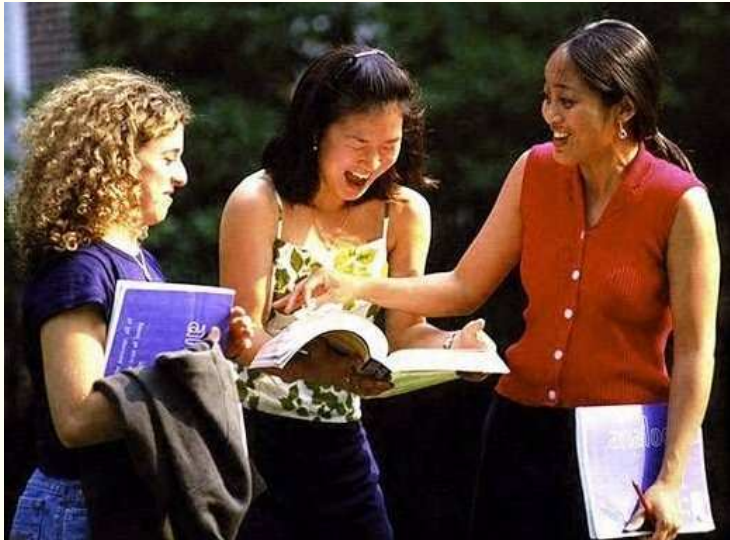


# Developmental neurobiology in animal models of adolescence: Implications of the action of addictive substances on a developing reward system



**Charles Landry, Ph.D.**  
**Department of Psychiatry**

# Adolescence

- **Asserting independence**
- **Interacting more with peers**
- **Increase in risk-taking**

**All directed toward taking on the responsibilities of adulthood**

## Maladaptive

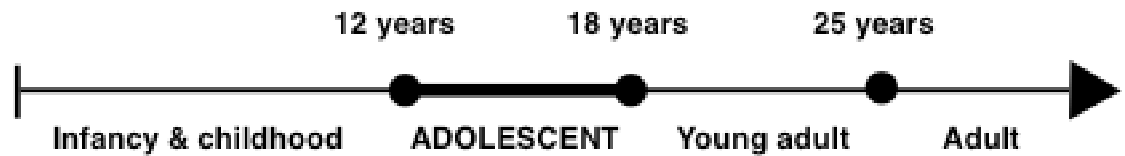
- **Risky behavior**
- **Substance abuse**



# Timeline of adolescence



## HUMAN

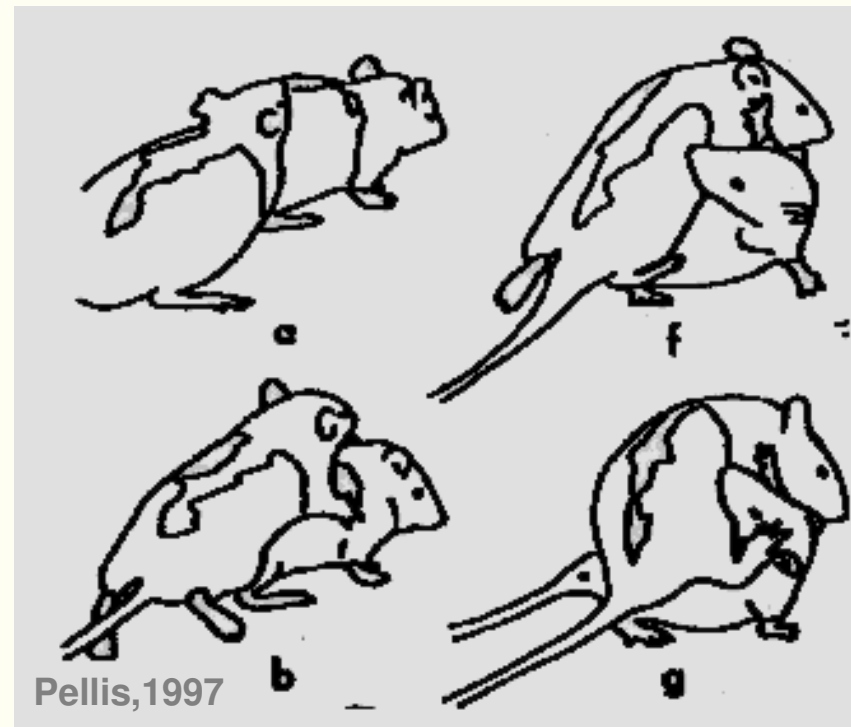


## RAT

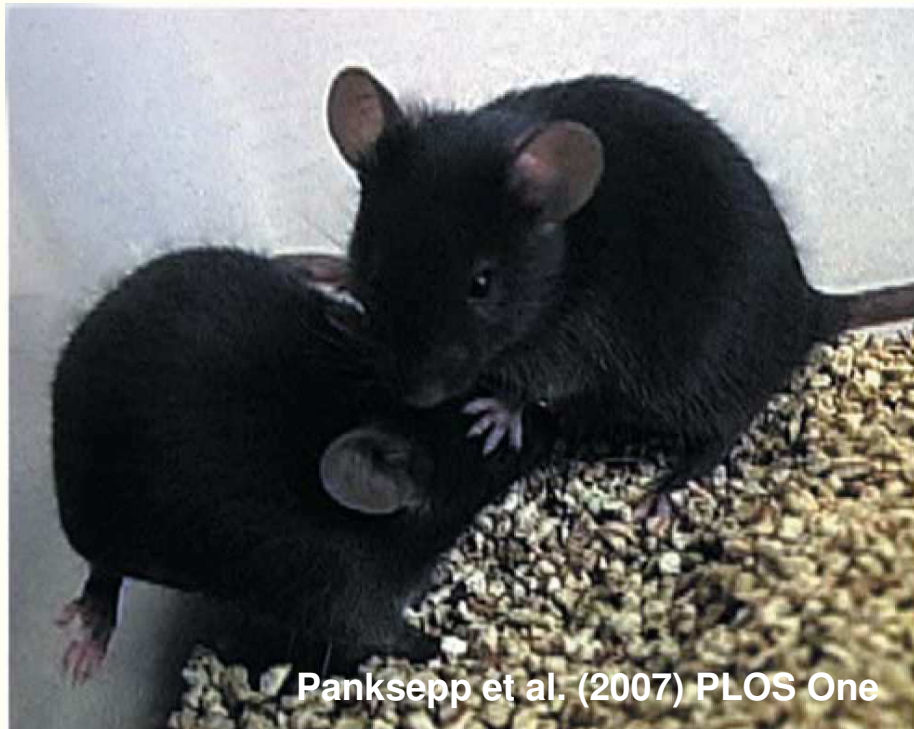


# Rodent model of adolescence

- hyperphagic
- pubertal changes
- increased risk-taking
- increased peer-directed social interaction



# The Adolescent Brain

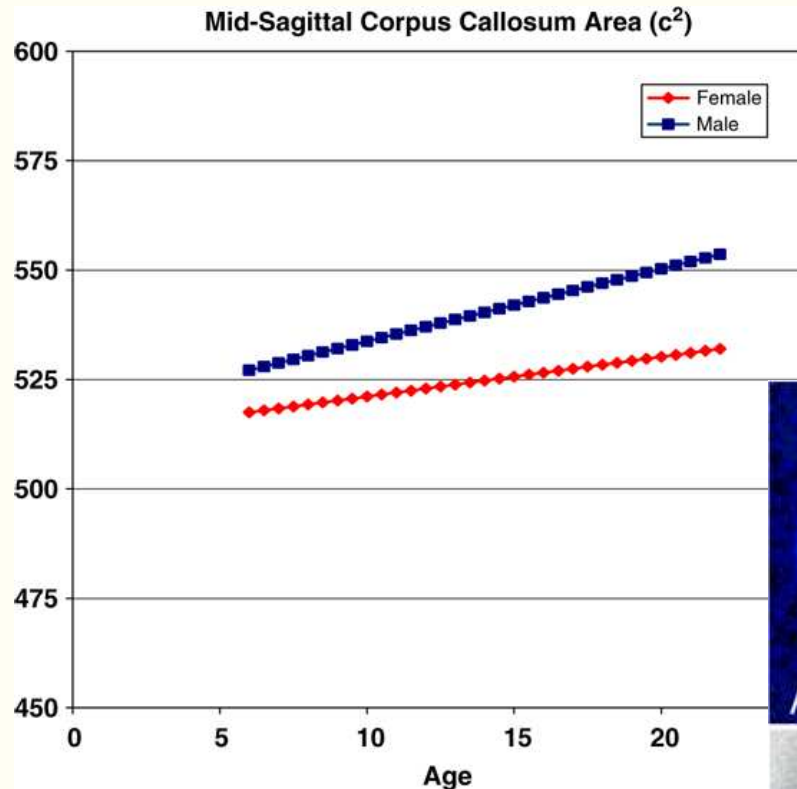


Panksepp et al. (2007) PLOS One

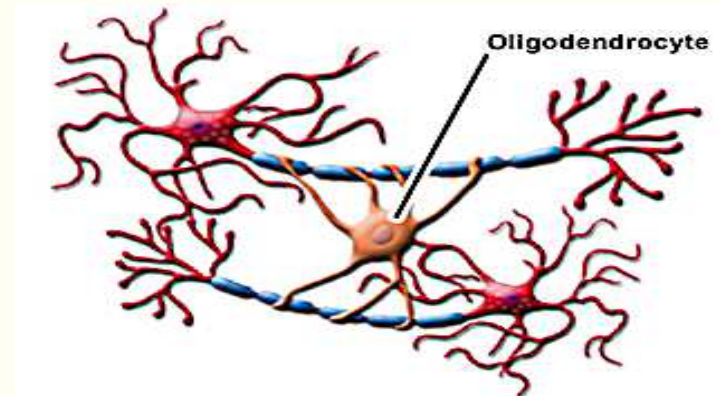
- Is it developmentally unique?
- Does it respond differently?
- Is it vulnerable?

# The developing adolescent brain

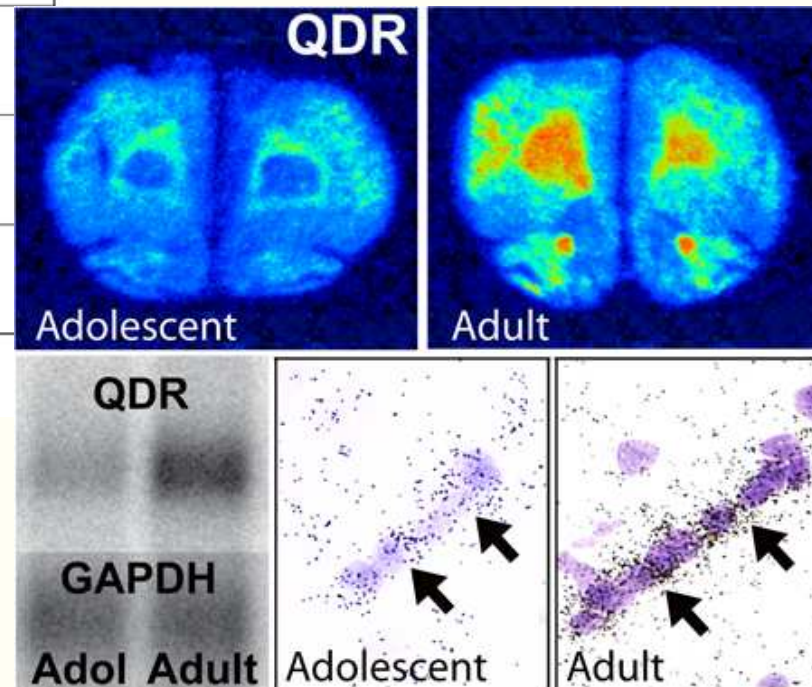
## Human



Lenroot and Geidd (2006) Neurosci Biobehav Rev

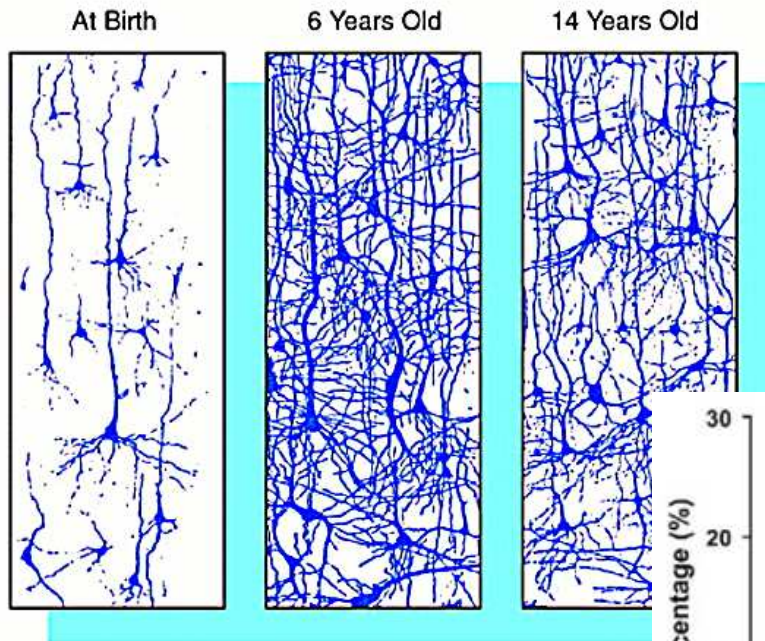


## Rodent

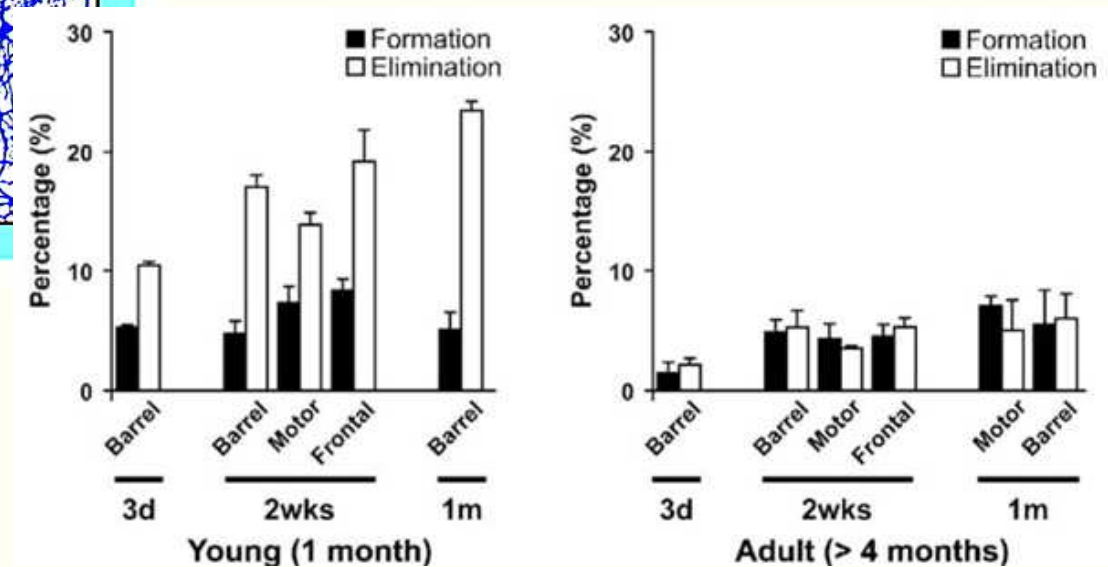


# The developing adolescent brain

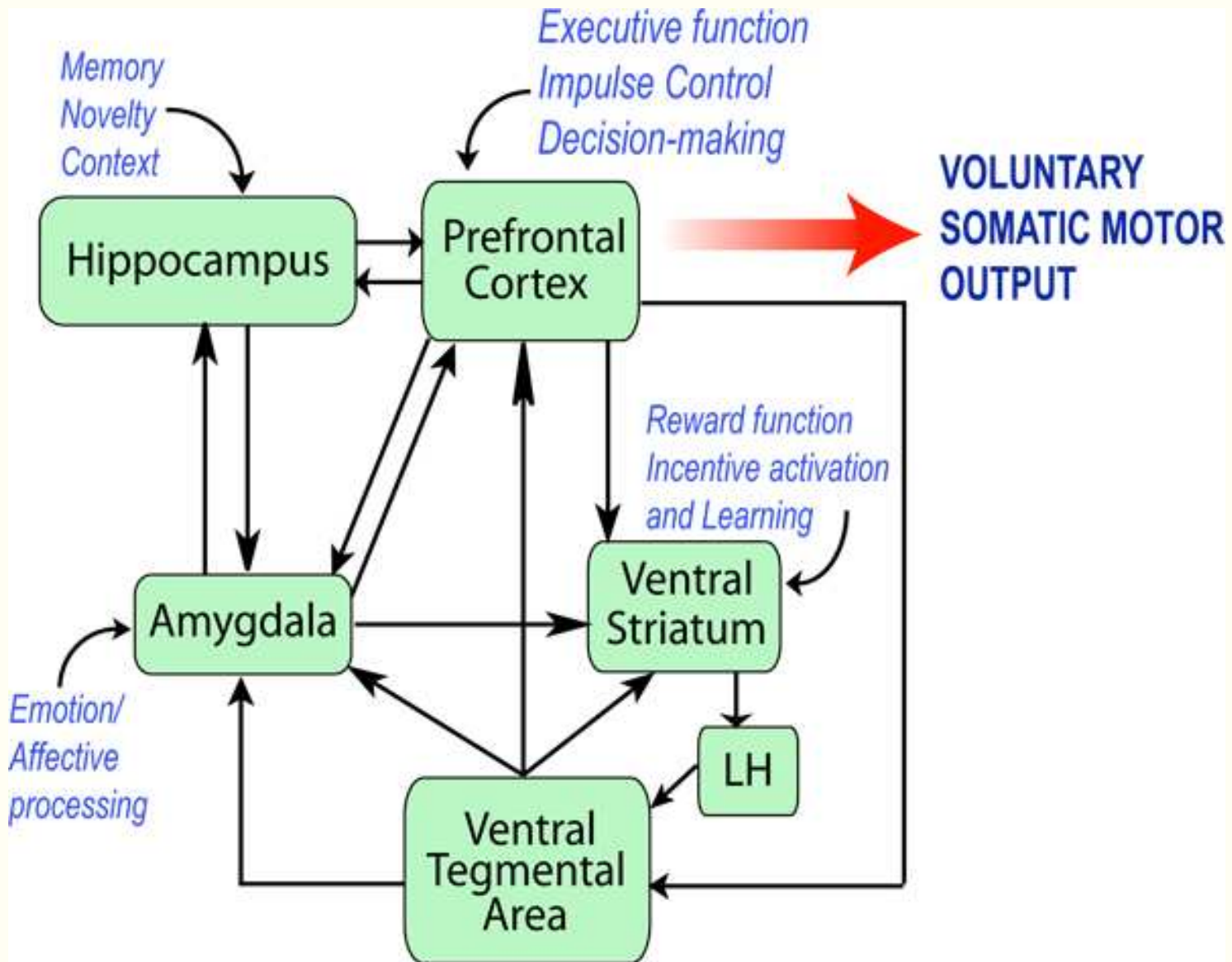
## Human



## Rodent



Zuo et al. (2005) Neuron



# Developmental changes in reward pathways

## Prefrontal cortex

- synaptic loss - especially excitatory inputs
- ↑ dopamine - serotonin inputs
- ↑ cholinergic innervation
- peak in glutamate binding then decline
- ↑ projections from amygdala
- changes in maturation of inhibitory neurons

## Striatum

- over production and subsequent pruning of dopamine receptors
- ↓ glutamate input from cortex

## Hippocampus, Amygdala

- pruning of excitatory inputs

# Does the adolescent brain respond differently?

## Nicotine:

↑ rewarding, reinforcing effects

## Cocaine:

↓ locomotor responses to acute cocaine

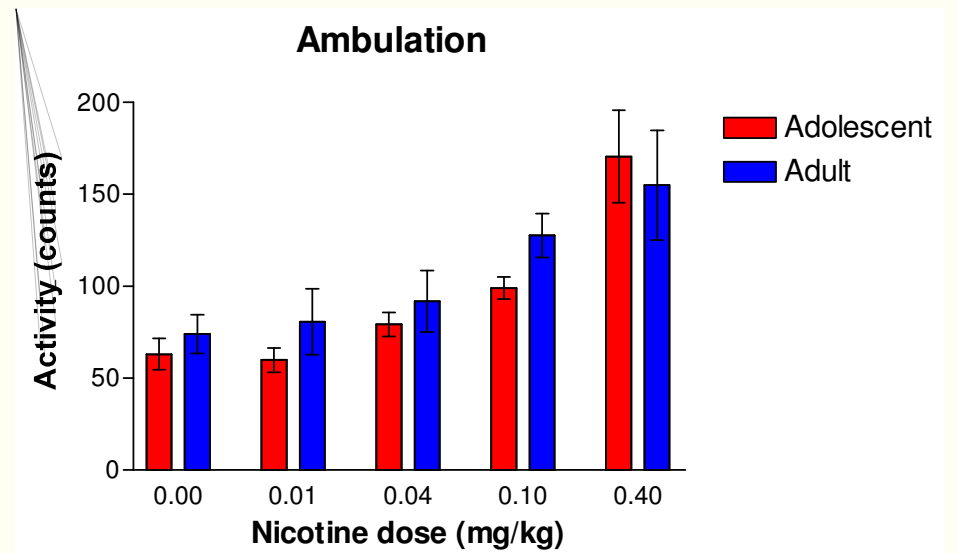
↑ aggression

## Alcohol:

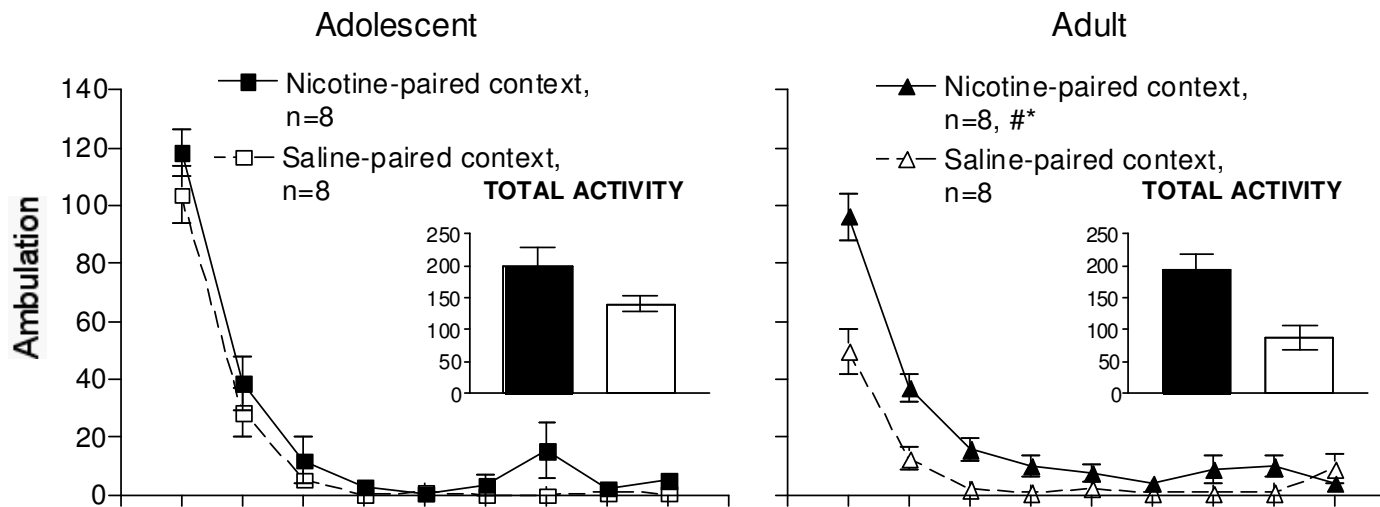
↓ sensitivity to sedative effects

↑ vulnerability to neurotoxicity

**Although adolescent rats have a similar dose response to nicotine as adults...**



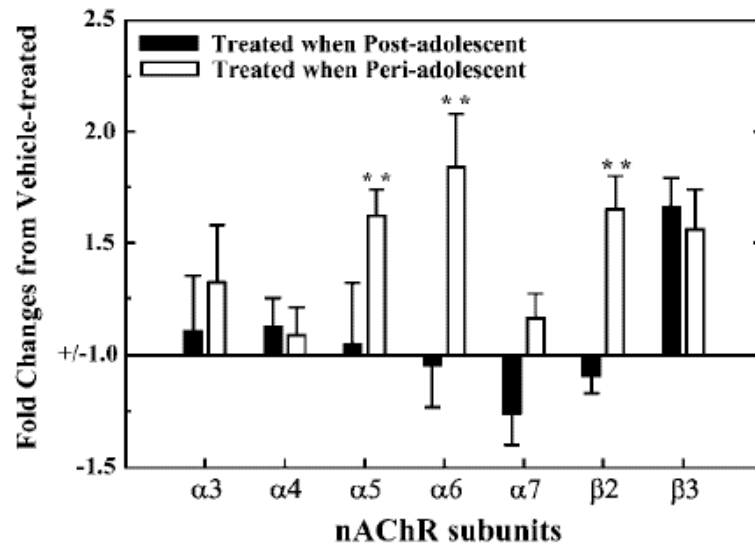
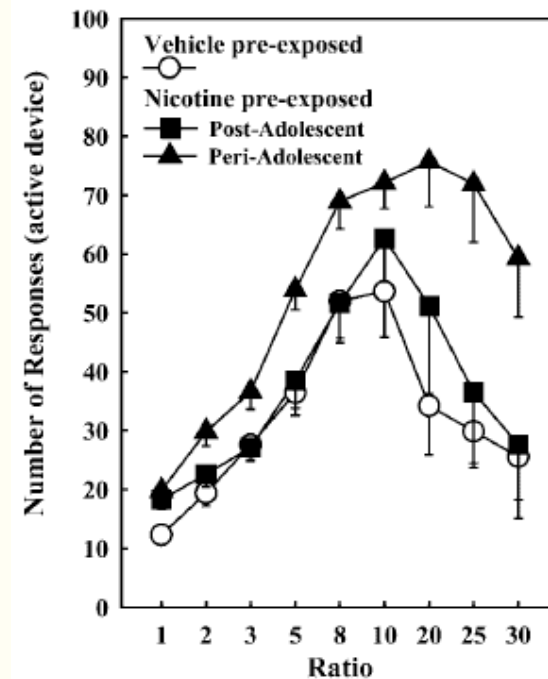
### Nicotine Conditioning



**...they fail to display nicotine cue conditioning.**

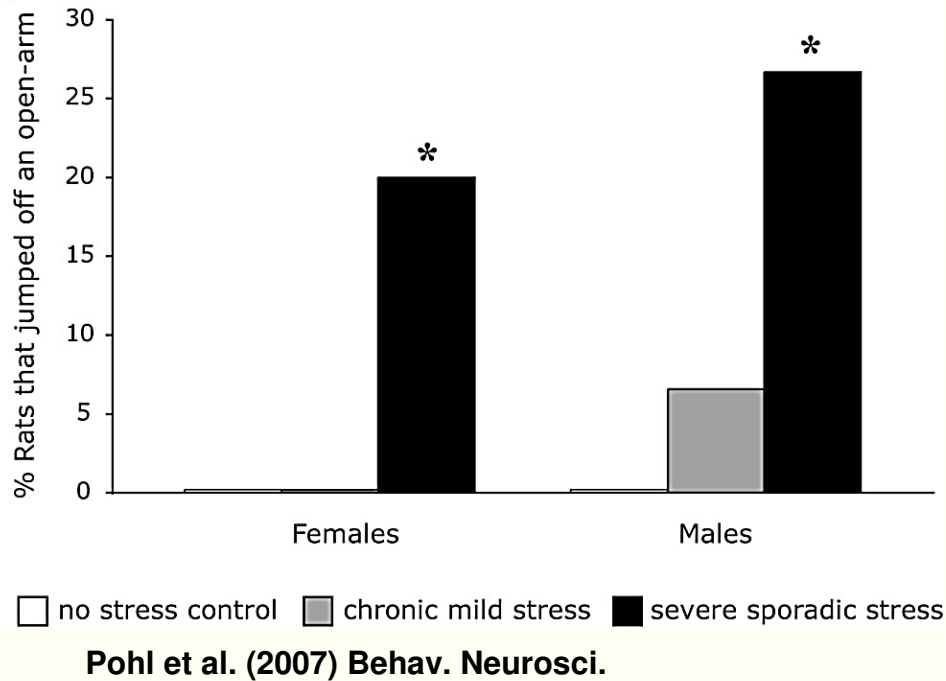
**May be linked to decreased attention to cues, or altered plasticity in PFC.**

## Nicotine in adolescence increases sensitivity to nicotine in adulthood...



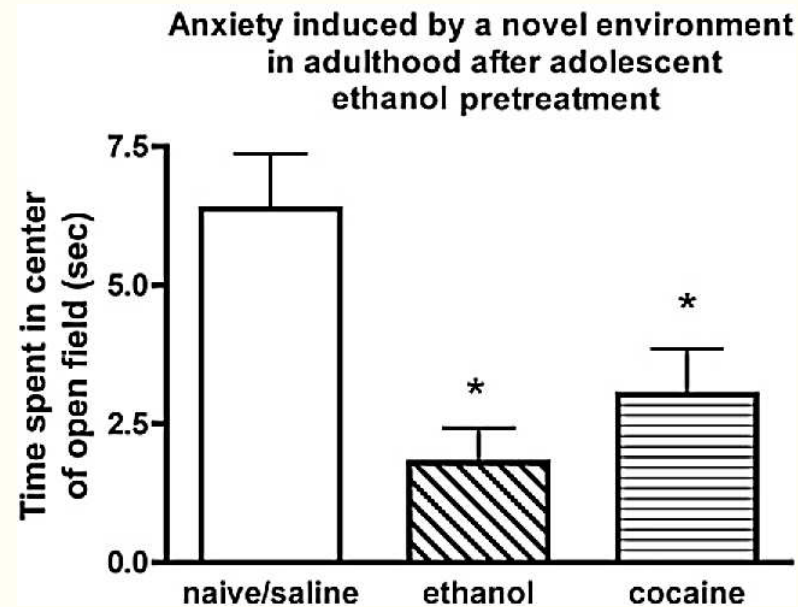
...and changes brain acetylcholine receptor expression.

# Stress...



...during the adolescent period  
alter behavior in adulthood.

...and **addictive substances**...



Stansfield and Kirstein (2007) Pharmacol. Biochem. Behav.

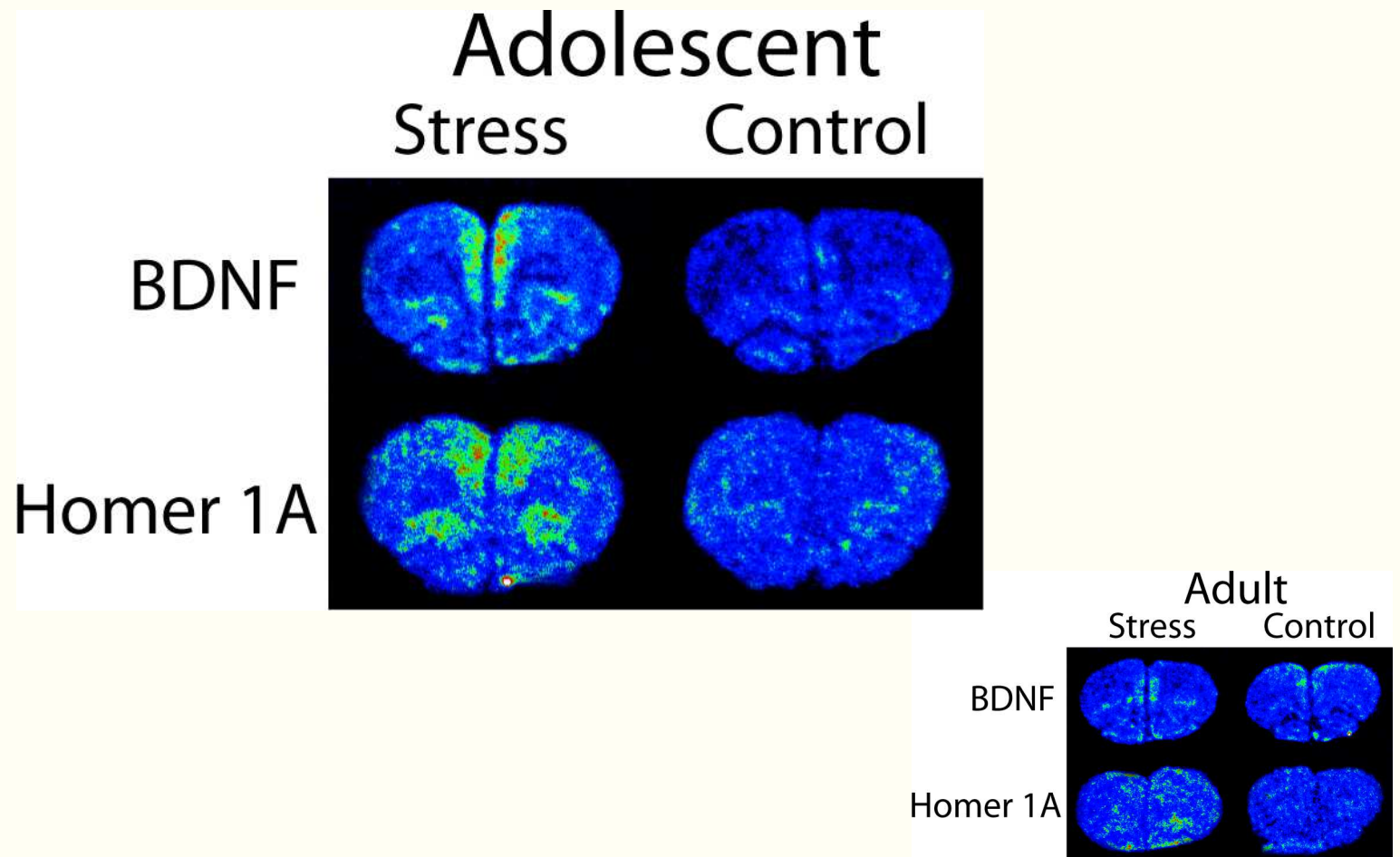
# Genes important in synaptic plasticity

- **Brain derived neurotrophic factor (BDNF)**
- **Homer 1A**
- **Arc**
- **Dendrin**

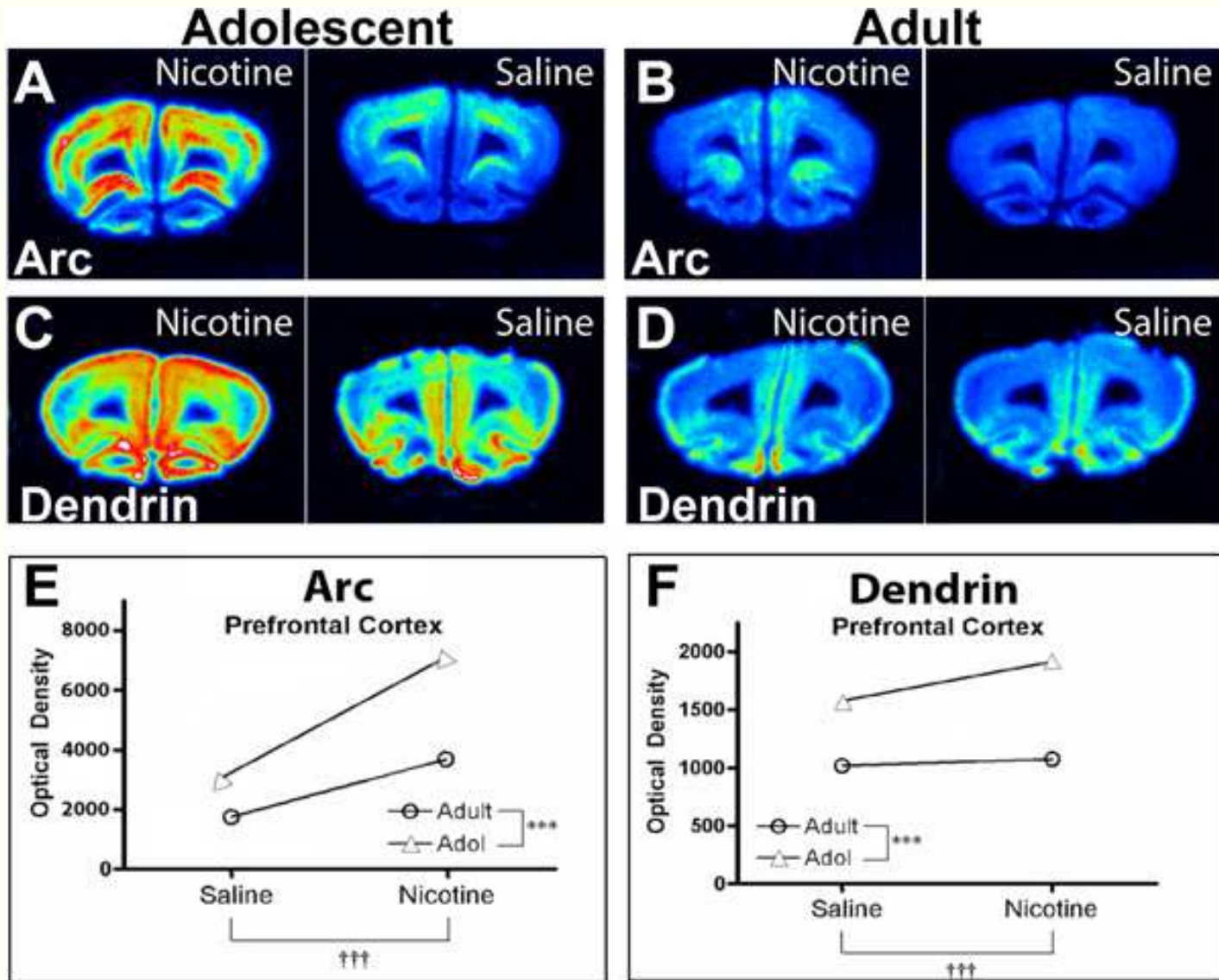


# Does the adolescent brain respond differently?

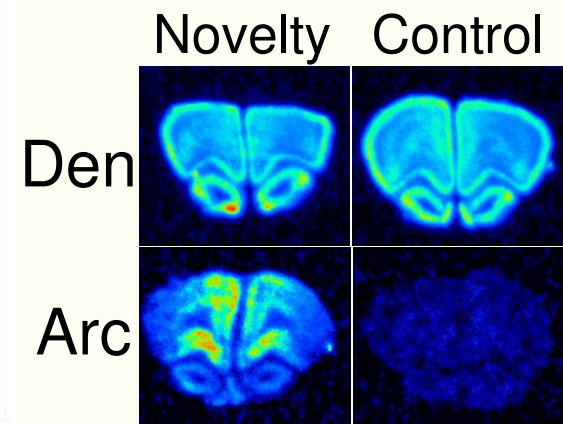
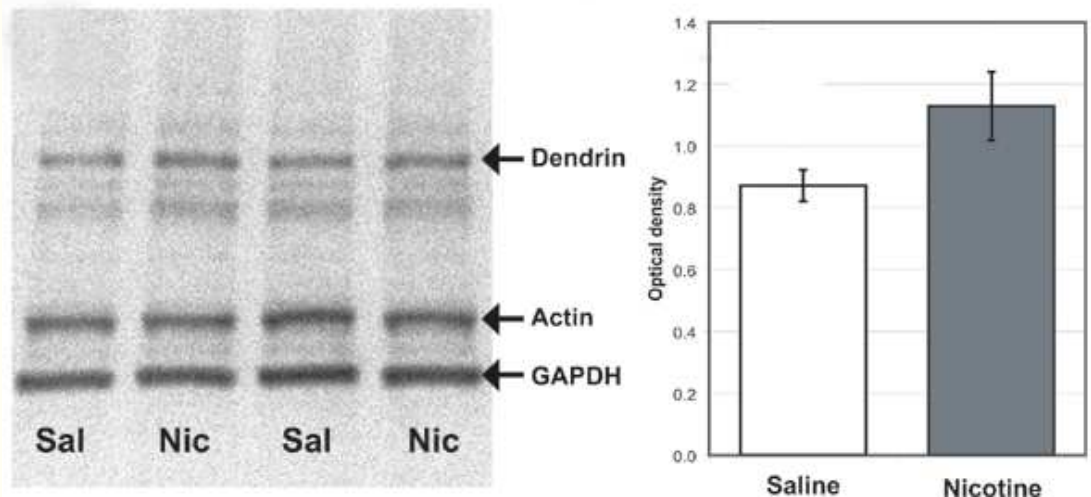
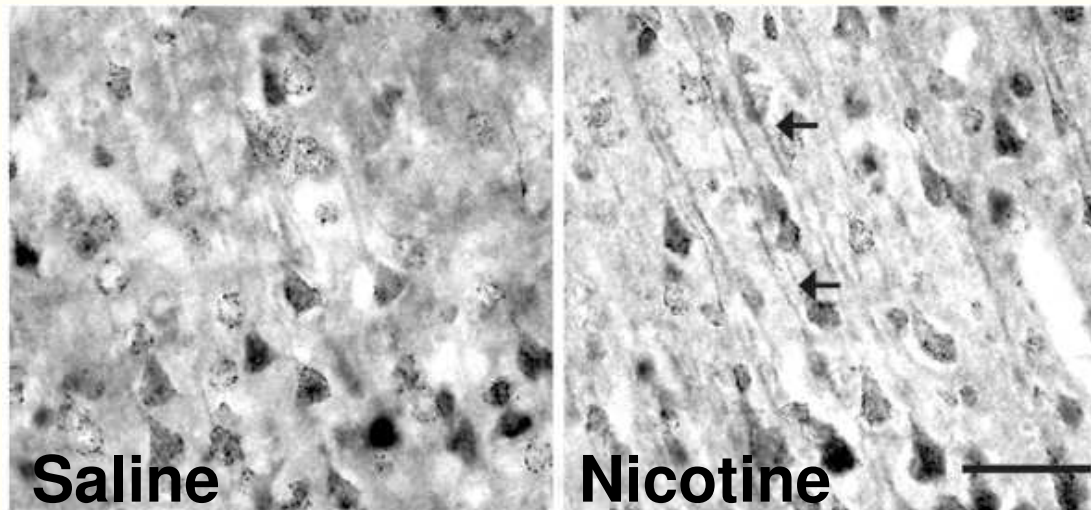
## Ferret stress



# Acute nicotine induces synaptic genes



# Dendrin is transiently induced following acute nicotine



- Adolescence is a unique period of development in terms of brain maturation
- Adolescents respond differently to drugs and stress and this has a molecular basis
- Neurochemical immaturity likely contributes to vulnerability
- Enhanced synaptic plasticity during adolescence may be a target for alterations caused by stimuli such as stress and addictive substances



**Ann Kelley**  
**Craig Schiltz**  
**Jason Gerstner**

**Terri Schochet**



**NIDA**  
NATIONAL INSTITUTE  
ON DRUG ABUSE  
DA19153

**Quentin Bremer**