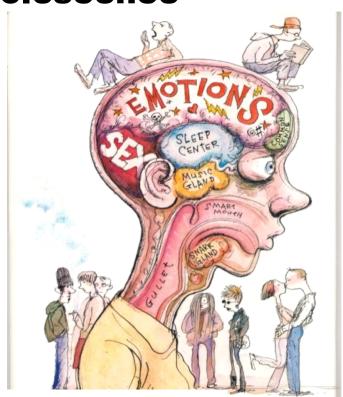
#### This is Your Brain on Adolescence

Ken Winters, Ph.D.

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Senior Scientist
Oregon Research Institute
&
Adjunct Faculty, Dept. of Psychology
University of Minnesota

44<sup>th</sup> Annual School on Addictions and Behavioral Health May 9, 2018 Anchorage, Alaska



Source: US News & World Report, 2005

### **Disclosures**

## None to report

### **Personal Disclosure**

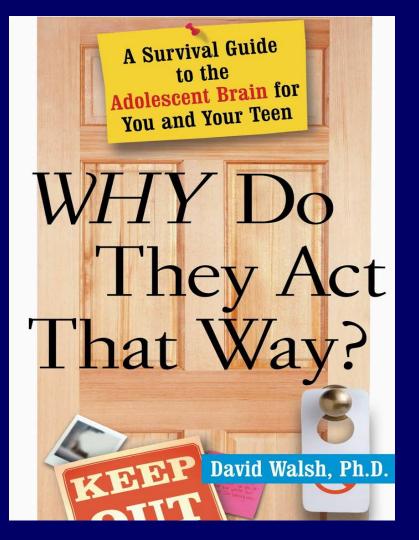
I hope to avoid a reaction from you that was voiced by the famous Italian-American physicist, Enrico Fermi, after he attended a seminar:

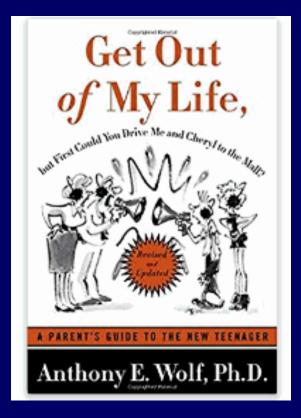
"Before I came here, I was confused about this subject. Having listened to your lecture, I am still confused -- but on a higher level."

### **Teen Brain Development Quiz**

- 1. It is an accepted fact the adolescent brain fully develops by about age 25. What 'privilege' in the U.S. requires a young person to be at least 25 years-old?
- There are several health indices suggesting that teenagers take less risk than in years past. T or F?
- 3. Which is more harmful to the developing brain?
  - a. chronic, heavy use of marijuana?
  - b. Chronic, heavy drinking?



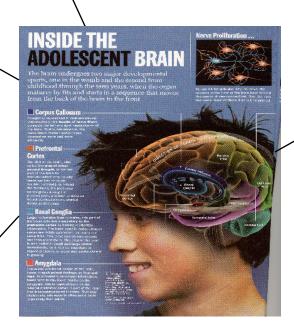




#### L. Brain development

4. Summary

3. Clinical implications



2. Developing brain, drug use and mental health

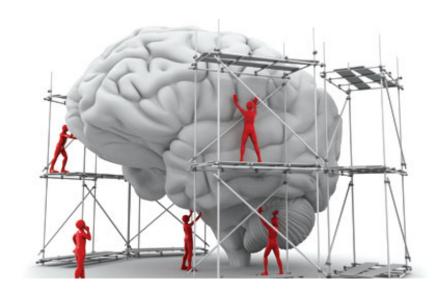
### **Major Points from My Talk**

- The maturation of the adolescent brain likely contributes to behaviors that are characteristic of this developmental period.
- This maturation also informs our understanding of risk for substance use disorders and other behavioral disorders.
- 3. Service providers can leverage teen brain science when working with adolescents and parents.

1. Teach youth about brain development and the science of addiction



2. Earlier the treatment the better



# 3. Use evidenced-based prevention & treatment approaches

- Prevention: keys to effective prevention, see NIDA's 2<sup>nd</sup> edition: "Preventing Drug Use among Children and Adolescents"
- Treatment: best approaches summarized in a recent meta analysis and literature summary (Hogue et al., 2018; Tanner-Smith et al., 2012)

# 4. Increase youth "cannabis IQ"

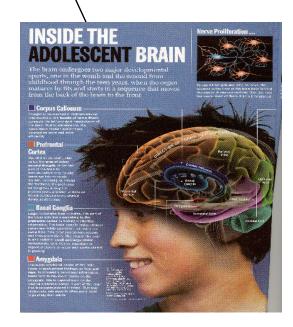
 Many misperceptions and myths about cannabis by are held by youth (and adults, too!)



5. Teach parents about brain development



### 1. Brain development

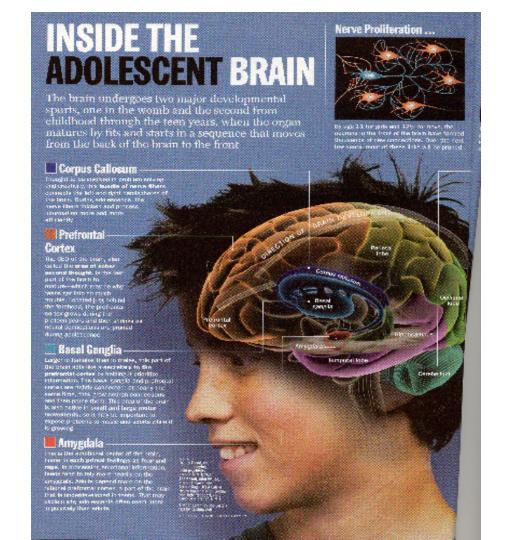


### **Cautions**



- Brain imaging studies of development are based on small samples
  - gender, ethnic and cultural differences may be significant.
- The role of hormones and early experiences on brain development are likely significant

**Based on** research by neuroscientists, brain maturation continues through adolescence, until approx. age **25** 



# Minimum age for various rights and privileges



16: driving, emancipation (in some instances)

- 18: voting, military, smoking (that is changing), gambling (in some instances), legal adult status
- 21: alcohol, marijuana (in some instances)
- 25? renting a car

# An Immature Brain = Less Brakes on the "Go" System

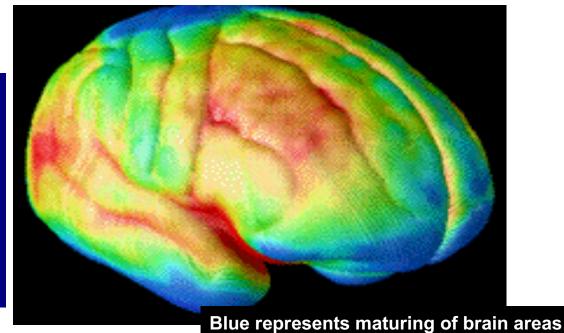


# Maturation Occurs from Back to Front of the Brain and Inside to Outside Images of Brain Development in Healthy Youth

(Ages 5 - 20)

Earlier: Limbic
Motor Coordination
Emotion
Motivation

**Later: Prefrontal Judgment** 



Source: PHAS USA 2004 May 25; 101(21): 8174-8179. Epub 2004 May 17.

#### **Implications of Brain Development for Adolescent Behavior**

- Preference for ....
  - physical activity
  - high excitement and rewarding activities
  - 3. activities with peers that trigger high intensity/arousal
  - novelty
- Less than optimal...
  - 5. control of emotions
  - 6. consideration of negative consequences
- Greater tendency to...
  - 7. be attentive to social information
  - 8. take risks and show poor self-control

### Risk-Taking & Self Control

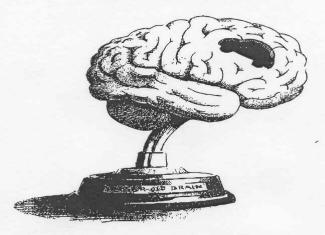
- Based on science of brain development, a modern view of risk taking in adolescence is...
  - evolutionarily adaptive

- normative; important to development
- significant individual differences
- is due primarily to <u>emotional and contextual</u>, not cognitive, factors

# Why do most 16-year-olds drive like they're missing a part of their brain?



BECAUSE THEY ARE.



### Allstate ad, *NY Times,* May, 2007

EVEN BRIGHT, MATURE TEENAGERS SOMETIMES DO THINGS THAT ARE "STUPID."

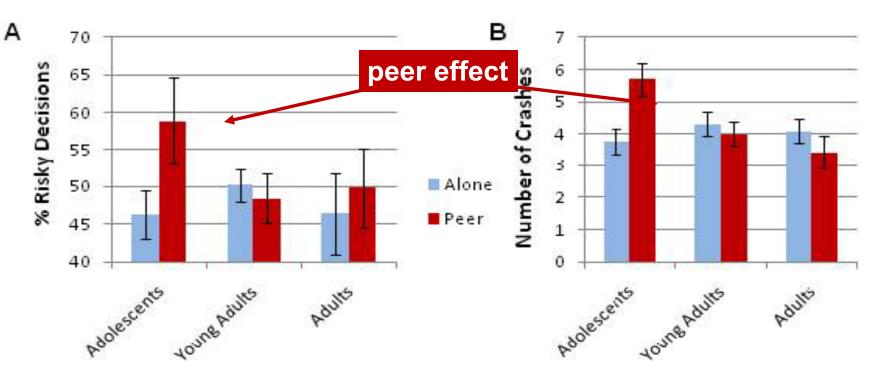
But when that happens, it's not really their fault. It's because their brain hasn't finished developing. The underdeveloped area is called the dorsal lateral prefrontal cortex. It plays a critical role in decision making, problem solving and understanding future consequences of today's actions. Problem is, it won't be fully mature until they're into their 20s.

It's one reason 16-year-old drivers have crash rates three times higher than 17-year-olds and five times higher crashes. These laws restrict the more dangerous kinds of driving teens do, such as nighttime driving and driving with teen passengers. Since North Carolina implemented one of the most comprehensive GDL laws in the country, it has seen a 25% decline in crashes involving 16-year-olds.

To find out what the GDL laws are in your state, visit Allstate.com/teen. Help enforce them—and if they aren't strong enough, ask your legislator to strengthen them.

Let's help our teenagers not miss out on tomorrow just

## Impact of Peer Presence on Risky Driving in Simulated Context



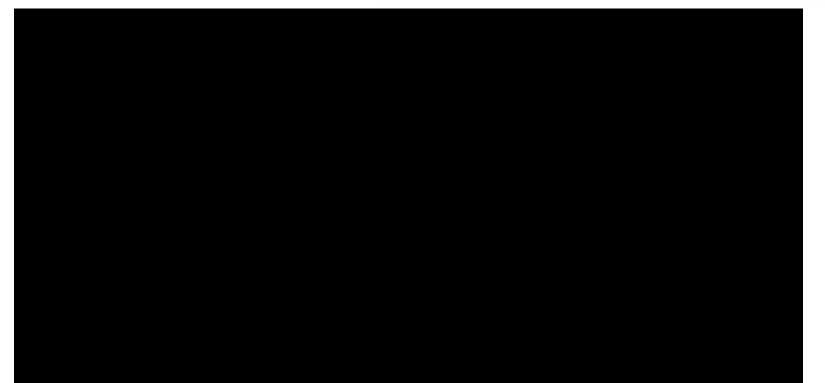
Chein et al., in press

# Risk-Taking & Self-Control



Resisting the marshmallow and the success of self-control

PBS NewsHour 
81K views

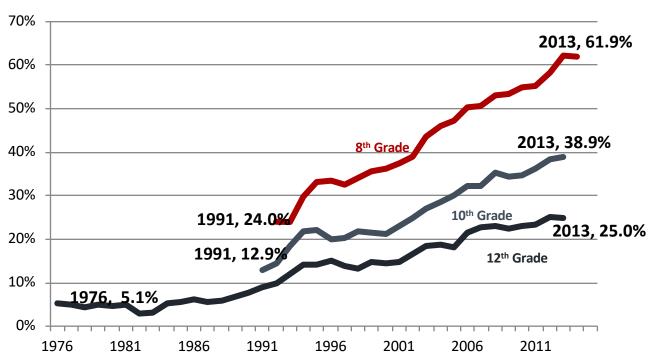


### **Adolescent Trends** in Risk Taking

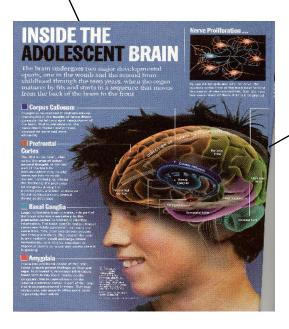
?

- There are several health indices suggesting that teenagers take less risk than in years past. True
- Declines in prevalence of...
  - Teenage pregnancy
  - Delinquency behaviors
- Increase in prevalence of abstaining from all substances

## Abstaining from Illicit Drugs, Alcohol and Cigarettes – Lifetime

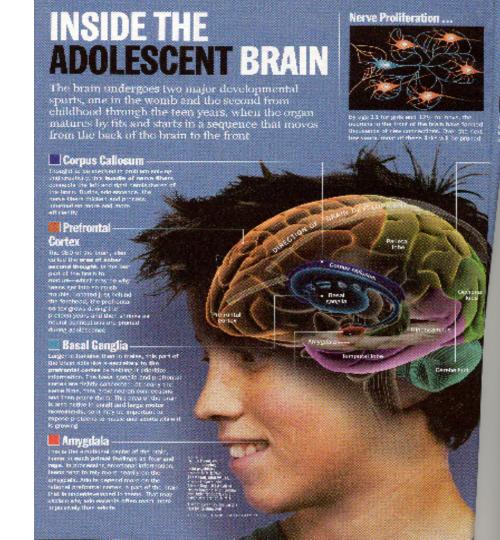


#### 1. Brain development



- 2. Developing brain, drug use and mental health
  1. drug use
- 2. behavioral disorders
  - 3. early experiences

### Health issue: Developing brain and drugs



## Implications of Brain Development for <u>Drug</u> **Abuse Vulnerability**

## Are adolescents more susceptible than adults to <u>drugs</u>?

## Several lines of evidence (acknowledgement to Linda Spear, Ph.D.)

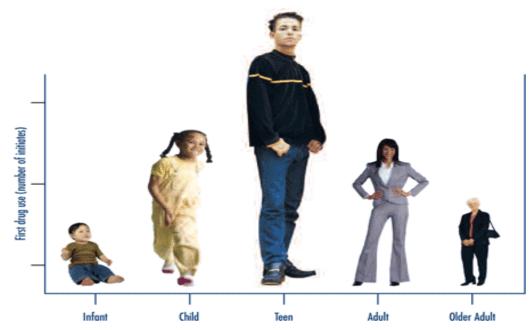
Unethical to give human adolescents alcohol in the laboratory; much of the best evidence comes from adolescent rat studies.





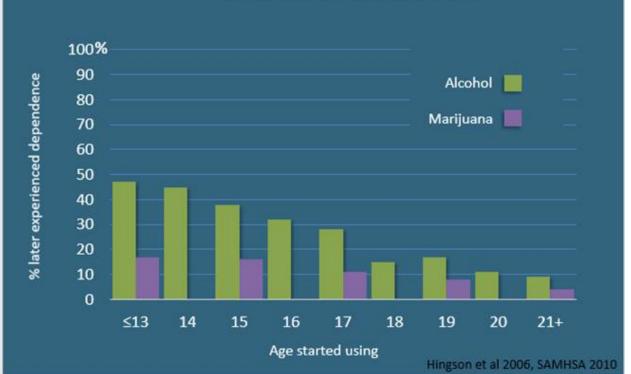
# Evidence from <u>epidemiological</u> studies

Drug use starts early and peaks in the teen years





## Age at substance use onset and later addiction



## Implications of Brain Development for <u>Drug</u> <u>Abuse Vulnerability</u>

# Alcohol



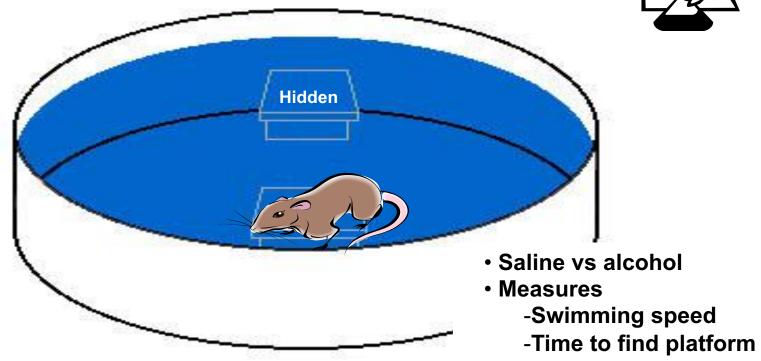
# Are adolescents more susceptible to alcohol than adults?

 Adolescent rats are <u>less sensitive</u> to the sedative and motor impairment effects of <u>intoxication</u>.

Adolescent rats are <u>more sensitive</u> to the social disinhibition effects of alcohol.

**#2** and **#3**: May contribute to binge drinking and increased risk to alcohol dependence.

### **The Water Maze Test**



Slide courtesy Sion Kim Harris, Ph.D.









# Impact of Binge Drinking



Contents lists available at ScienceDirect

NeuroImage: Clinical



journal homepage: www.elsevier.com/locate/ynicl

Adolescent binge drinking disrupts normal trajectories of brain functional organization and personality maturation



**Ruan et al., 2019** 

- Longitudinal design; assessed at ages 14, 16 and 19
- Accumulating effect of binge drinking....
  - Neuroimaging data: maturation of frontal connectivity disrupted
  - Personality data: the developmental improvement of impulsivity was slowed down

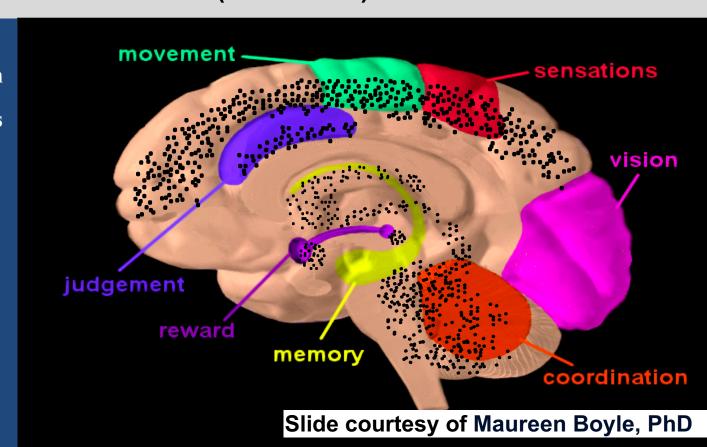
## Implications of Brain Development for <u>Drug</u> <u>Abuse Vulnerability</u>

# Marijuana



# Marijuana Binds Cannabinoid Receptors Located Throughout the Brain (source NIDA)

- Brain Development
- Memory & Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia



# Adverse Health Effects of Chronic Marijuana Use: Those Effects Strongly Associated with Initial Marijuana Use Early in Adolescence (Volkow et al., 2014)

#### "Low Level of Confidence"

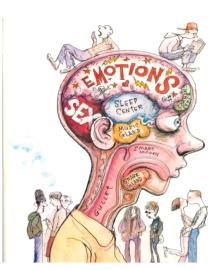
1. Lung cancer

#### "Medium Level of Confidence"

- 2. Altered brain development
- **3.** Progression to use of other drugs
- 4. Cognitive impairment
- 5. Increased risk of chronic psychosis disorders (including schizophrenia and depression) in persons with a predisposition to such disorders

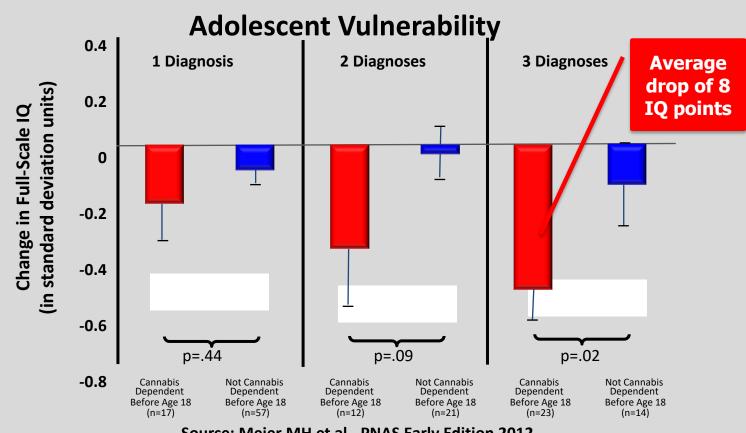
#### "High Level of Confidence"

- 6. Addiction
- 7. Diminished life satisfaction and achievement (including poor educational outcome)
- 8. Symptoms of chronic bronchitis



Source: US News & World Report, 2005



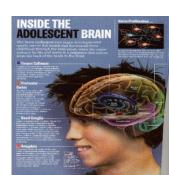


Source: Meier MH et al., PNAS Early Edition 2012.

# 

### 1. Could there be inherent risk factors of brain development that contribute to drug use?

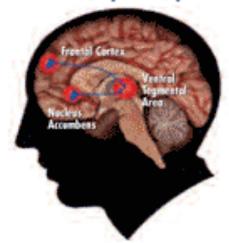
- Preference for ....
  - physical activity
  - 2. high excitement and rewarding activities
  - 3. activities with peers that trigger high intensity/arousal
  - 4. novelty
- Less than optimal...
  - 5. control of emotions
  - 6. consideration of negative conseq.
- Greater tendency to...
  - 7. be attentive to social information
  - 8. take risks and show less self control



# 2. Adolescent pleasure centers in the brain may be more sensitive to the acute effects of drugs than pleasure centers in the adult brain.

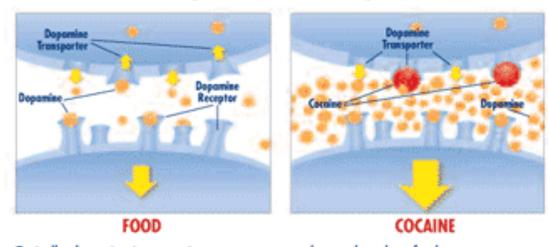
#### ALL DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

#### Brain reward (dopamine) pathways



These brain circuits are important for natural rewards such as food, music, and art.

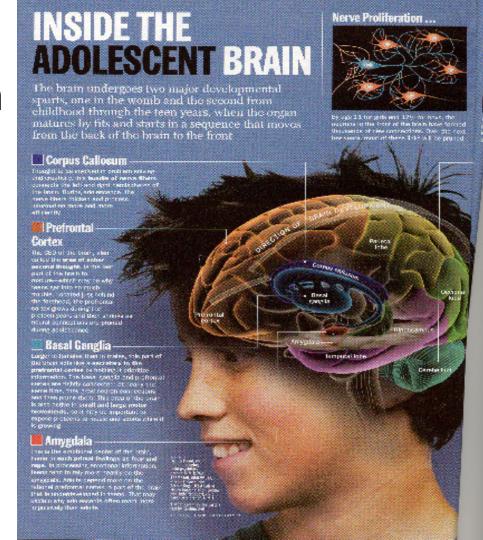
#### All drugs of abuse increase dopamine



Typically, dopamine increases in response to natural rewards such as food.

When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

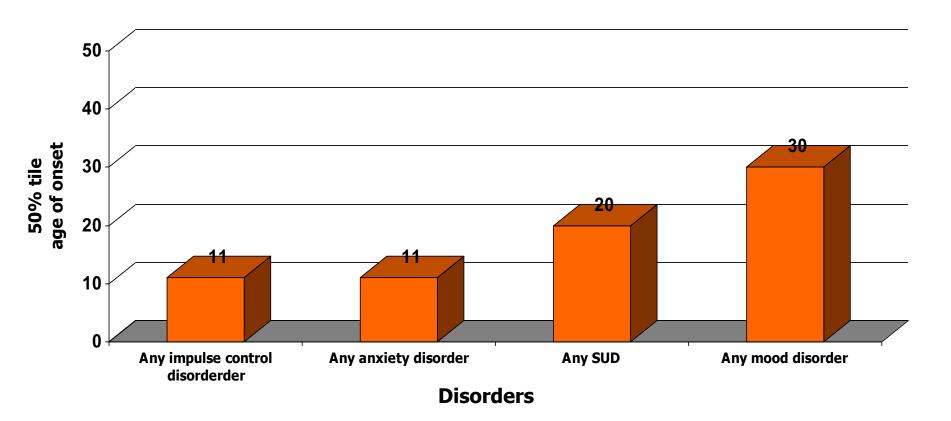
2. Health issue: Brain development and behavioral disorders



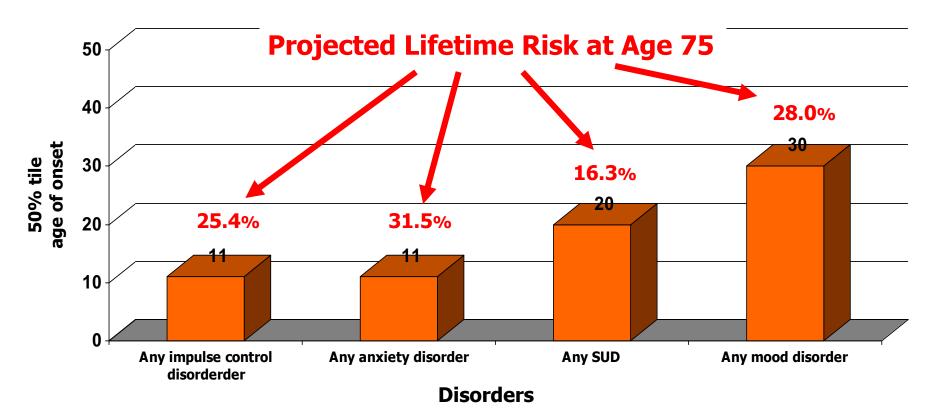
### **Adolescence and Behavioral Disorders**

- Alterations in neurodevelopment have been linked to several adolescent-onset mental and behavioral disorders (Charney et al., 2013):
  - ADHD
  - Affective Disorders
  - Anxiety Disorders
  - Autism
  - Obsessive-Compulsive Disorders
  - PTSD
  - Schizophrenia

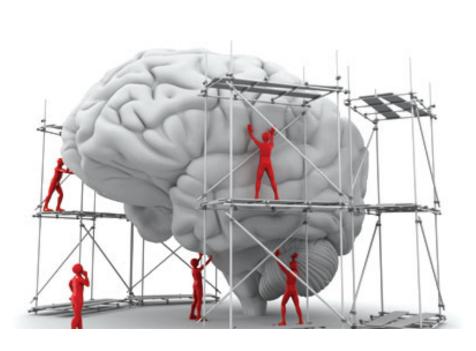
### Ages at the 50 Percentile of the Age-at-Onset Distribution for Major Disorders (Kessler et al., 2005)



### Ages at the 50 Percentile of the Age-at-Onset Distribution for Major Disorders (Kessler et al., 2005)



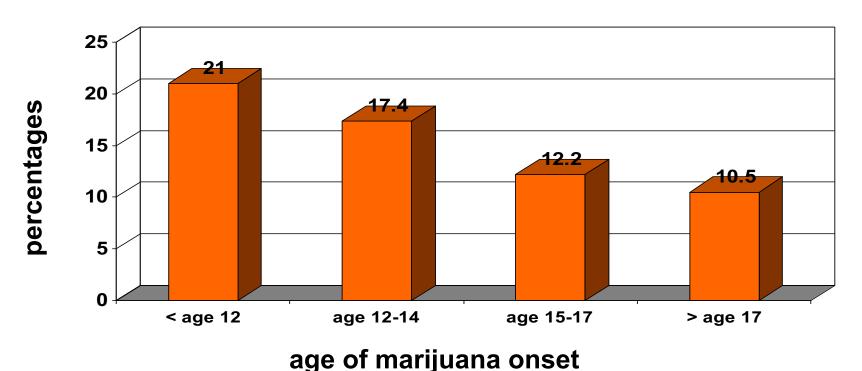
# **Adolescent Use of Marijuana and Behavioral Disorders**





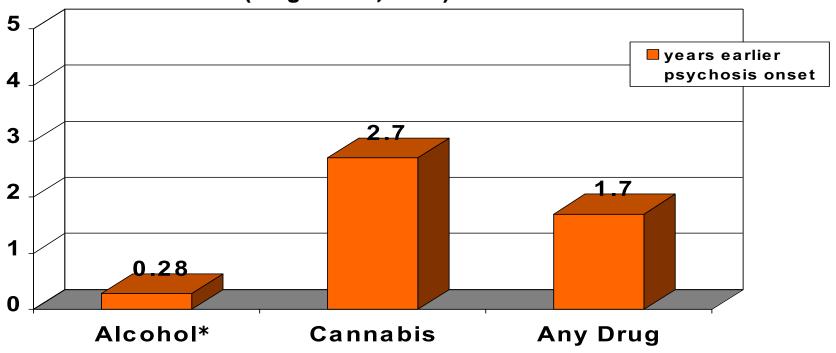
# **Psychosis:** Prevalence of Past Year Serious Mental Illness Among Lifetime Marijuana Users Aged 18+

(SAMHSA, 2005; data collected 2002-2003)



# **Psychosis:** Drug Use and Age at Onset of Psychosis Based on a Meta-Analysis

(Large et al., 2011)



mean years earlier of age at onset of psychosis compared to non-drug using controls \* = nonsig. with controls

#### Miller's Review of the Marijuana and Mental Health Connection

Disorder	Cross-Sectional Data	Longitudinal Data
Schizophrenia	++	++
Bipolar	+	
Anxiety Disorders	+	+
Depressive Disorders	+	+
Risk of Suicide	+	

**Key: ++ = several studies; +a few studies** 

Yellow box = risk greater when MJ use onset during youth.

Miller, C. L. (in press). The impact of marijuana on mental health. In K. Sabet & K.C. Winters, Contemporary health issues on marijuana. NY: Oxford Press.

The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study

Marta Di Forti, PhD R O Diego Quattrone, MD • Tom P Freeman, PhD • Giada Tripoli, MSc • Charlotte Gayer-Anderson, PhD • Harriet Quigley, MD • et al. Show all authors •

- 901 patients with first episode psychosis across 11 clinic sites in Europe
- Compared 1237 population controls from those same sites
- Cannabis use was associated with increased odds of psychotic disorder compared with never users
  - Daily use of low potency cannabis = adjusted odds ratio,
     3.2 (95% CI 2.2 – 4.1)
  - Daily use of high potency cannabis = adjusted odds ratio,
     4.8 (95% CI 2.5 – 6.3)

#### **Source: Lancet Psychiatry, 2019**

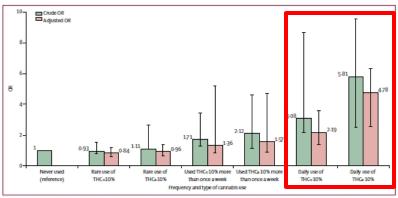


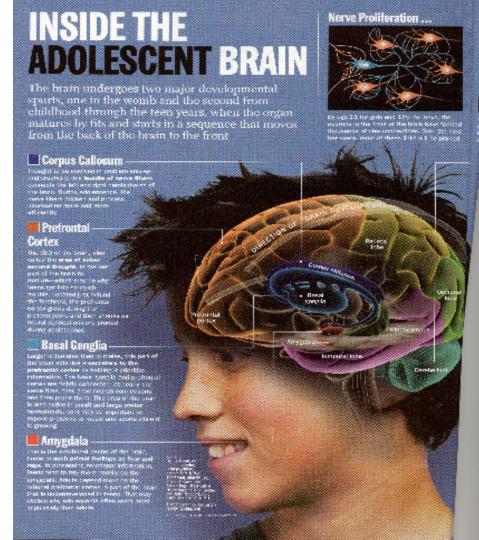
Figure 1: Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample Crude ORs are adjusted only for age, gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and use of tobaccs, stimulant, ketamine, legal highs, and hallocinogenics. Error bars represent 95% ICs OR-odds ratio.

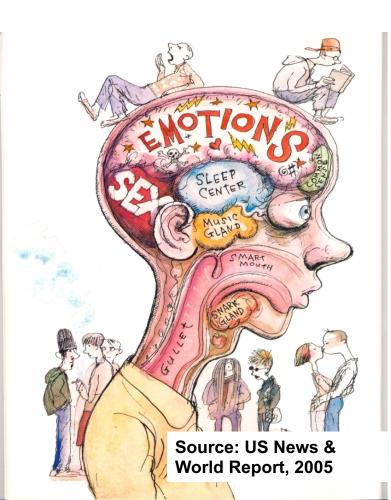
### **Cautionary Notes**

 Reverse causation (selfmedication).



 Early drug use may be a marker of underlying genetic risk and not causative, or only partially causative. 3. Health issue: **Impact of early** experiences on the developing brain can alter health and well-being





### **A Developing Brain**

- > Impact from Environment?
  - "Exposure to both positive and negative elements before adolescence can imprint on the final adult topography in a manner that differs from exposure to the same elements after adolescence."

(Anderson, 2003, *Neuroscience* & *Biobehavioral Reviews*)

#### Early experiences can alter brain development in positive ways





"Nurturing and responsive care for the child's body and mind is the key to supporting healthy brain development."



#### Early experiences can alter brain development in positive ways.



Preschool is a sensitive period for the influence of maternal support on the trajectory of hippocampal development

Joan L. Luby<sup>a,1</sup>, Andy Belden<sup>a</sup>, Michael P. Harms<sup>a</sup>, Rebecca Tillman<sup>a</sup>, and Deanna M. Barch<sup>a,b,c</sup>

<sup>a</sup>Department of Psychiatry, Washington University in St. Louis, St. Louis, MO 63110; <sup>b</sup>Department of Psychological & Brain Sciences, Washington University in St. Louis, St. Louis, MO 63130; and <sup>c</sup>Department of Radiology, Washington University in St. Louis, St. Louis, MO 63110

More parental support = more hippocampus volume



#### Early experiences can alter brain development in negative ways





### The impact of child traumatic stress can last well beyond childhood. Associated with...

- Learning problems
- Increased use of health services, including mental health services



#### Early experiences can alter brain development in negative ways

### Infant Stress Affects Teen Brain (Davidson et al., 2012; *Nature Neuroscience*)



- For some girls, stressful experiences in the first year of life was associated with.....
  - altered hormonal changes and abnormal development of connections between regions of the brain that control fear and stress responses.

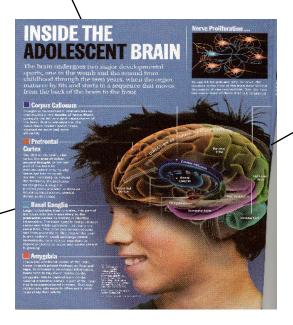
#### Early experiences can alter brain development in negative ways





- Children deprived of parents early in life (orphans), compared to children with parents, revealed....
  - increased gastrointestinal symptoms
  - pattern of gut microbiomes linked to concurrent and future anxiety, and prefrontal cortex activation to emotional faces

#### 1. Brain development



2. Developing brain, drug use and mental health

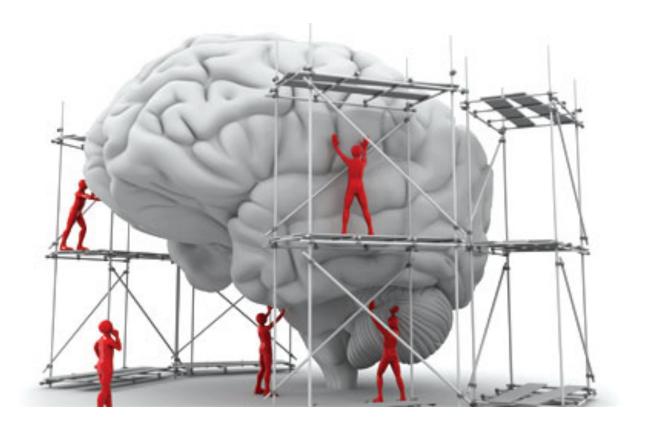
#### 3. Clinical implications

1. Teach youth about brain development and the science of addiction

See NIDA's website:

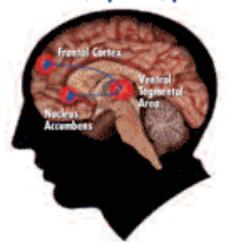
https://www.drugabuse.gov/publications/drugfacts/





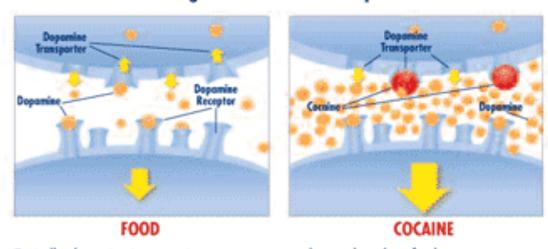
#### ALL DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

#### Brain reward (dopamine) pathways



These brain circuits are important for natural rewards such as food, music, and art.

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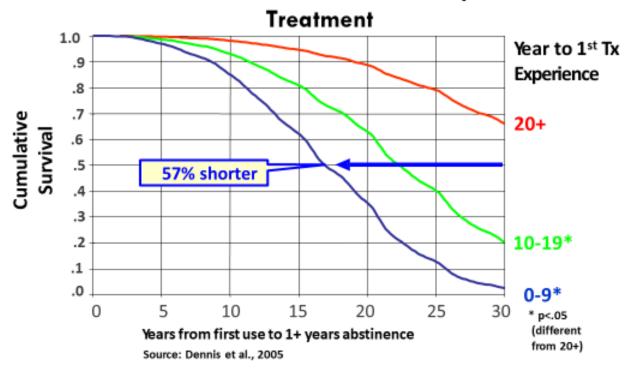
Typically, dopamine increases in response to natural rewards such as food.

When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

Source: https://www.drugabuse.gov.

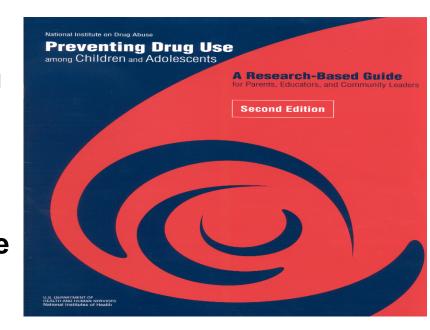
2. Earlier the treatment the better

"Careers" are Shorter the Sooner People Access



# 3. Use evidenced-based approaches prevention

 Prevention: 16 principles of effective prevention summarized in NIDA's 2<sup>nd</sup> edition of their research guide



http://www.drugabuse.gov

#### 3. Use evidenced-based treatment

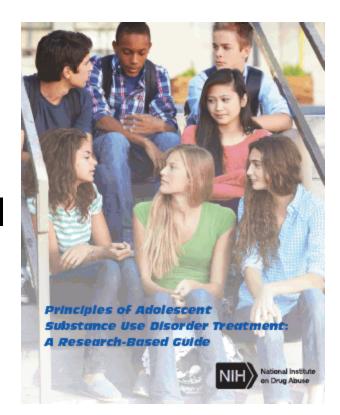
- Treatment: Recent literature summary and meta-analysis (Tanner-Smith et al., 2012; Hogue et al., 2018)
  - Treatment "as usual" is no better than prevention education only or no treatment.
  - A wide range of more recent evidenced-based treatments (EBTs) do significantly better.



#### **Evidenced-Based Treatment**

NIDA (2014): Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide

- Motivational Interviewing
- Cognitive Behavioral Therapy (CBT)
- Family Treatment



### Characteristics of Motivational Interviewing (Miller & Rollnick, 2013)

- De-emphasize labels
- Emphasis on personal choice and responsibility
- Therapist focuses on eliciting the client's own concerns
- Resistance is met with reflection and non-argumentation
- Treatment goals are negotiated;
   client's involvement is seen as vital



### **Characteristics of CBT**

Focus on immediate, relevant and specific problems

 Solutions are realistic, concrete, specific



# **CBT Helpful for Teaching and Supporting Self-Regulation**

- impulse control
- "second" thought processes
- social decision making
- dealing with risk situations
- taking healthy risks



# New 12-Step Program for Adolescents?

Tipsteps of Self-Regulation

impulse control

- 2. "second thought" processes
- 3. social decision making
- 4. dealing with risk situations
- 5. taking healthy risks
- 6. attention regulation
- 7. anger control
- 8. modulating reward incentives
- 9. choosing options
- 10. considering consequences
- 11. minimizing arousal
- 12. dealing with peer influences

# Characteristics of Family-Based Approaches (Bobek et al., in press)

- Adolescent's drug problem is part of a family unit problem
- Engage the whole family; key to long-term health of the youth
- Address poor family communication, cohesiveness and problem solving

- 4. Increase the "Cannabis IQ" of Adolescents
  - Sources of exercises and quizzes
    - www.dfaf.org (Busting the Top Ten Myths of Marijuana)
    - www.learnaboutsam.org



### 5. Teach parents about brain development

- = <u>Promote</u> activities that capitalize on the strengths of the developing brain.
- = Assist children with challenges that require planning.
- = Reinforce their seeking advice from adults; teach decision making.
- = <u>Encourage</u> a lifestyle that promotes good brain development.
- = <u>Never</u> underestimate the impact of a parent being a good role model.
- = <u>Tolerate</u> the "oops" behaviors due to an immature brain.



### **Parent Resources**

THE PARTNERSHIP\*
AT DRUGFREE,ORG

Prevent\_Intervene\_Get Treatment\_Recover

www.drugfree.org

National Institute
on Drug Abuse for Teens
Advancing Addiction Science

3.



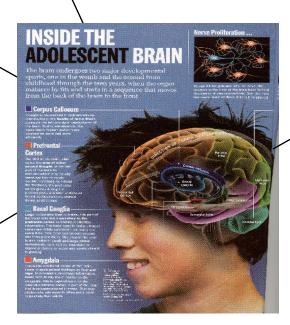
#### **Preventing Teen Drug Use**

Prevent your teen from starting or continuing drug use.

#### 1. Brain development

4. Summary

3. Clinical Implications



2. Developing brain, drugs and mental health

- Adolescence is an extended period of transition from reliance on adults to independence
- Normal adolescence is characterized by....
  - increase in conflicts with family members
  - desire to be with one's friends
  - resistance to messages from authority
  - irritability
  - risk taking
  - proclamations of sheer boredom



reward incentives > perception of consequences



 Several lines of evidence suggesting that adolescence is a period of vulnerability to the effects of drugs, and a period linked to the onset of some mental disorders.



- Employ teen-brain friendly and evidence-based prevention and treatment
  - Prevention: decrease risk, increase protective factors
  - Tx: employ these techniques
    - Motivational interviewing
    - CBT
    - Family therapy
  - Teach parents about brain development



### **Teen Brain Development Quiz**

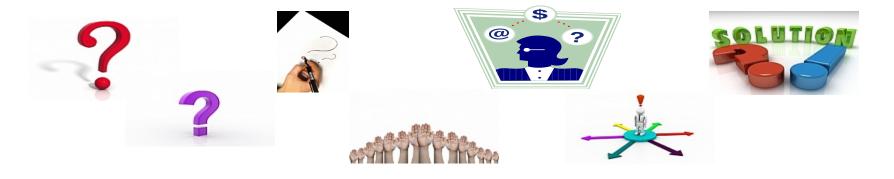
- 1. It is an accepted fact the adolescent brain fully develops at about age 25. What privilege or milestone in the U.S. requires a young person to be 25 years-old? Renting a car
- There are several health indices suggesting that teenagers take less risk than in years past.
   True
- 3. Which is more harmful to the developing brain: Chronic, heavy use of marijuana? Chronic heavy drinking? Debatable



### **THANK YOU**

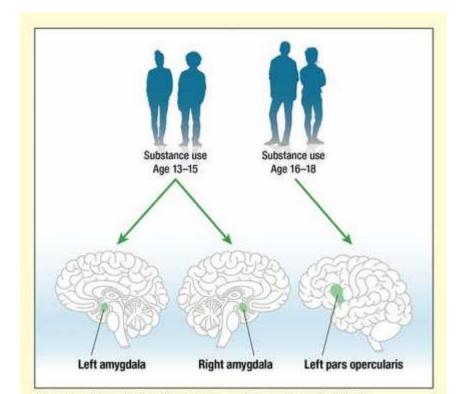
winte001@umn.edu

### **Questions and Discussion**



### **Poly-Substance Abuse**

(Windle et al. 2019)



- Pr. Michael Windle at Emory University and colleagues from other institutions performed magnetic resonance imaging of the brains of 110 25-year-old African Americans. The young men and women had participated in a study of Strong African American Families, a program designed to reduce the impact of childhood poverty on rural African Americans. During the study, they had reported their substance use to researchers annually from age 11 to 21.
- The researchers found that higher levels of alcohol, cigarette, and marijuana use before age 19 correlated with smaller gray matter volume in two brain areas (see Figure). The amygdala was smaller in youths who had reported higher use of the substances at ages 12 to 15. The pars opercularis, a subregion of the inferior frontal gyrus, was smaller in those who reported higher use of the substances at ages 16 to 18. To the researchers' knowledge, theirs is the first study to show a relationship between substance exposure and the pars opercularis.