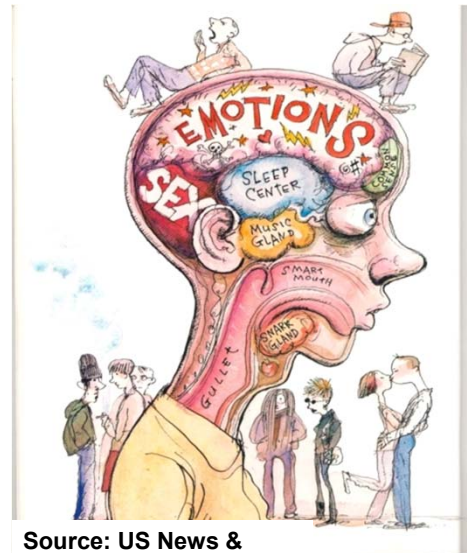


Adolescent Brain Maturation and Health: Intersections on the Developmental Highway

Ken Winters, Ph.D.

Senior Scientist
Oregon Research Institute (MN location)
&
Adjunct Faculty, Dept. of Psychology
University of Minnesota
winte001@umn.edu

September 4, 2019
Webinar Series, National American Indian
and Alaska Native Technology Transfer
Center



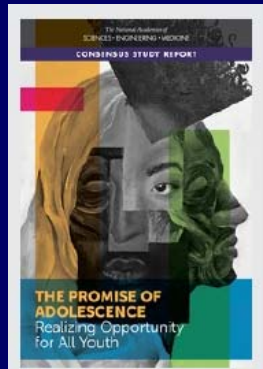
Source: US News &
World Report, 2005

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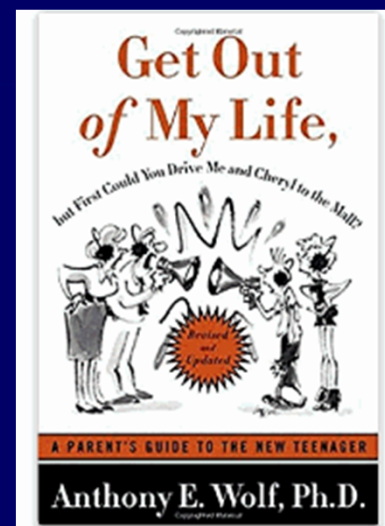
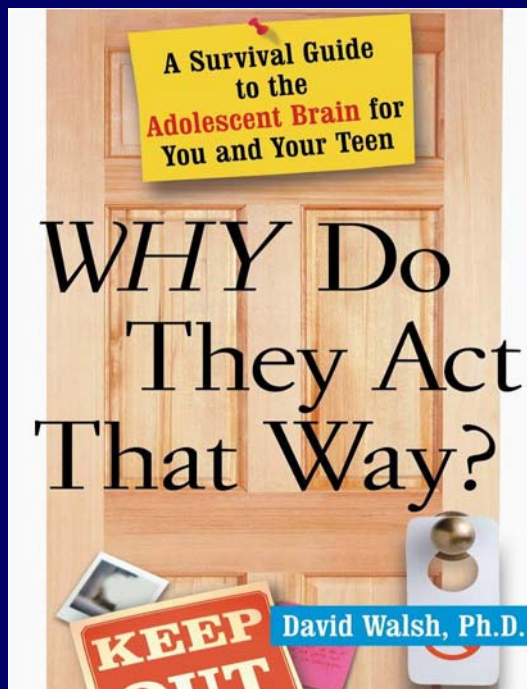
Professional Disclosures

None to report

2



3



4

Teen Brain Development Quiz



1. There are several health indices suggesting that teenagers take less risk than in years past. T or F ?
2. What lifestyle choices during adolescence promote good brain development?
3. Which is more harmful to the developing brain?
 - a. Chronic, heavy use of marijuana
 - b. Chronic, heavy drinking



5

I. Brain development

IV. Summary

III. Clinical implications



II. Developing brain: drug use, mental health, early experiences

6

Major Points from My Talk



1. The maturation of the adolescent brain likely contributes to behaviors that are characteristic of this developmental period.
2. 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.

7

Brain Development: Implications for Service Providers

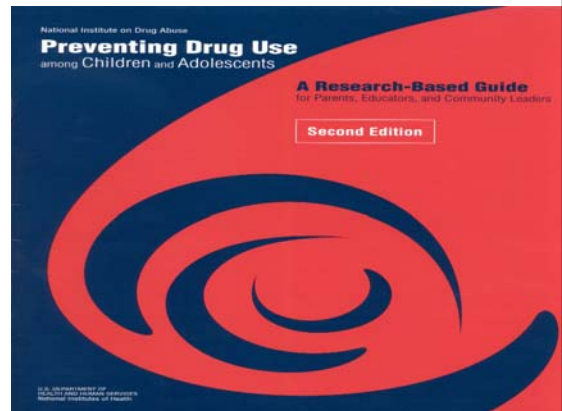
1. Teach youth about *brain development* and how it impacts mental health



8

Brain Development: Implications for Service Providers

2. Promote evidenced-based *prevention* programs



<http://www.drugabuse.gov>

9

Brain Development: Implications for Service Providers

3. Earlier the treatment, the better



10

Brain Development: Implications for Service Providers

4. Use evidenced-based treatment strategies

- Evidenced-based treatment programs are “teen-brain friendly.”

11

Brain Development: Implications for Service Providers

5. Increase youth “cannabis IQ”

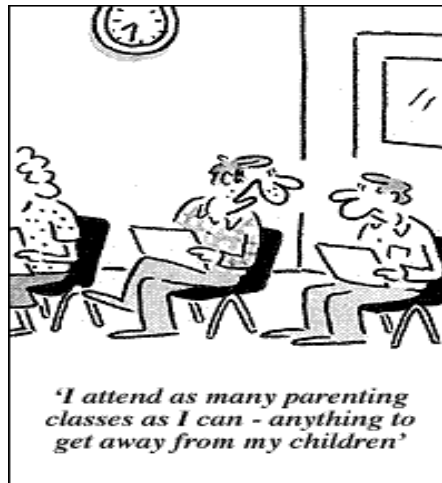
- Many misperceptions and myths about cannabis are held by youth (and adults, too!)



12

Brain Development: Implications for Service Providers

6. Teach parents about brain development



13

I. Brain development



14

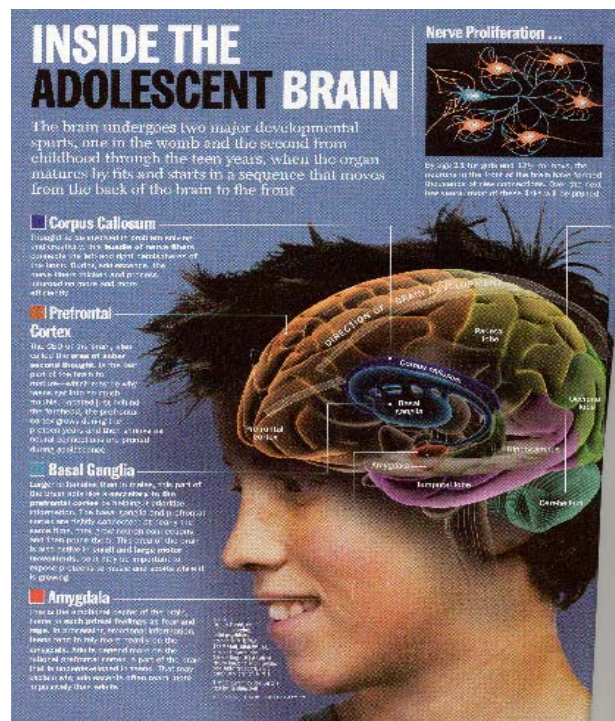
Cautions



- **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**

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



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



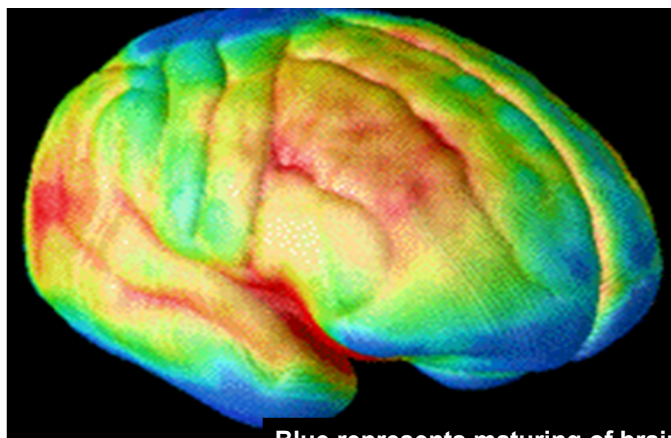
17

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: Frontal
Judgment



Blue represents maturing of brain areas

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

18

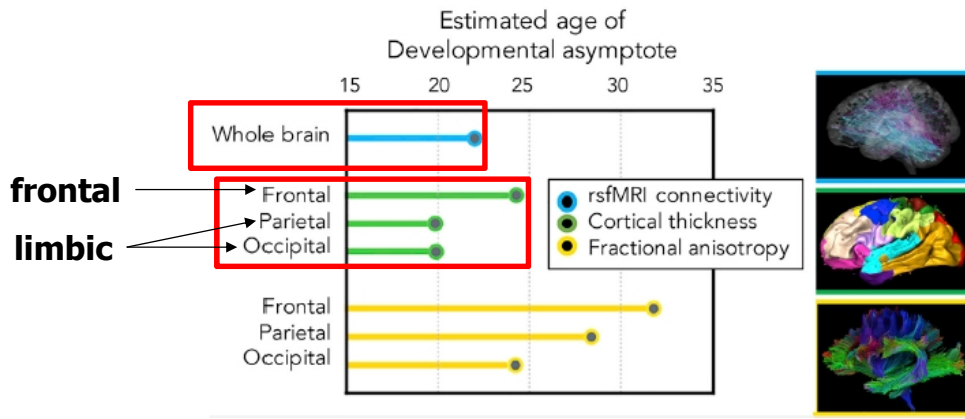


Figure 2. Indices of Brain Maturity
Adapted from Somerville (2016).

19

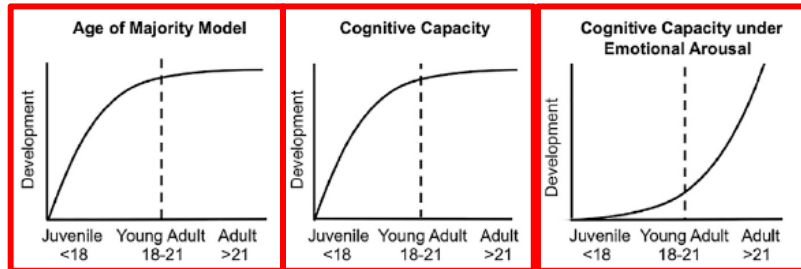


Figure 1. Legal, Psychological, and Brain-Based Accounts of When an Adolescent Is an Adult
Adapted from Cohen et al. (2016b) and Icenogle et al. (2019).

20

Implications of Brain Development for Adolescent Behavior



- **Preference for**
 1. 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 consequences
- **Greater tendency to...**
 7. be attentive to social information
 8. take risks and show poor self-control

21

Risk-Taking & Self Control

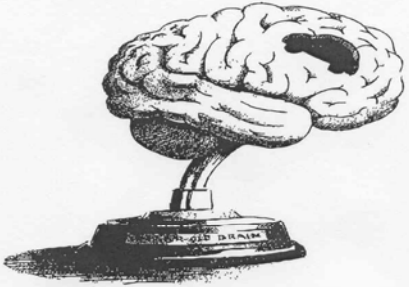
- **Based on science of brain development, a modern view of risk taking in adolescence is...**
 - evolutionarily adaptive
 - normative; important to development
 - significant individual differences
 - is due primarily to emotional and contextual, not cognitive, factors

22

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

— (V) —

BECAUSE THEY ARE.

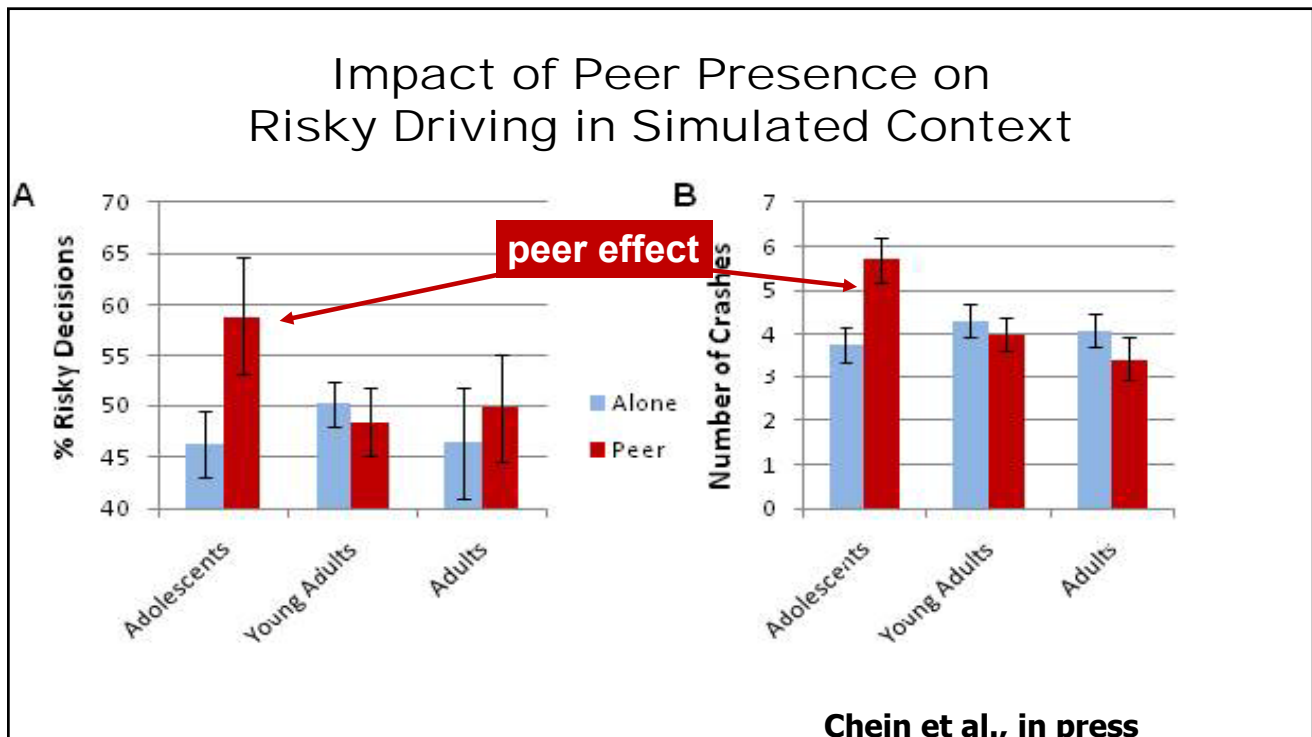


Allstate ad, NY Times, May, 2007

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

23



24

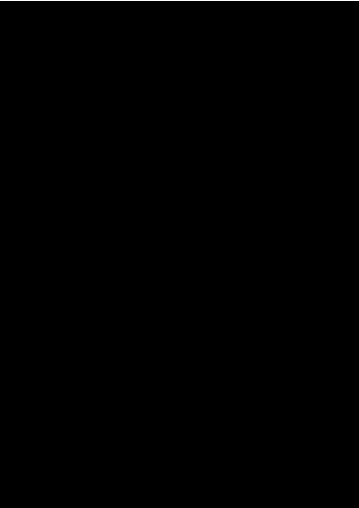
Risk-Taking & Self-Control



Resisting the marshmallow and
the success of self-control

PBS NewsHour

81K views



25

I. Brain development



**II. Developing brain:
drug use, mental
health, early experiences**

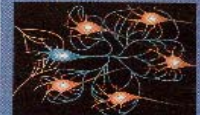
26

1. Developing brain and 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 fits and starts in a sequence that moves from the back of the brain to the front.

Nerve Proliferation ...



By age 2.5, for girls and 3.5 for boys, the increase in the size of the brain has stopped. This is due to the retraction of the connections. Two-thirds of the connections are retracted, leaving only one-third left to be pruned.

Corpus Callosum

Thought to be the most important structure in the brain, the corpus callosum connects the left and right hemispheres of the brain. It is a bundle of nerve fibers that allows the two hemispheres to communicate with each other.

Prefrontal Cortex

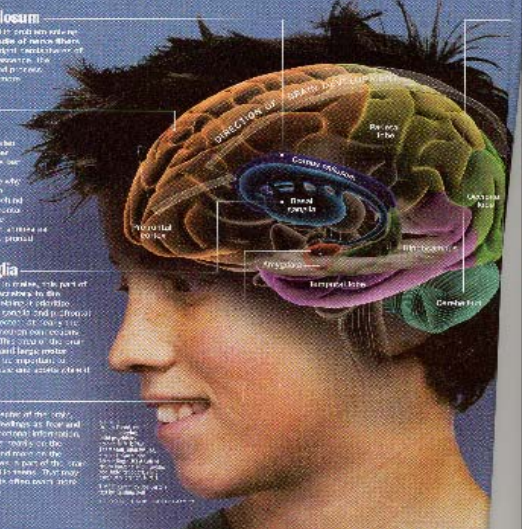
The prefrontal cortex is the part of the brain that is responsible for planning, decision-making, and impulse control. It is the part of the brain that is most affected by drugs, and it is the part of the brain that is most important for the development of the adolescent brain.

Basal Ganglia

Large in children, the basal ganglia is a part of the brain that is responsible for movement, learning, and emotion. It is the part of the brain that is most affected by drugs, and it is the part of the brain that is most important for the development of the adolescent brain.

Amygdala

The amygdala is a part of the brain that is responsible for emotion, learning, and memory. It is the part of the brain that is most affected by drugs, and it is the part of the brain that is most important for the development of the adolescent brain.



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Implications of Brain Development for Drug Abuse Vulnerability

Are adolescents more susceptible than adults to drugs?

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

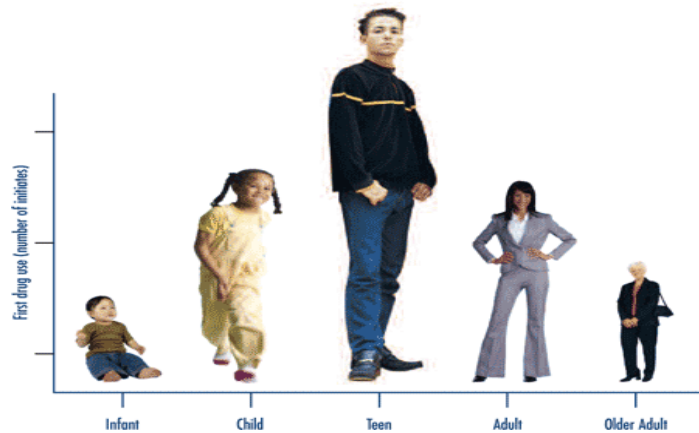
Unethical to give human adolescents alcohol in the laboratory;
much of the best evidence comes from adolescent rat studies.



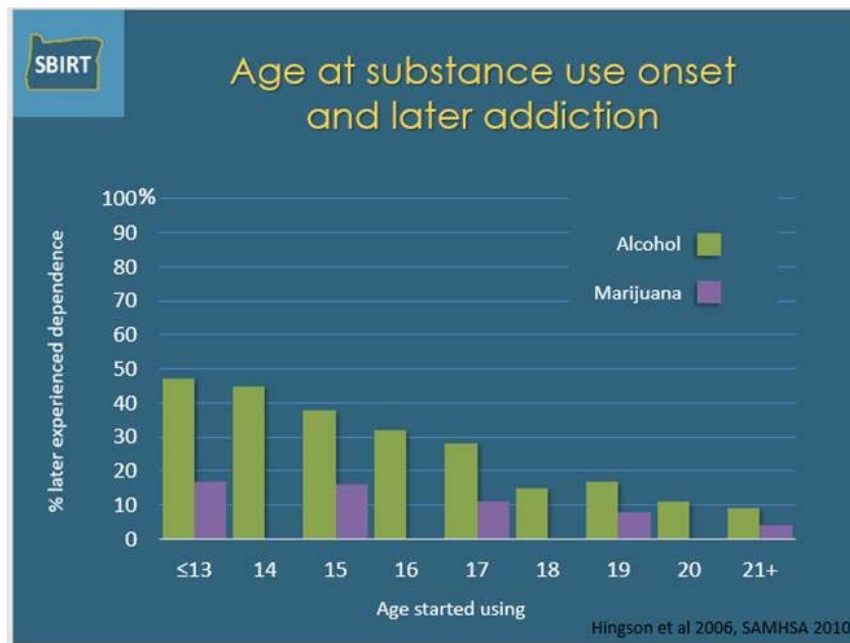
28

Evidence from epidemiological studies

Drug use starts early and peaks in the teen years



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Implications of Brain Development for Drug Abuse Vulnerability

Alcohol



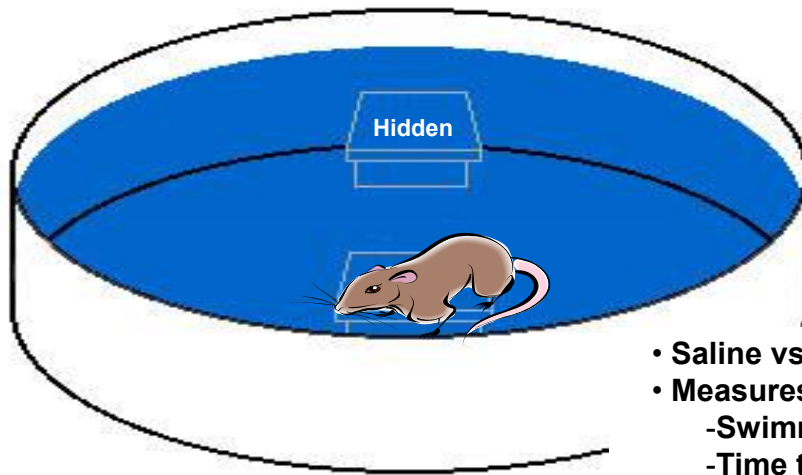
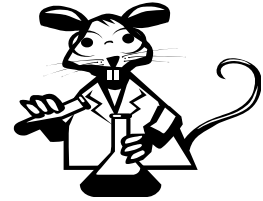
31

Are adolescents more susceptible to alcohol than adults?

1. Adolescent rats are **less sensitive** to the sedative and motor impairment effects of **intoxication**.
2. Adolescent rats are **more sensitive** to the social disinhibition effects of alcohol.

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The Water Maze Test



- Saline vs alcohol
- Measures
 - Swimming speed
 - Time to find platform

Slide courtesy
Sion Kim Harris, Ph.D.

33

Are adolescents more susceptible
to alcohol than adults?

1. Adolescent rats are less sensitive to the sedative and motor impairment effects of intoxication.
2. Adolescent rats are more sensitive to the social disinhibition effects of alcohol.

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

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35

Impact of Binge Drinking



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: slower developmental improvement of impulse control**

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Implications of Brain Development for Drug Abuse Vulnerability

Marijuana

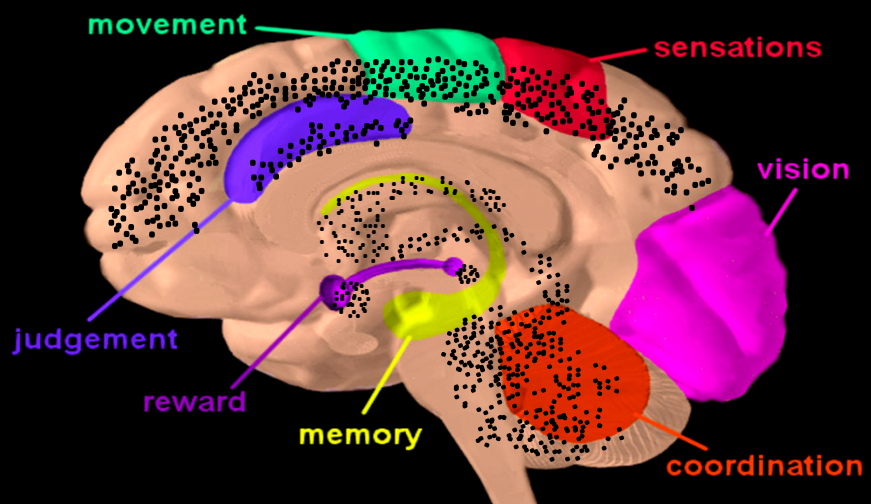


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Marijuana Binds Cannabinoid Receptors Located Throughout the Brain

(source NIDA)

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



Slide courtesy of Maureen Boyle, PhD

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Eight Adverse Health Effects of Chronic Marijuana Use (Volkow et al., 2014)

"Low Level of Confidence"

- Lung cancer

"Medium Level of Confidence"

- Altered brain development
- Progression to use of other drugs
- Increased risk of schizophrenia, depression and anxiety disorders (in persons with a predisposition to such disorders)

"High Level of Confidence"

- Addiction
- Motor vehicle accidents
- Diminished life achievement (including cognitive impairment and poor educational outcome)
- Symptoms of chronic bronchitis



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The Health Effects Strongly Associated with Initial Cannabis Use Early in Adolescence (Volkow et al., 2014)

"Low Level of Confidence"

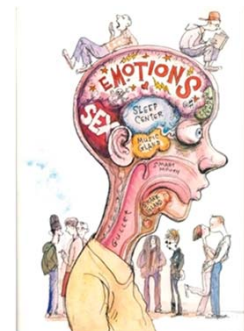
- Lung cancer

"Medium Level of Confidence"

- Altered brain development
- Progression to use of other drugs
- Increased risk of chronic psychosis disorders (including schizophrenia and depression) in persons with a predisposition to such disorders

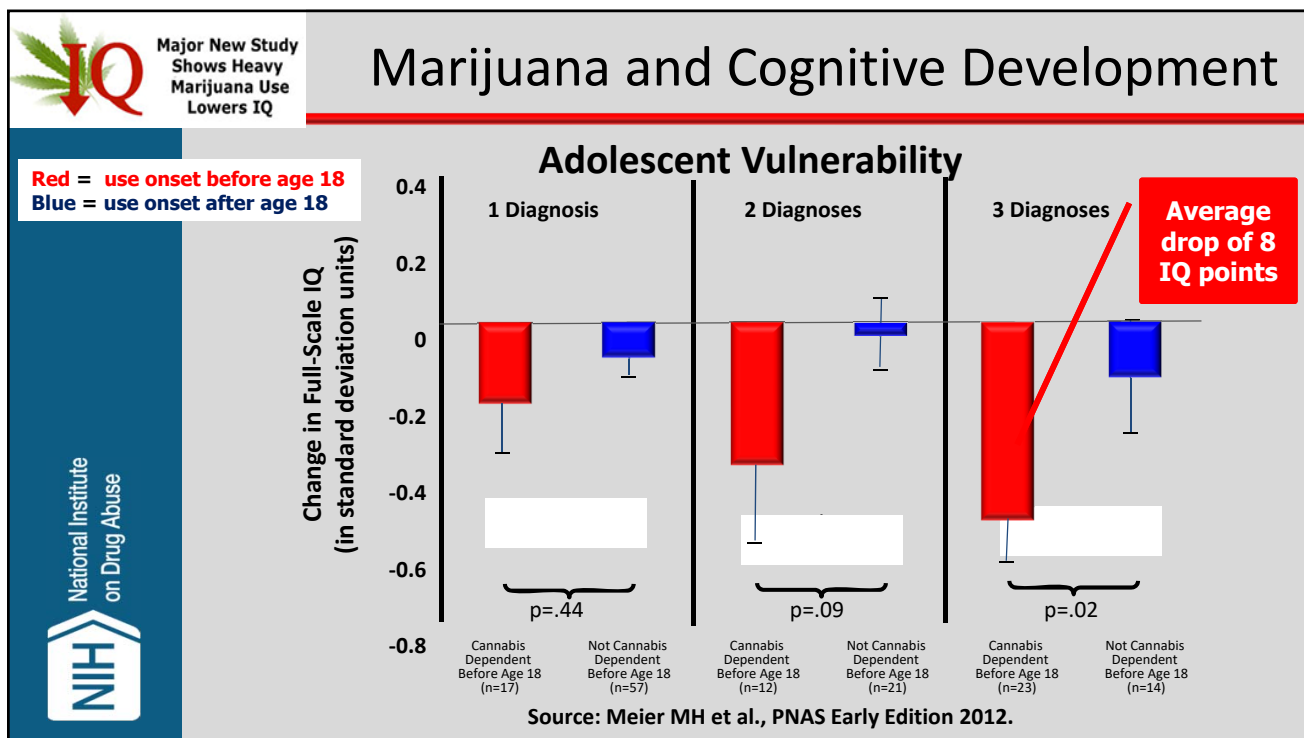
"High Level of Confidence"

- Addiction
- Motor vehicle accidents
- Diminished life satisfaction and achievement (including cognitive impairment and poor educational outcome)
- Symptoms of chronic bronchitis



Source: US News & World Report, 2005

40



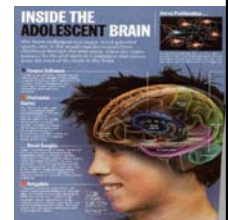
41

WHY?

42

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

- **Preference for**
 1. **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**

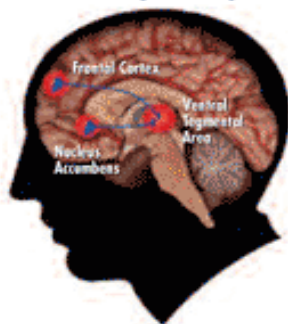


43

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

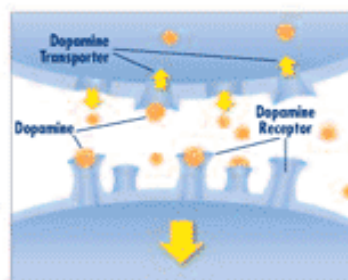
ALL DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

Brain reward (dopamine) pathways



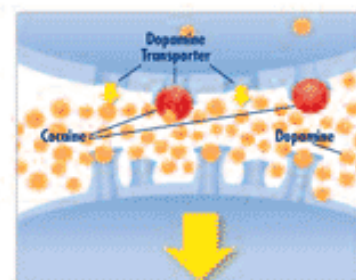
These brain circuits are important for natural rewards such as food, music, and art.

All drugs of abuse increase dopamine



FOOD

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

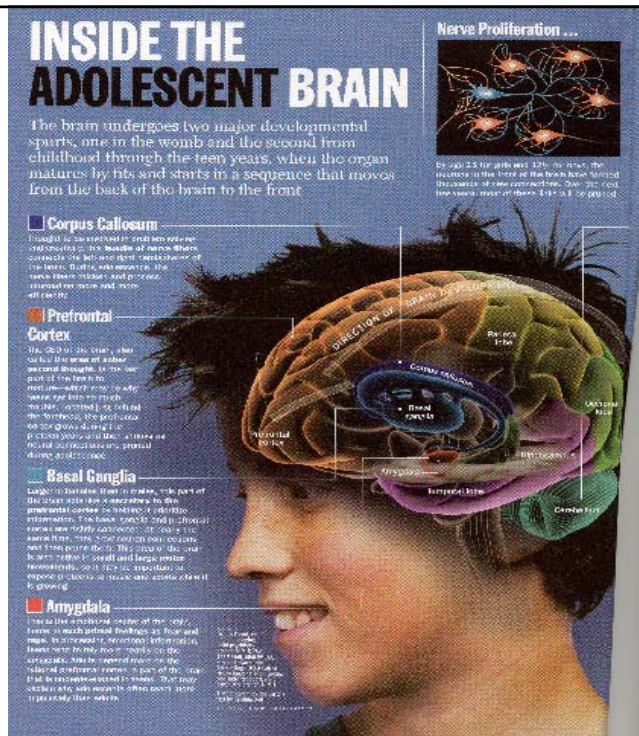


COCAINE

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

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2. Brain development and behavioral disorders



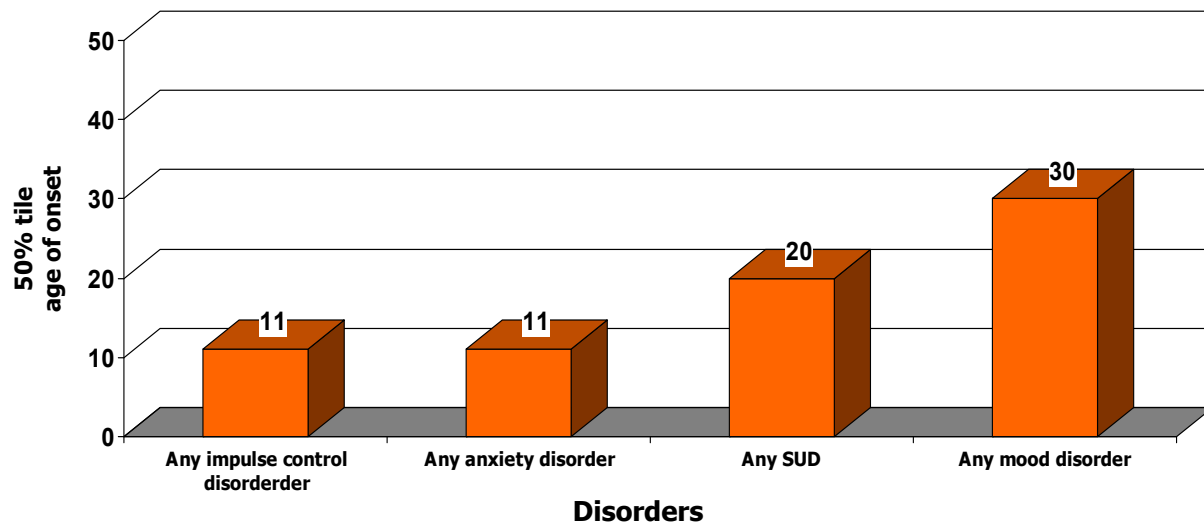
45

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**

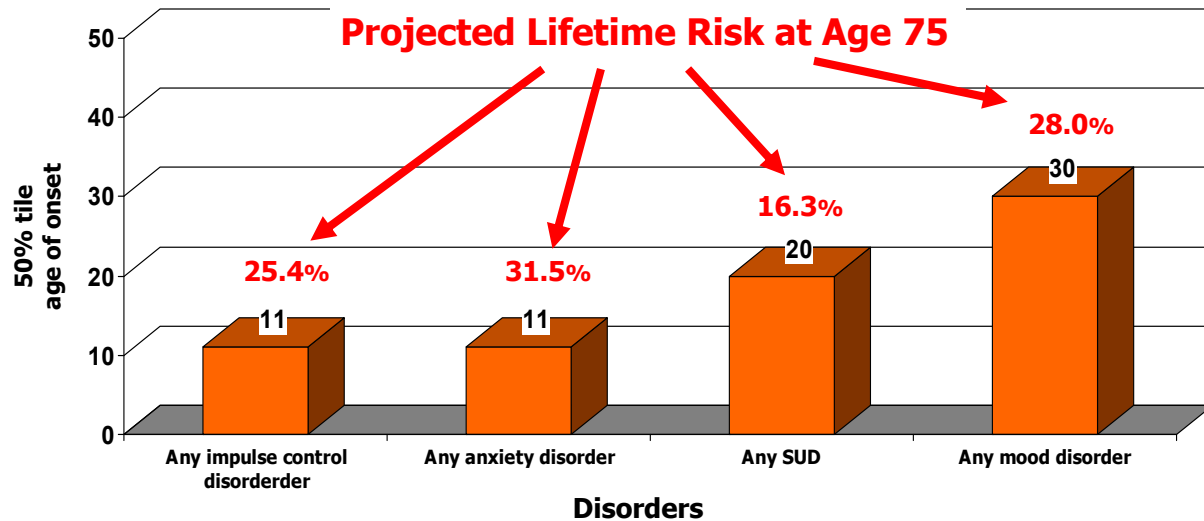
46

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



47

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



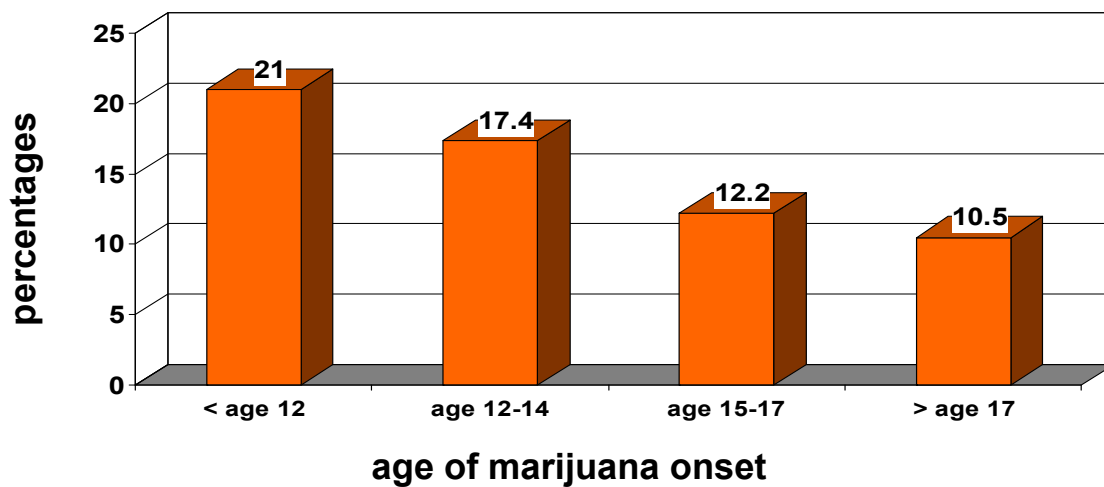
48

Adolescent Use of *Marijuana* and Behavioral Disorders



49

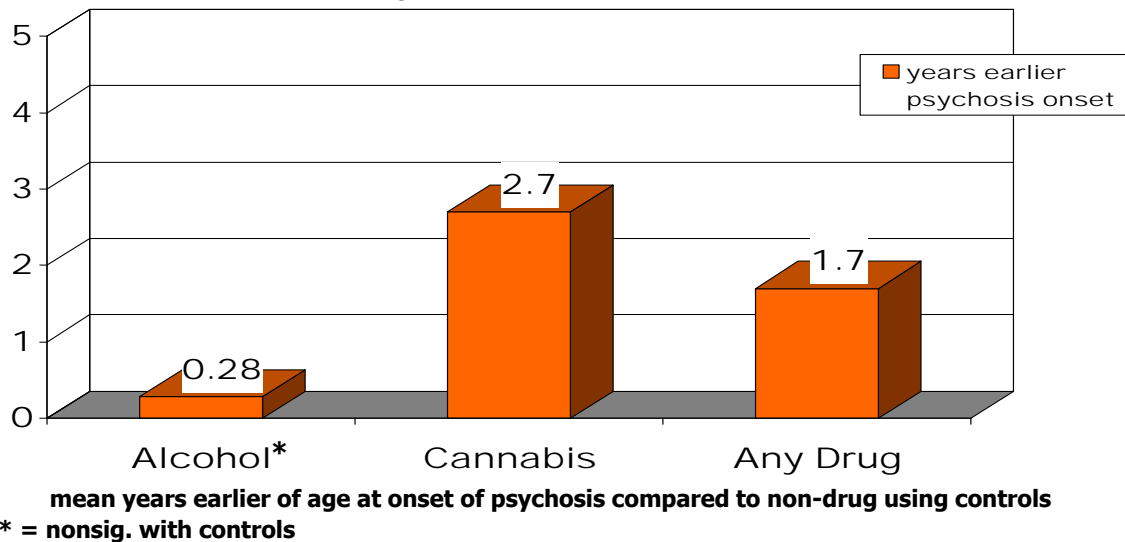
Psychosis: Prevalence of Past Year Serious Mental Illness Among Lifetime Marijuana Users Aged 18+ (SAMHSA, 2005; data collected 2002-2003)



50

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

(Large et al., 2011)



51

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.

52

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   • Diego Quattrone, MD • Tom P Freeman, PhD • Giada Tripoli, MSc • Charlotte Gayer-Anderson, PhD • Harriet Quigley, MD • et al. [Show all authors](#) •

Source: Lancet Psychiatry, 2019

- 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)

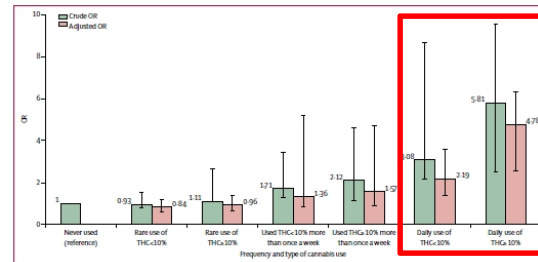


Figure 1: Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample. Crude ORs are adjusted only for age, gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and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

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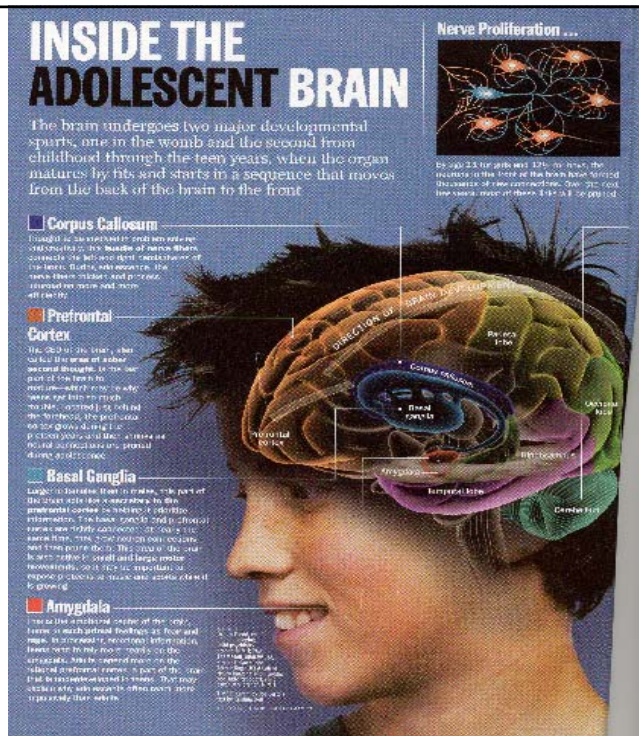
Cautionary Notes

- **Reverse causation (self-medication).**
- **Early drug use may be a marker of underlying genetic risk and not causative, or only partially causative.**



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3. Impact of early experiences on the developing brain and subsequent health and well-being



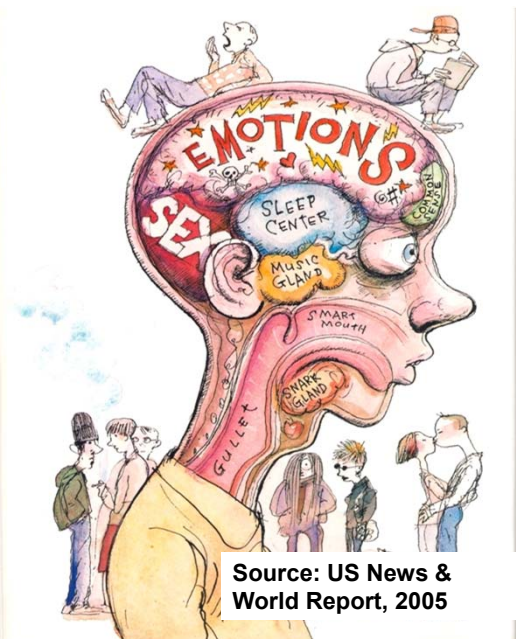
55

A Developing Brain

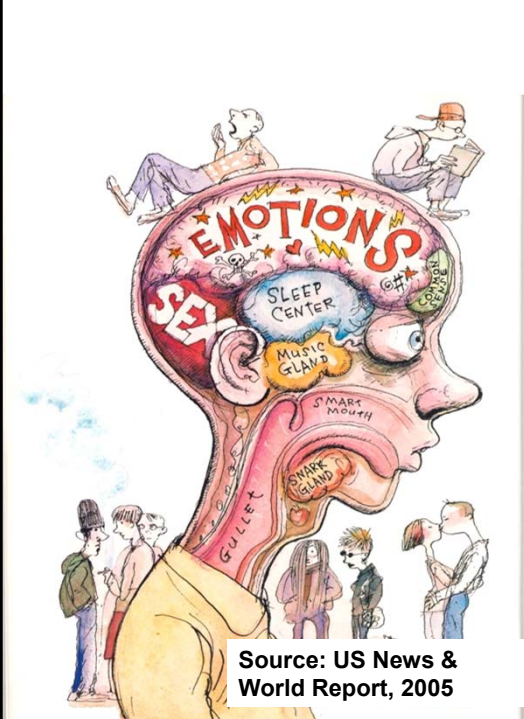
> Impact from Environment?

- "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*)



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A Developing Brain

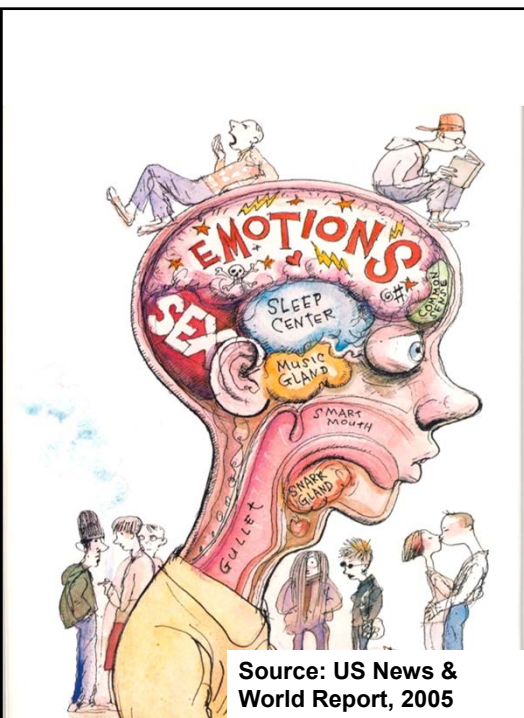
> Impact from Environment?

<https://developingchild.harvard.edu/science/deep-dives/mental-health/>

- **"Genes are not destiny. The interaction between genetic predispositions and sustained, stress-inducing experiences early in life can lay an unstable foundation for mental health that endures well into the adult years."**



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A Developing Brain

> Impact from Environment?

<https://developingchild.harvard.edu/science/deep-dives/mental-health/>

Rays of Hope!

- **"Some individuals demonstrate remarkable capacities to overcome the severe challenges of early, persistent maltreatment, trauma, and emotional harm."**
- **"Most potential mental health problems will not become mental health problems if we respond to them early."**

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Early experiences can alter brain development in positive ways



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

“Nurturing and responsive care for the child’s body and mind is the key to supporting healthy brain development.”



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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^{a,1}, Andy Belden^a, Michael P. Harms^a, Rebecca Tälman^a, and Deanna M. Barch^{a,b,c}

^aDepartment of Psychiatry, Washington University in St. Louis, St. Louis, MO 63110; ^bDepartment of Psychological & Brain Sciences, Washington University in St. Louis, St. Louis, MO 63130; and ^cDepartment of Radiology, Washington University in St. Louis, St. Louis, MO 63110

More parental support = more hippocampus volume



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Early experiences can alter brain development in negative ways

WHAT ARE ACES?
AND HOW DO THEY RELATE TO TOXIC STRESS?

SAMHSA
Substance Abuse and Mental Health
Services Administration



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

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



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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.



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Early experiences can alter brain development in negative ways

Development and Psychopathology

Article Supplementary materials Metrics

First View

Mind and gut: Associations between mood and gastrointestinal distress in children exposed to adversity

Bridget L. Callaghan¹*, Andrea Fields¹*, Dylan G. Gee¹*, Laurel Gabard-Durnam¹*, <https://doi.org/10.1017/S0954579419000087> Published online: 28 March 2019



- 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



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I. Brain development



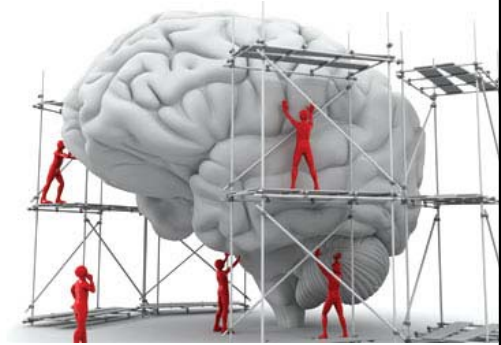
!! Developing brain, drug use and mental health

III. Clinical implications

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Brain Development: Implications for Service Providers

1. Teach youth about brain development and its importance to health



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Brain Development: Implications for Service Providers

RESOURCES

- **Drug Abuse**
<https://www.drugabuse.gov/publications/drugfacts/>
- **Mental Health**
<https://developingchild.harvard.edu/science/deep-dives/mental-health/>
- **Adolescent Health**
<https://collegeofphysicians.org/uploads/attachments/cjrs2yopd3z76dczh8h60bs4j-federal-resources-for-adolescent-health.pdf>

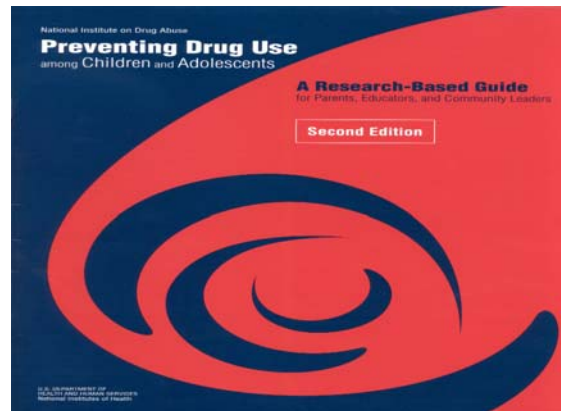


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Brain Development: Implications for Service Providers

2. Promote evidenced-based *prevention* programs

Prevention: 16 principles of effective prevention summarized in NIDA's 2nd edition of their research guide
Key: reduce risk and increase assets

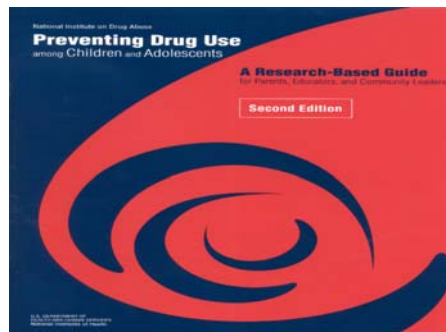


<http://www.drugabuse.gov>

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Sources of Evidence-Based Prevention Programs

1. <http://www.drugabuse.gov>



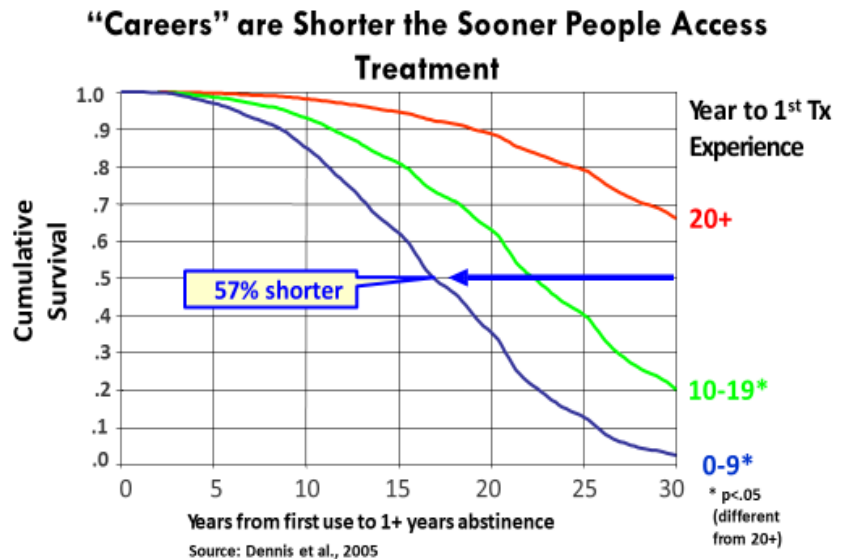
2.  **Cochrane** Trusted evidence.
Informed decisions.
Better health.

Interventions for preventing multiple risk behaviours in young people

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Brain Development: Implications for Service Providers

3. Earlier the treatment, the better



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Brain Development: Implications for Service Providers

4. 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 treatment (EBTs) do significantly better.

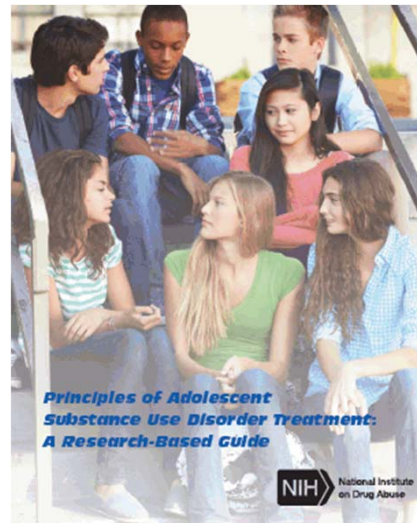


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Evidenced-Based Treatment

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

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



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CBT and MI Are Helpful for Teaching and Supporting Self-Regulation

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



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New 12-Step Program for Adolescents ?

12-Steps of Self-Regulation

1. 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

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Brain Development: Implications for Service Providers

5. Increase the "Cannabis IQ" of Adolescents

- **Sources of exercises and quizzes**
 - **www.dfaf.org (Busting the Top Ten Myths of Marijuana)**
 - **www.learnaboutsam.org**



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Brain Development: Implications for Service Providers

6. Teach parents about brain development

P = Promote activities that capitalize on the strengths of the developing brain.

A = Assist children with challenges that require planning.

R = Reinforce their seeking advice from adults; teach decision making.

E = Encourage a lifestyle that promotes good brain development.

N = Never underestimate the impact of a parent being a good role model.

T = Tolerate the "oops" behaviors due to an immature brain.



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Parent Resources



**Prevent_Intervene_Get
Treatment_Recover**

www.drugfree.org

2.



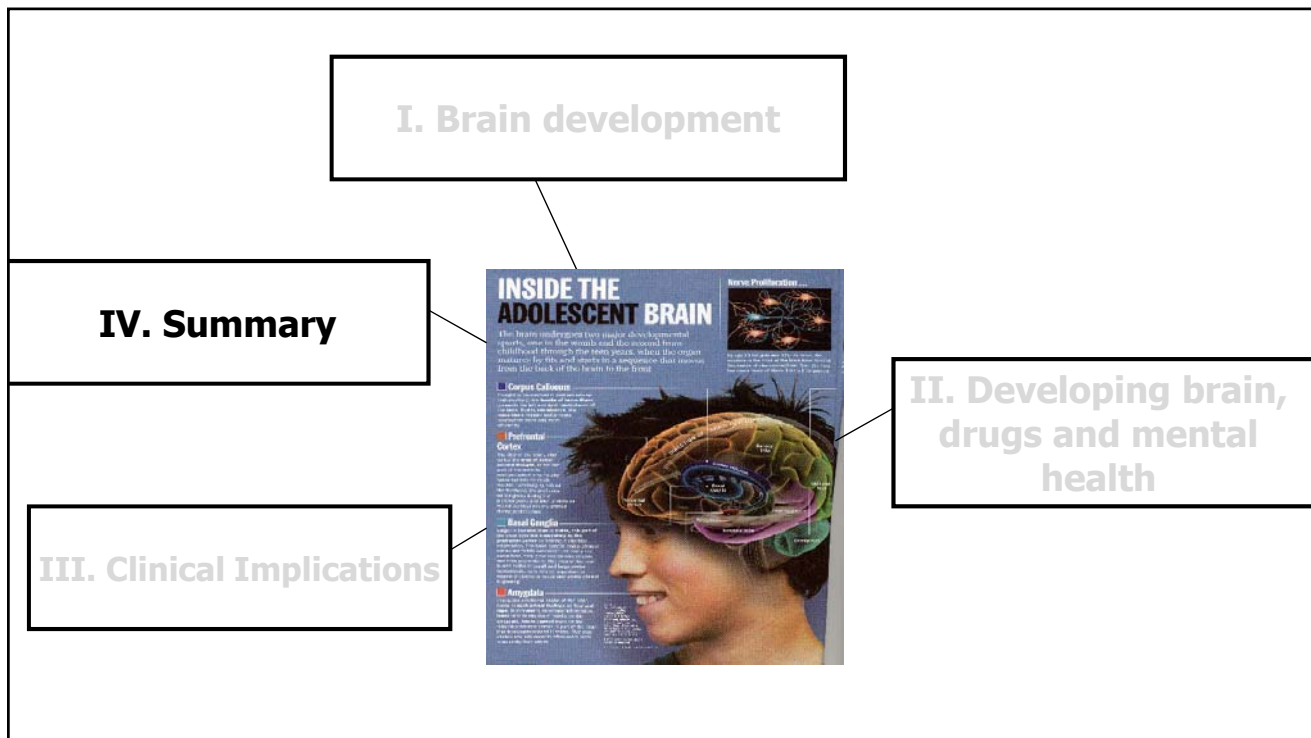
3.



Preventing Teen Drug Use

Prevent your teen from starting or continuing drug use.

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Summary

- **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



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Summary

**reward incentives >
perception of
consequences**



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Summary

- **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.**



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Summary

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



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Adolescent Brain Cognitive Development National Longitudinal Study

U.S. longitudinal study of 13,000 children enrolled at age 9-10 years to assess effects of drugs on individual brain development trajectories



Slide courtesy of Maureen Boyle, PhD

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Teen Brain Development Quiz

1. There are several health indices suggesting that teenagers take less risk than in years past.
True (increased rate of "abstaining" from all substances; lower rate of teenage pregnancies and certain delinquency behaviors)
2. What lifestyle choices during adolescence promote good brain development?
Healthy diet; sufficient sleep; involvement in music; daily exercise; no drug use
2. Which is more harmful to the developing brain?
 - a. Chronic, heavy use of marijuana
 - b. Chronic, heavy drinking**Good question!!**

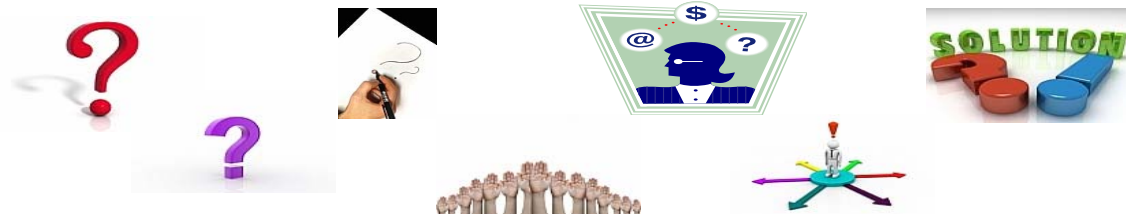


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THANK YOU

winte001@umn.edu

Questions and Discussion



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