
  - The maturation process is not complete until about age 25!!!

# INSIDE THE ADOLESCENT BRAIN

The brain undergoes two major developmental spurts, one in the womb and the second from childhood through the teen years, when the organ matures by fits and starts in a sequence that moves from the back of the brain to the front.

## Nerve Proliferation ...



By age 13 for girls and 17 for boys, the neurons in the back of the brain have formed thousands of new connections. On the red line above, most of them still are being pruned.

## Corpus Callosum

Though it is believed to contain only a few million of the 100 billion neurons that connect the left and right hemispheres of the brain, the corpus callosum is the most important bridge between the two halves of the brain and is crucial to many of its functions.

## Prefrontal Cortex

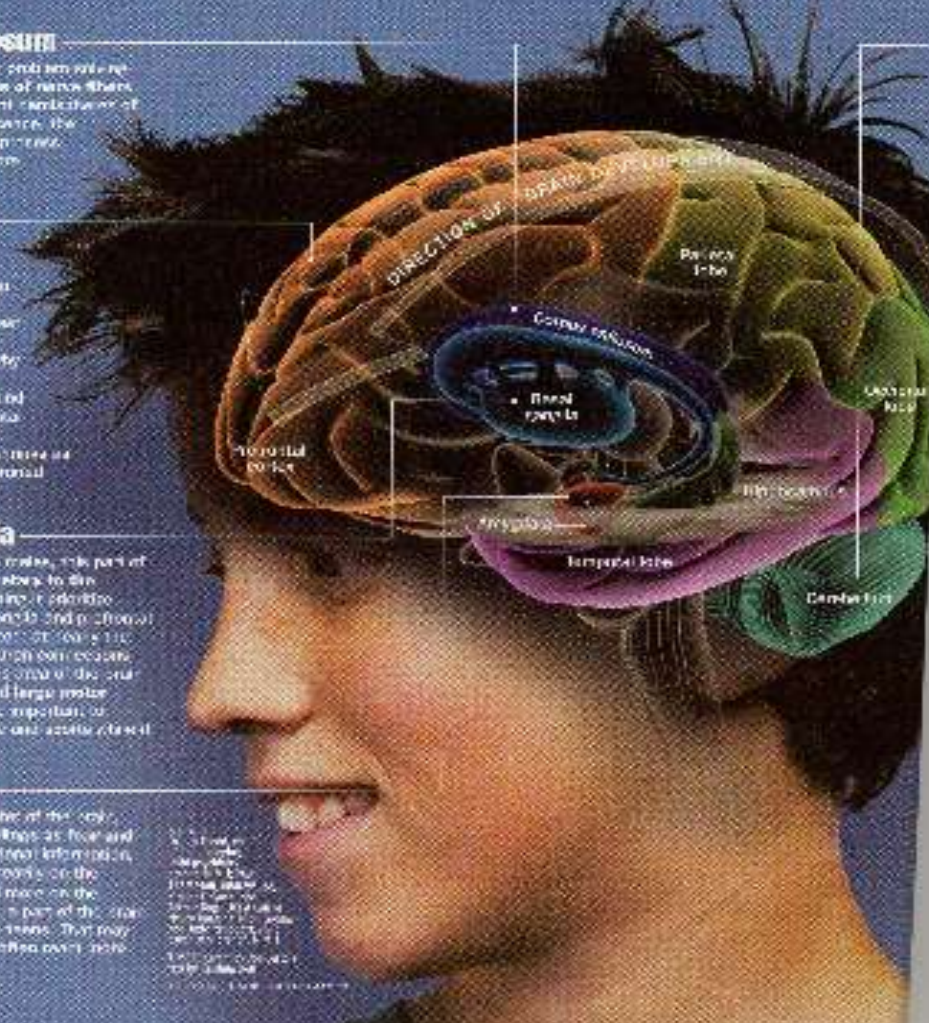
The CEO of the brain, also called the seat of higher thought, is the seat of the brain's executive functions, such as planning, decision-making, and impulse control. It is the last part of the brain to mature, and it is still developing during the teenage years and into the early 20s.

## Basal Ganglia

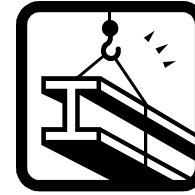
Large subcortical structures, the basal ganglia are involved in motor control, learning, and decision-making. They are also involved in the brain's reward system, which is responsible for the brain's ability to learn from its experiences.

## Amygdala

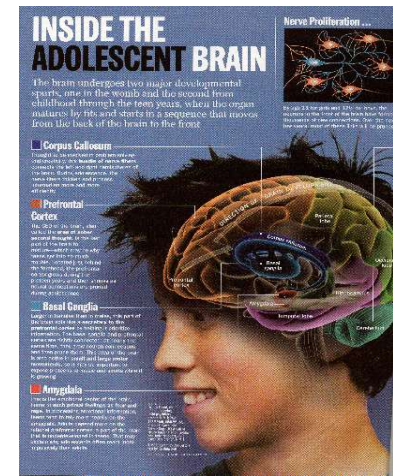
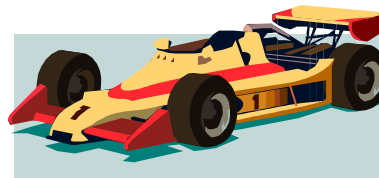
The amygdala is the seat of the brain's emotions, and it is involved in processing information about the environment. It is also involved in the brain's reward system, which is responsible for the brain's ability to learn from its experiences.



# Construction Ahead



- During late childhood, neurons get bushier and increase in the number of connections.
- At about age 11 in girls and age 12½ in boys, this thickening undergoes pruning.
- At the same time, the myelin sheaths that encase nerve cells thicken.
  - Myelin sheaths are like insulation on a wire; they make nerve cell transmissions faster and more efficient
- Net effect when complete is faster, yet fewer, connections in the brain.



# Pruning occurs in stages, from back of the brain to the front



**emotional processing center; evaluates relative pleasure vs aversiveness**

**PFC**

**amygdala**

**nucleus accumbens**

**cerebellum**

**planning; setting priorities; organizing thoughts; suppressing impulses; weighing consequences of one's actions**

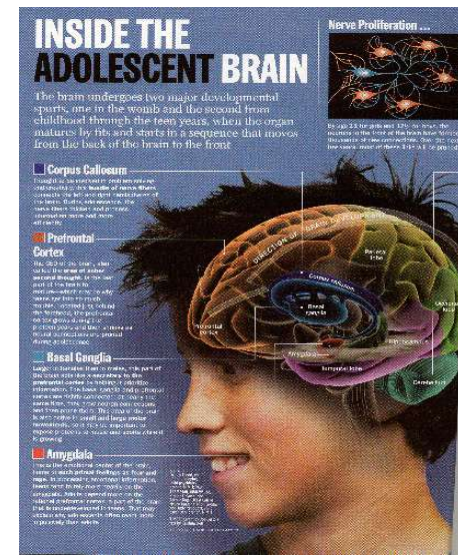
**regulates motivation to seek rewards**

**physical coordination; sensory processing; learning linked to math and music**

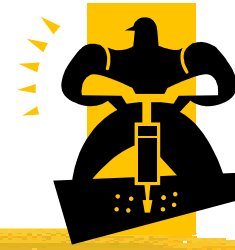
# Arrested Development



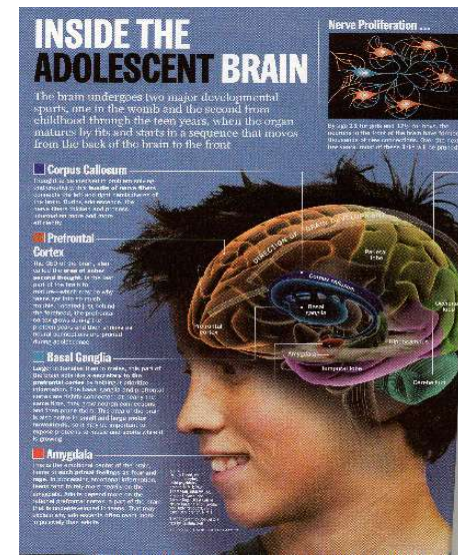
- **Back of brain matures before to the front of the brain...**
  - **sensory and physical activities favored over complex, cognitive-demanding activities**
  - **propensity toward risky, impulsive behaviors**
    - **group setting may promote risk taking**
  - **poor planning and judgment**



# Arrested Development



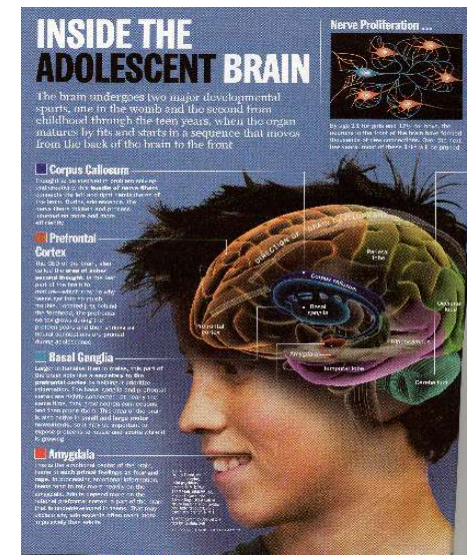
- **Immature nucleus accumbens**
  - activities with high excitement and low effort are preferred
- **Under-developed amygdala**
  - poor modulation of emotions (hot emotions more common than cold emotions)
  - misinterpret the emotions and intentions of others
    - over-interpret non-angry facial expressions as a sign of anger



# Construction Plans Can Change



- **Experiences may alter the brain maturation process**
  - **piano practicing quickly thickens neurons in the brain region that control the fingers**
  - **engaging in high-level memory tasks has been shown to increase the size of the hippocampus**
  - **Stress may slow down the maturation of the prefrontal cortex**



# The Developing Adolescent Brain is Susceptible to Drugs

## INSIDE THE ADOLESCENT BRAIN

The brain undergoes two major developmental spurts, one in the womb and the second from childhood through the teen years, when the organ matures by 18 and starts in a sequence that moves from the back of the brain to the front.

### Nerve Proliferation



By age 25, the adolescent brain has nearly the neurons in the size of the brain have formed thousands of new connections. Still, the brain's wiring is not yet fully formed.

### Corpus Callosum

Thought as an evolutionary oddity, the corpus callosum is the bundle of fibers that connects the left and right hemispheres of the brain. It's a major highway for information, and it's still growing in the adolescent brain.

### Prefrontal Cortex

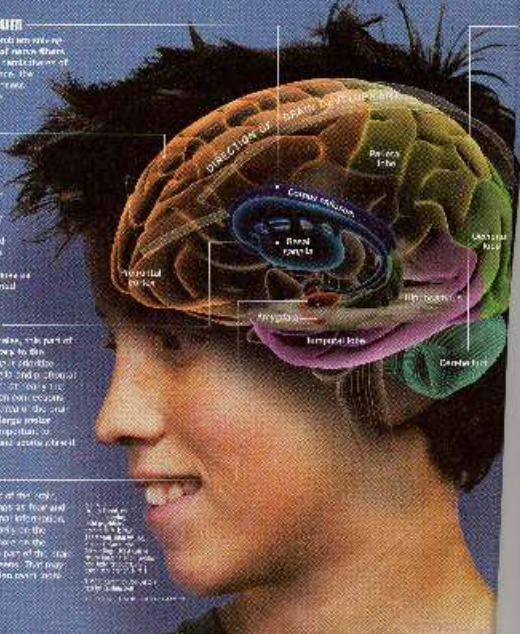
The CEO of the brain, the prefrontal cortex is the area of the brain that is most affected by drugs. It's the part of the brain that is still developing in the adolescent brain, and it's the part that is most vulnerable to the effects of drugs.

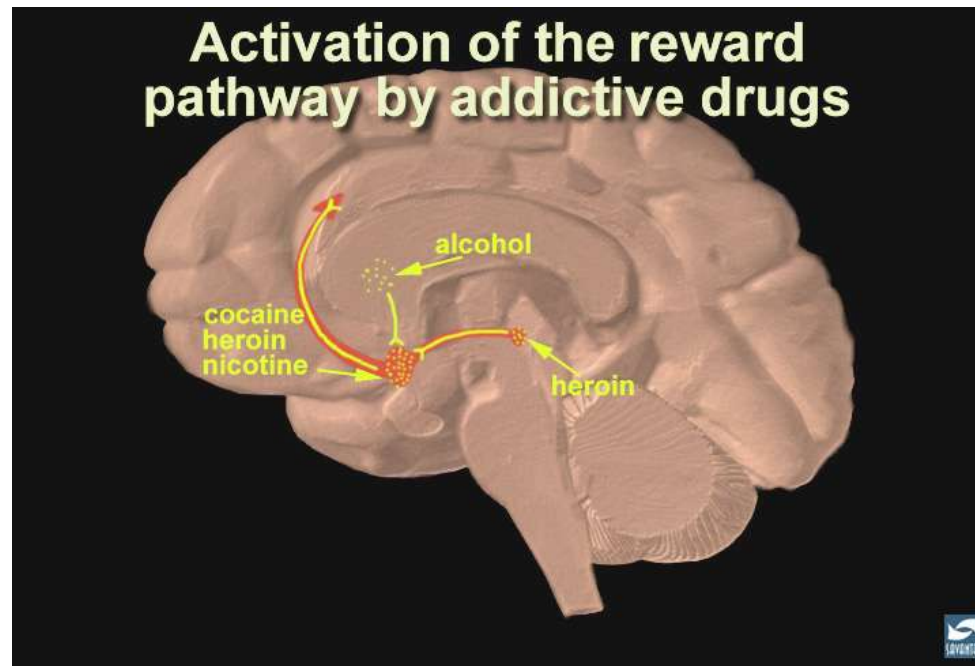
### Basal Ganglia

Thought of as the brain's control center, the basal ganglia is the part of the brain that is most affected by drugs. It's the part of the brain that is still developing in the adolescent brain, and it's the part that is most vulnerable to the effects of drugs.

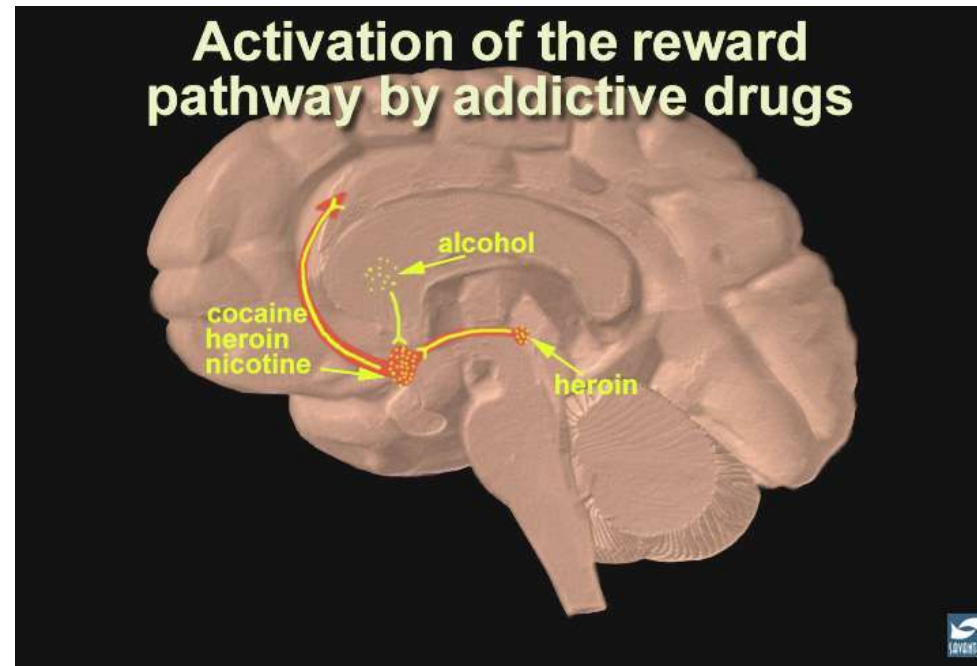
### Amygdala

The brain's emotional center, the amygdala is the part of the brain that is most affected by drugs. It's the part of the brain that is still developing in the adolescent brain, and it's the part that is most vulnerable to the effects of drugs.



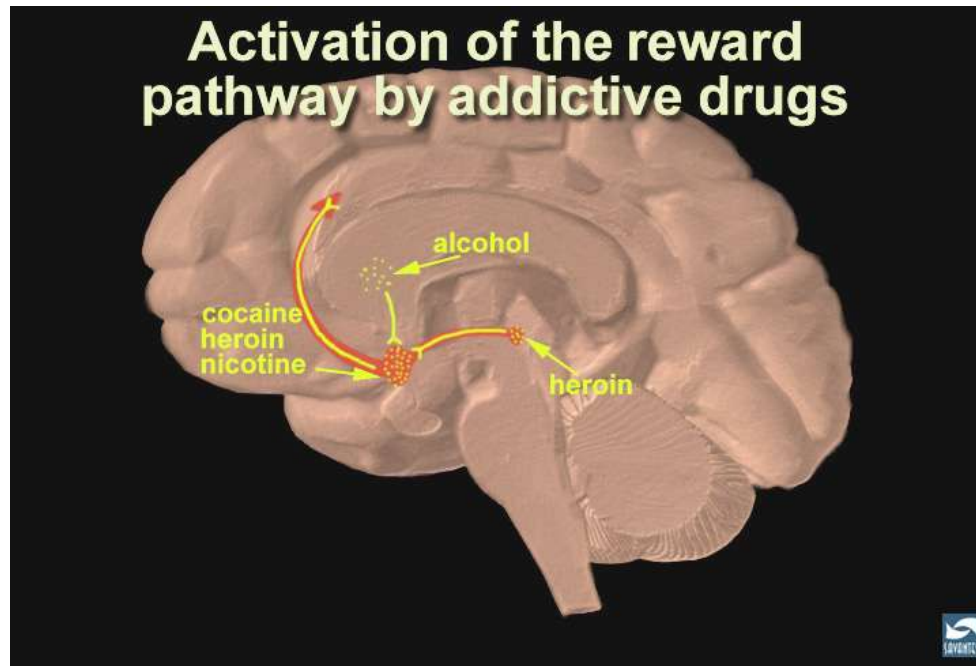


- **Drugs activate or “light-up” the brain’s reward pathway**
- **The reward pathway directs behaviors essential for survival value**
  - **seeking food, water, sex, and nurturance**



**How does this activation of a “survival” system lead to addiction for some individuals?**

## Activation of the reward pathway by addictive drugs

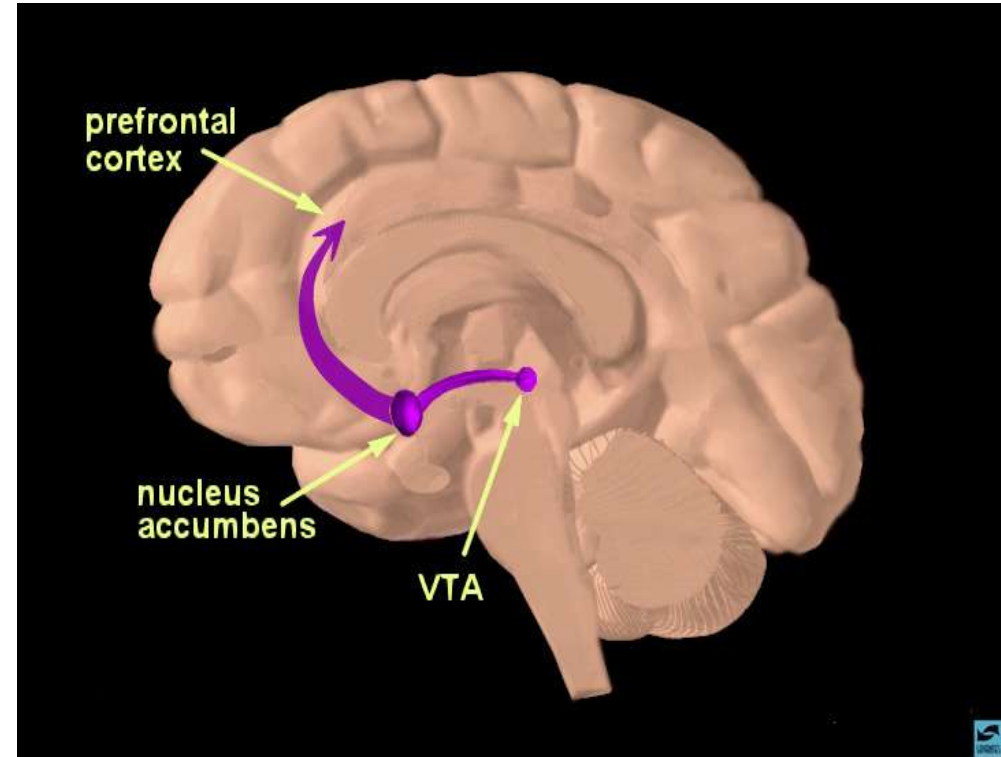


**Veni, Vidi, Vici**

# Veni, Vidi, Vici

**Veni: The drug came (to the user's brain)**

drug ingested → **VTA**  
signals nucleus accumbens  
(**na**) → levels increase of a  
euphoria-inducing  
neurotransmitter,  
dopamine (**"wow"**)



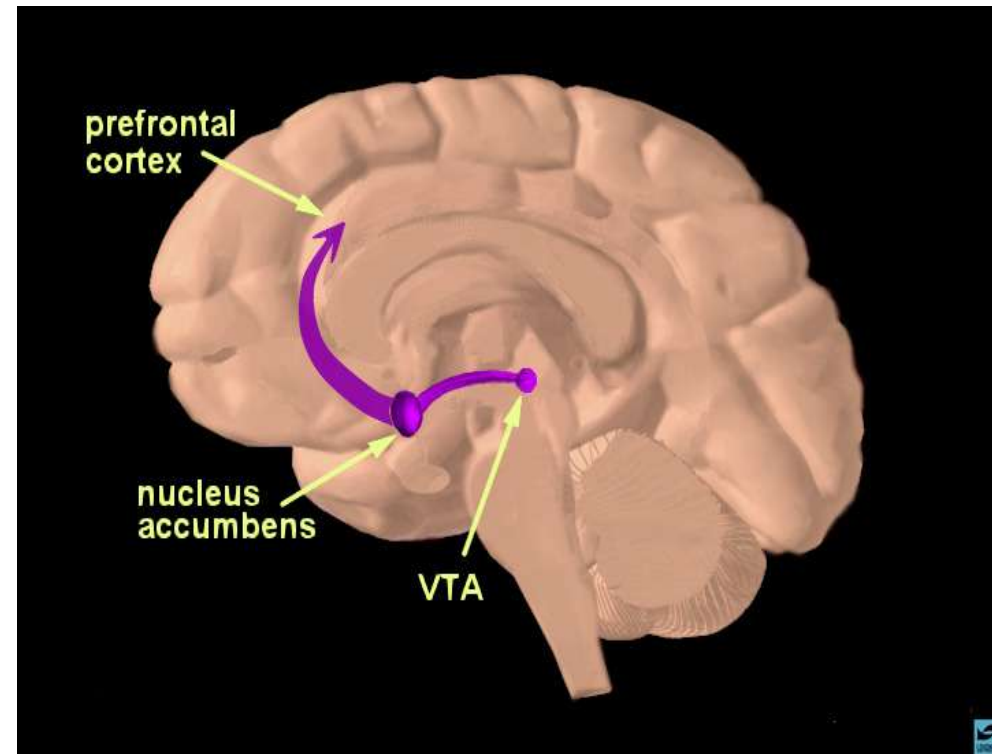
# Veni, **Vidi**, Vici

**Vidi: The drug saw (its impact on the brain)**

**na** signals the **amygdala** → weighs the relative pleasure and aversiveness of the experience  
("This is worth repeating.")

**amygdala** signals the **hippocampus** → records memory of the experience, including where and when ("I am going to remember this drug experience.")

**PFC** → receives, coordinates and processes this molecular experience, and shapes future behavior and attitudes of the drug experience  
("Go for it again?" vs. "Too risky?")



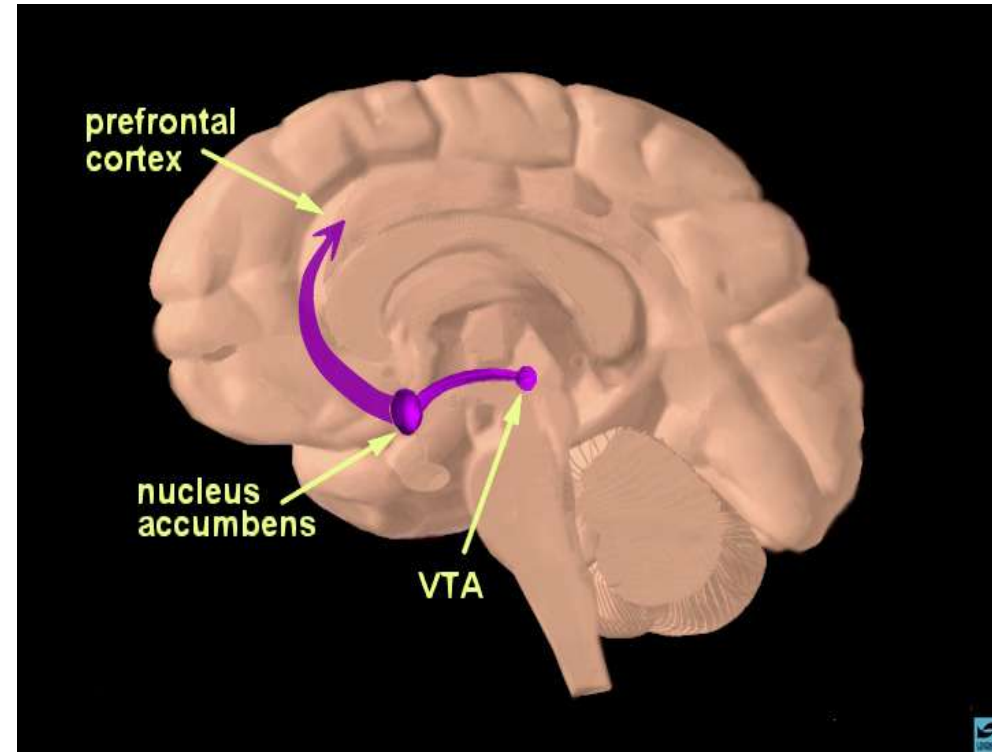
# Veni, Vidi, Vici

**Vici: The drug conquered (by commandeering the brain) continued use of the drug.....**

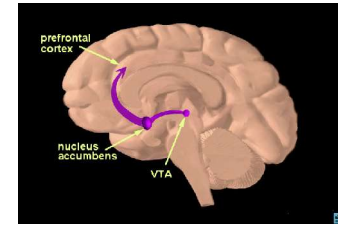
**CREB**, a protein is activated → reduction in dopamine levels and dampening to the overall reward system (“I crave the drug. I need to take more of the drug.”)

**delta FosB**, another protein is activated → creates sensitization to drugs and the cues associated with prior use (“I am prone to relapsing.”)

- May promote growth of dendrite buds in the **na**, which are “tagged” with memories of the drug



# Review: Veni, Vidi, Vici



- **Drugs of abuse immediately activate the brain's reward pathway, particularly by increasing levels of a euphoria-inducing neurotransmitter, dopamine.**
- **Continued, chronic heavy drug use leads to several adaptations in the brain that promote the ingredients of addiction: tolerance, craving and relapse.**
- **Future research:**
  - **How much and how quickly can reversal or correction of the brain adaptations occur when drug use is reduced or stopped?**
  - **What new-age pharmacotherapies can promote this restoration?**
  - **Can high-risk individuals be identified for genetic profiles that increase one's susceptibility to the "commandeering of the brain" by drugs?**

# Evidence

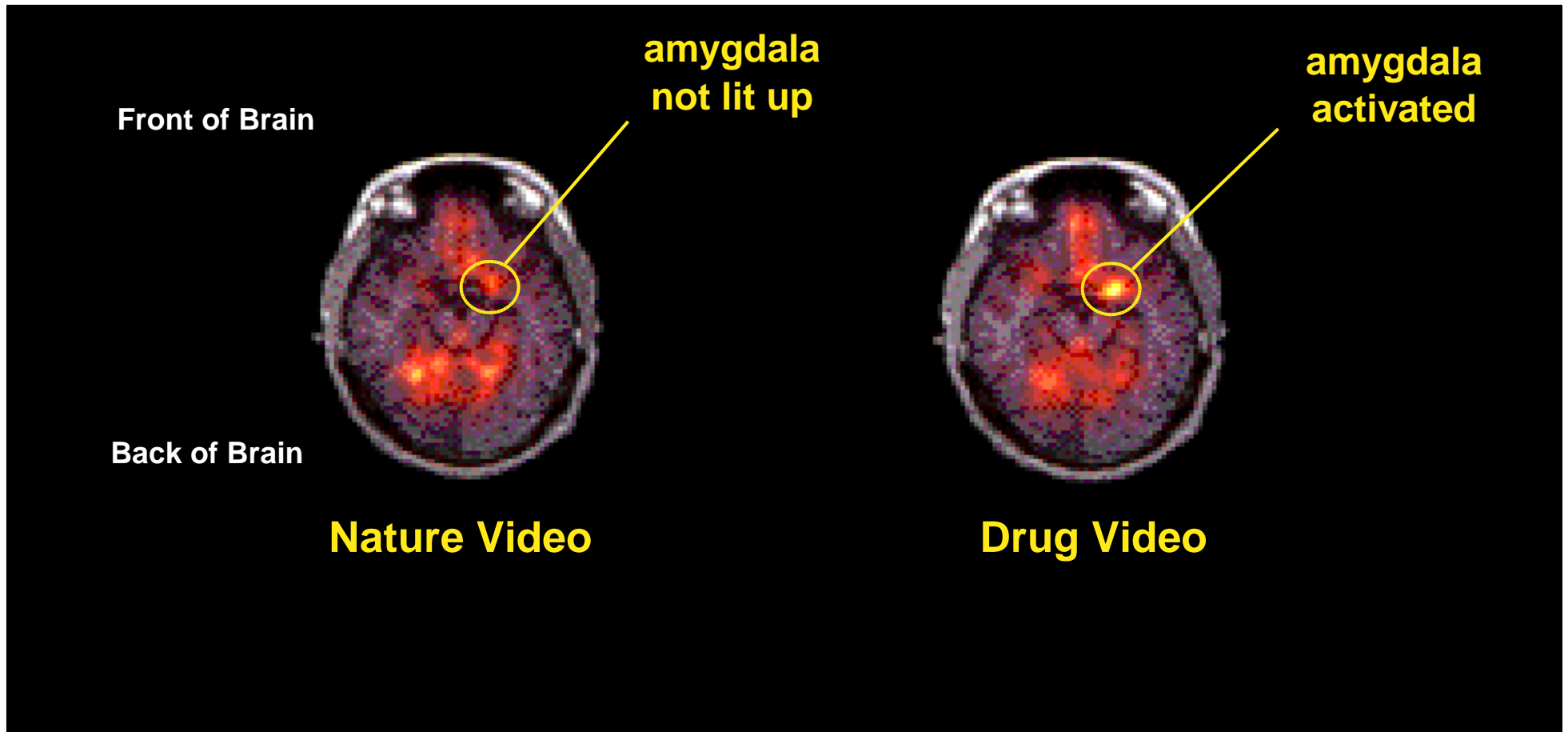
- **Animal Studies:**

- **animal investigations support the “hijacking” of the brain’s reward system by alcohol and other drug use**
  - **when electrodes attached to the reward circuitry, drug use continues until collapse from exhaustion**
  - **when rats are bred for excessive delta FosB, heightened sensitization is observed**

- **Behavioral Genetics Studies:**

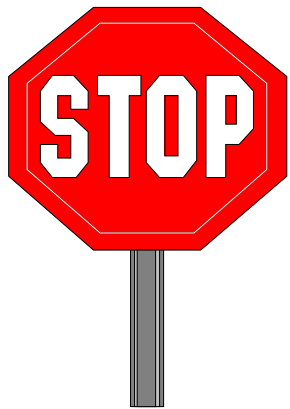
- **heredity plays a role**
  - **identical twins: > chance of becoming alcoholics than fraternal twins**
  - **adoptive children of alcoholics: > chance of becoming alcoholic, even true when raised by non-alcoholic parents**
  - **further research needed regarding other drugs and by gender**

**Human Studies: Amygdala (with help from the hippocampus and PFC) has memory of the drug after discontinuation. This “memory” can occur months after discontinuation.**

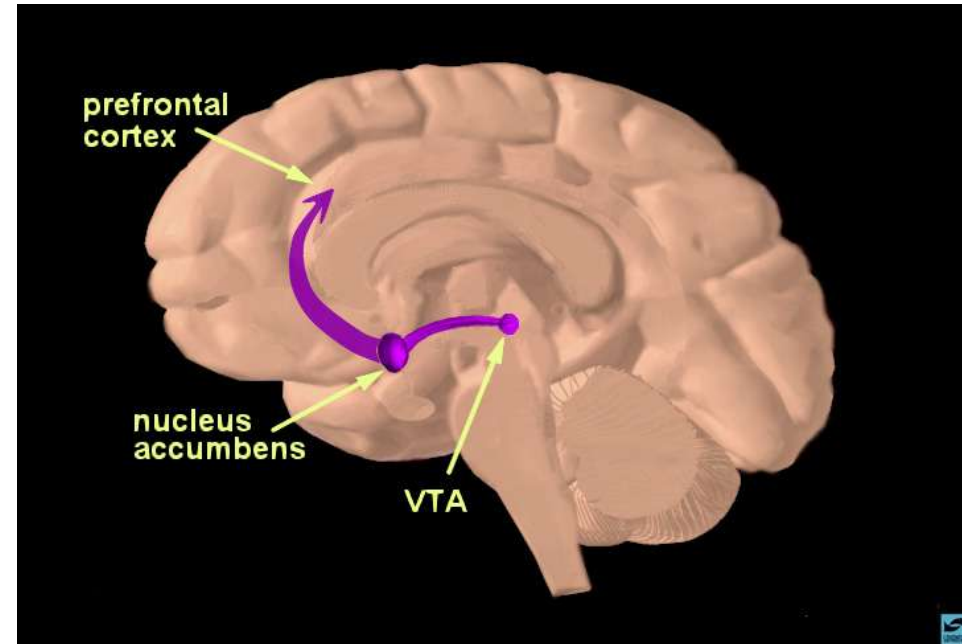


# Are adolescents more susceptible to alcohol than adults?

- **Adult studies suggest that the areas of the adolescent brain that are remodeled are sensitive to the effects of alcohol**



**Difficult scientifically and ethically to study adolescent sensitivity to alcohol**



# **Are adolescents more susceptible to alcohol than adults?**

---



- **Animal models can be easily used to explore this issue**
- **Role of psychosocial factors can not be studied**

# Are adolescents more susceptible to alcohol than adults?

- 1** Adolescent rats are less sensitive to effects of intoxication and less sensitive to the “hangover” that follows use



# Are adolescents more susceptible to alcohol than adults?

**2** Adolescent rats are more sensitive to the social disinhibition induced by alcohol use

Wanna look for some cheese with me?



Sure!



# Are adolescents more susceptible to alcohol than adults?

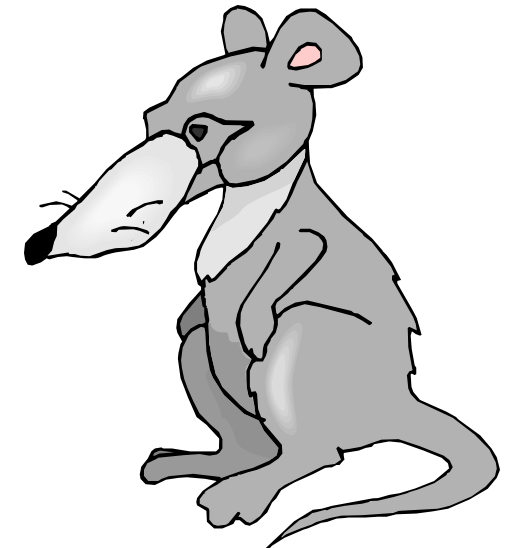
**3 Adolescent drunk rats perform worse on memory tasks than adult drunk rats**

converts  
information  
to memory

disrupts the hippocampus

brain damage in the PFC

Ugh?  
?



planned  
thinking

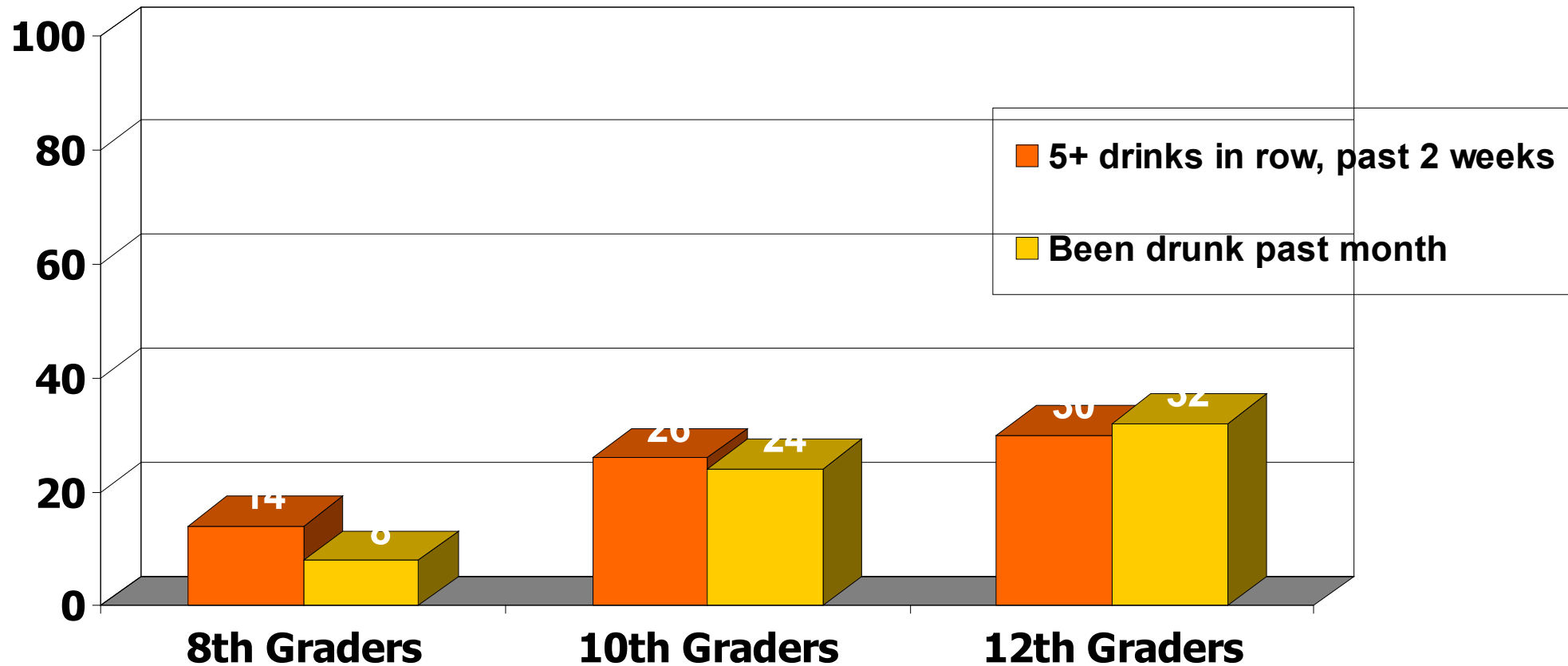
# Supporting Human Studies

- 1. Reduced sensitivity to intoxication**
- 
- 3. Greater adverse effects to cognitive functioning**



# Survey Data Suggest that Adolescents Are Less Sensitive to Alcohol's Effects

Monitoring the Future, 2001



# Alcohol's Effects

(Brown, 2002; Wuethrich, 2001)

- **Adolescents with a history of extensive use....**

↓ **Hippocampus (50%)**

converts  
informatio  
n to  
memory

↓ **brain activity during memory tasks**

↑ **brain activation when shown alcohol images**

trigger  
for  
relapse

# Are adolescents more susceptible to alcohol than adults?

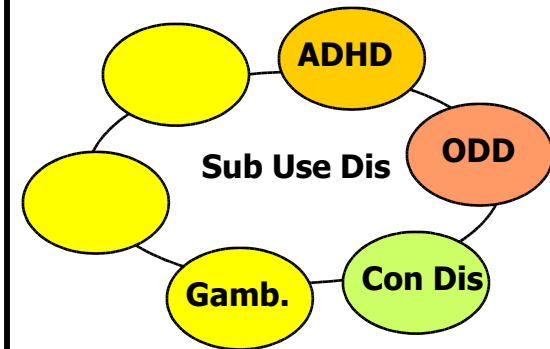


**4 Hyperexcitability issue**

# Are adolescents more susceptible to alcohol than adults?

## 4. Hyperexcitability issue

- Alcohol relieves hyperexcitability state
- Relief is temporary; continued seeking of alcohol is reinforced
- Hyperexcitability is a key characteristic of conduct disorders, ADHD & other impulsive behaviors
- Hyperexcitability found in non-alcoholic relatives - suggests inheritance of this trait



# **Are adolescents more susceptible to alcohol than adults?**

**Most certainly YES**

- 1. Reduced sensitivity to intoxication**
- 2. Increased sensitivity to social disinhibitions**
- 3. Greater adverse effects to cognitive functioning**
- 4. Medicates "excitability"**

# **Are adolescents more susceptible to alcohol than adults?**

## **Increases reinforcing properties**

- 1 Reduced sensitivity to intoxication**
- 2 Increased sensitivity to social disinhibitions**
- 3 Medicates "excitability"**
- 4 Medicates "excitability"**

# **Are adolescents more susceptible to alcohol than adults?**

**Greater deficits**

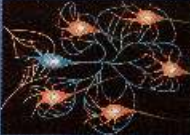
- 3 Greater adverse effects to cognitive functioning**

# The Developing Adolescent Brain May be Susceptible to Gambling

## INSIDE THE ADOLESCENT BRAIN

The brain undergoes two major developmental spurts, one in the womb and the second from childhood through the teen years, when the organ matures by 18 and starts in a sequence that moves from the back of the brain to the front.

### Nerve Proliferation ...



By age 25, the adolescent brain has the neurons in the front of the brain have formed thousands of new connections. Over the next few years, more of these connections will form.

### Corpus Callosum

Thought as an evolutionary oddity, the corpus callosum is the bundle of fibers that connects the left and right hemispheres of the brain. It's a major highway for information, and it's still growing in the adolescent brain.

### Prefrontal Cortex

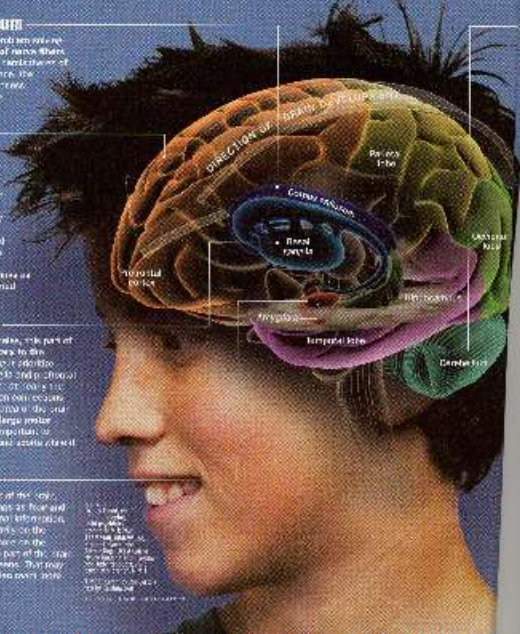
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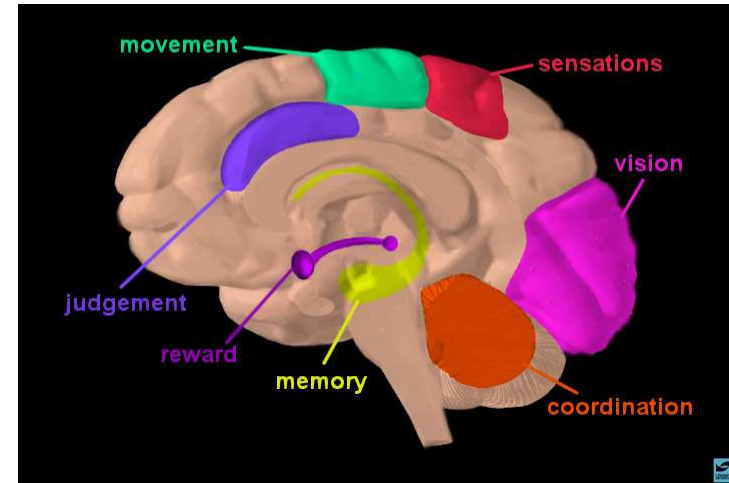
### Amygdala

The brain's emotional center, the amygdala is the part of the brain that's responsible for processing emotions. It's the part of the brain that's still developing in the adolescent brain.



# Implications for Prevention and Treatment

- **Prevention**
  - **The earlier the better**
  - **Educate them about the susceptibility of the adolescent brain and risk taking behaviors**
  - **Developmentally adjust given the maturation of brain development**



# Glossary

- **mesolimbic dopamine system:**  
VTA (ventral tegmental area) and nucleus accumbens
- **amygdala:**  
brain region that helps assess whether an experience is pleasurable or aversive, and whether it should be repeated or not
- **hippocampus:**  
records memories of an experience, including where and when
- **frontal cortex:**  
coordinates and processes brain information
- **glutamate:**  
neurotransmitter that communicates with various brain regions and systems
- **CREB:**  
protein key to tolerance; regulates expression of genes that result in a dampening of the reward circuitry
- **delta FosB:**  
protein key to drug sensitization (relapse); increases due to prolonged drug use; regulates genes that increase sensitivity to drugs, perhaps by two mechanisms: promoting growth of new dendrite buds or sprouts in the nucleus accumbens that may be wired to "ID" stimuli associated with the prior drug use; and triggering an increase in dopamine activity in the presence of drug-specific stimuli (craving).