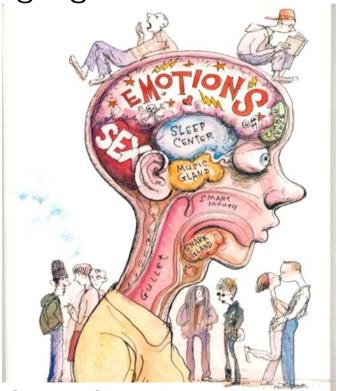
#### Adolescents and the Changing Brain

#### Ken Winters, Ph.D.

Senior Scientist, Oregon Research Institute (MN location)

Retired Professor, Dept. of Psychiatry University of Minnesota winte001@umn.edu

July 8, 2020 Webinar Series National American Indian and Alaska Native Mental Health Technology Transfer Center



Source: US News & World Report, 2005

#### Professional Disclosures

### None to report

#### Personal Disclosure

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

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

The National Academies of SCIENCES ENGINEERING MEDICINE

#### THE NATIONAL ACADEMIES PRESS

This PDF is available at http://nap.edu/25388

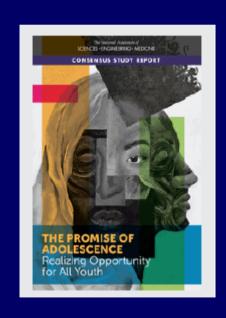












#### **Podcast Series**

 Harvard's Center on the Developing Child new podcast series, The Brain Architects

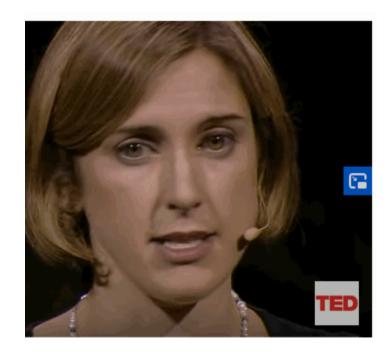




- "Learn the science behind how brains are built and what it means how to build a strong brain."
- https://developingchild.harvard.edu/ science/key-concepts/brainarchitecture/

#### YouTube Video

https://youtu.be/6zVS8HIPUng Sarah-Jayne Blakemore's Ted Talk: The mysterious workings of the adolescent brain



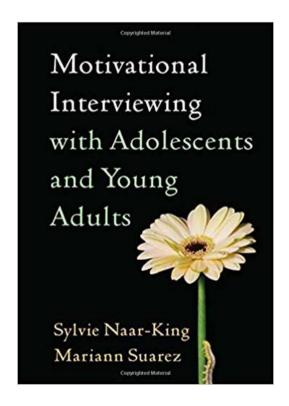
## Publication on the Intersection of Brain Development and Treatment

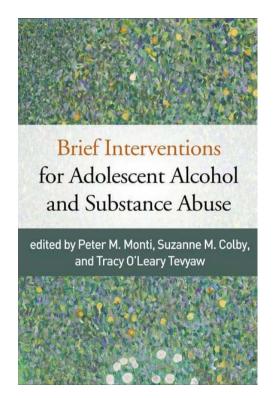
Wetherill, R., & Tapert, S. F. (2013). Adolescent brain development, substance use, and psychotherapeutic change. *Psychology of Addictive Behaviors*, *27*(2), 393–402.

https://doi.org/10.1037/a0029111

#### Recent "Treatment" Publications

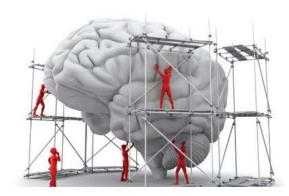
(that integrate teen brain development)





#### Teen Brain Development Quiz

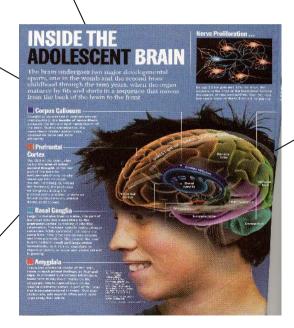
- 1. There are several health indices suggesting that teenagers take less risk than in years past. T or F?
- 2. What lifestyle choices during adolescence promote good brain development?
- 3. Which is more harmful to the developing brain?
  - a. Chronic, heavy use of marijuana?
  - b. Chronic, heavy drinking?



## I. Overview of brain development

**IV. Summary** 

III. Youth Serving Workers



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

### Possible Sources of Confounds when Interpreting Studies on Brain Development and Health



- 1. Confirmation bias
- 2. Small sample sizes
- 3. Too small a time window
- 4. Community-level vs. individual-level data
- 5. Direct links between brain functions and structures and human behavior are problematic





## Possible Sources of Confounds when Interpreting Studies on Brain Development and Health



One more introductory note about this talk: My "spotlight" on brain development and its impact on adolescent behavior and health does not diminish the impact of environment and social determinants on adolescent behavior.



 I will be integrating into today's discussion the important role of nonbiological influences.



#### Major Points from My Talk

- 1. 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. Youth serving workers & educators can leverage teen brain science when working with adolescents and parents.

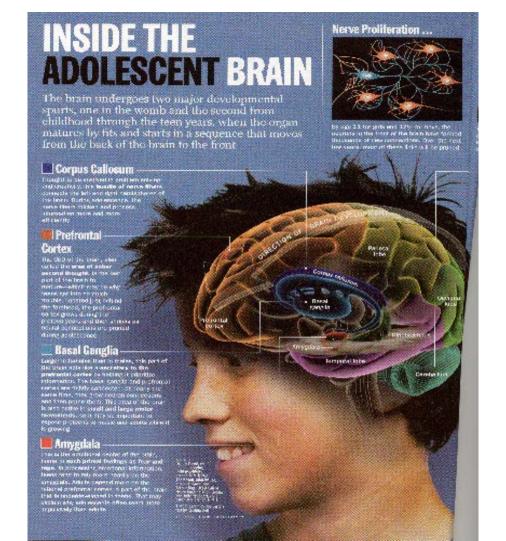
#### Major Points from My Talk

- 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. Youth serving workers & educators can leverage teen brain science when working with adolescents and parents.
  - i. teaching youth about brain development
  - ii. use evidenced-based prevention programs
  - iii. treat teen behavioral disorders as early as possible
  - iv. use evidence-based treatment programs
  - v. increase youth "cannabis and vaping IQ"
  - vi. educate parents

## I. Overview of brain development



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



### A Developing Brain = Less Brakes on the "Go" System

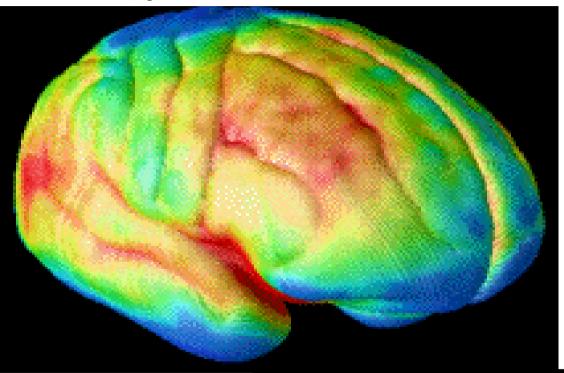


### Maturation Occurs from Back to Front of the Brain and Inside to Outside

Images of Brain Development in Healthy Youth (Ages 5 - 20)

Frontal: later (judgment)

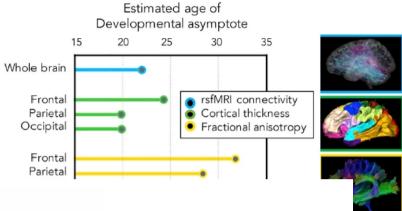
Limbic: earlier (emotion, motivation)



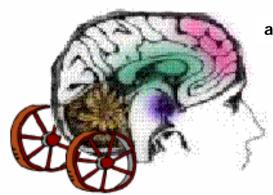
Blue represents maturing of brain areas

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





 During adolescent brain development, the brain is not functioning at full and optimal capacity.



adapted from Somerville, 2016

#### Implications of Brain Development for Adolescent Behavior (Winters et al., 1995)



- Preference for ....
  - physical activity
  - 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 overly attentive to social information
  - 3. take risks

#### Implications of Brain Development for Adolescent Behavior (Winters et al., 1995)



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Contributors for unhealthy behaviors?

#### Implications of Brain Development for Adolescent Behavior (Winters et al., 1995)



- Preference for ....
  - physical activity
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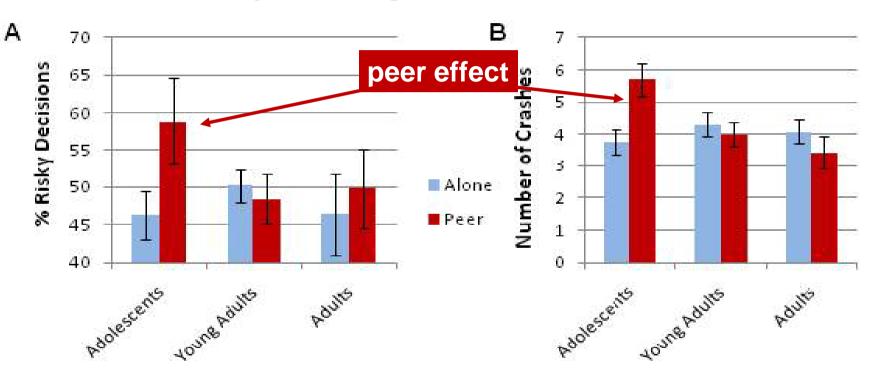
Contributors for healthy or personal growth?

#### Risk-Taking - Context Matters!

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

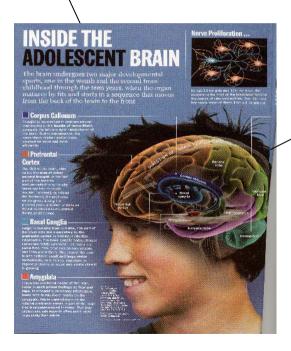
- normative; important to development
- significant individual differences
- is due primarily to <u>emotional and contextual</u>, not cognitive, factors

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



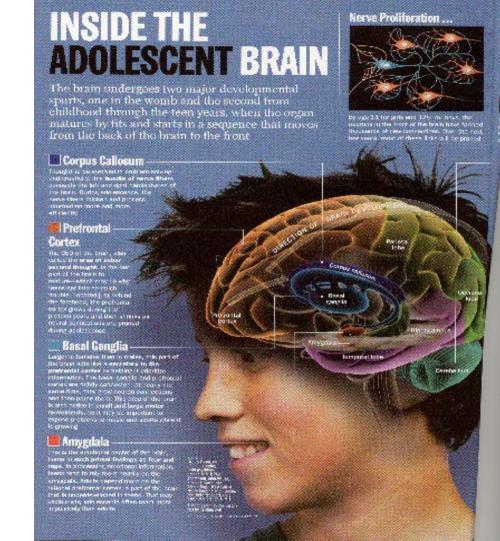
Chein et al., in press

#### I. Brain development



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

#### Developing brain and drugs



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

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

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

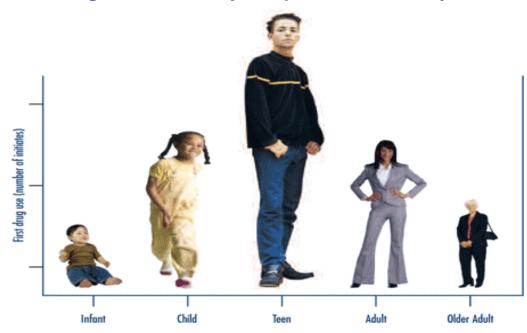
Unethical to give human adolescents alcohol in the laboratory; much of the best evidence comes from adolescent rat studies.





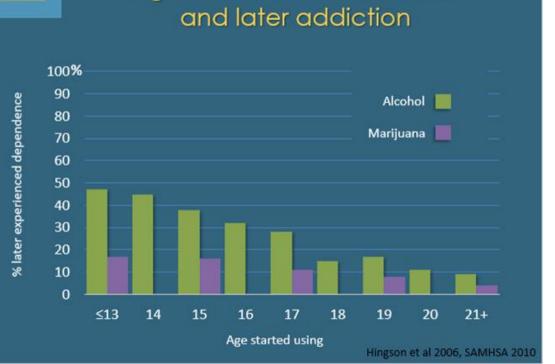
## Evidence from <u>epidemiological</u> studies

Drug use starts early and peaks in the teen years



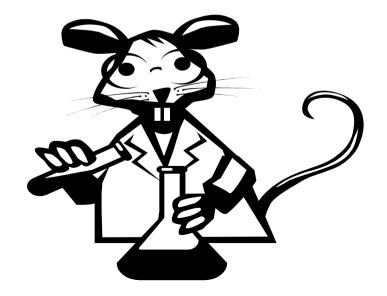


## Age at substance use onset and later addiction



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

## Alcohol





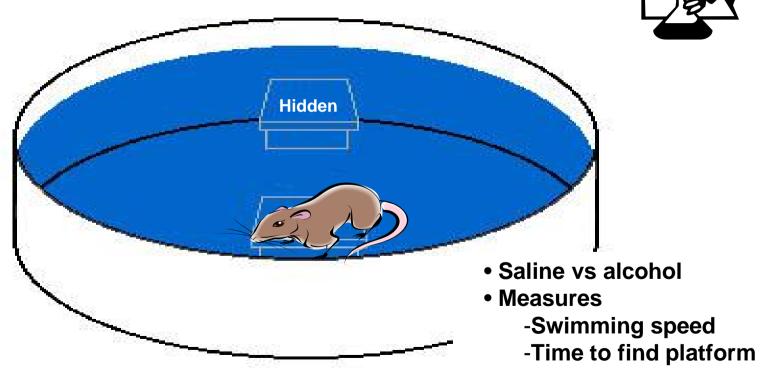
## Are adolescents more susceptible to <u>alcohol</u> than adults?

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

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



#### The Water Maze Test



Slide courtesy Sion Kim Harris, Ph.D.

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

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

 Adolescent mice are more sensitive to the social disinhibition effects of alcohol.

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









#### Impact of Binge Drinking

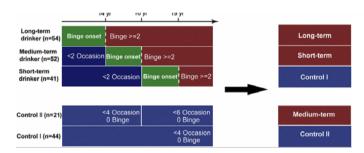


Adolescent binge drinking disrupts normal trajectories of brain functional organization and personality maturation

Ruan et al., 2019



- Longitudinal design; assessed at ages 14, 16 and 19
- Accumulating effect of binge drinking....
  - Neuroimaging data: disruption in the maturation of frontal connectivity (caution: small sample with neuroimaging data at baseline)
  - Personality data: slower developmental improvement of impulse control



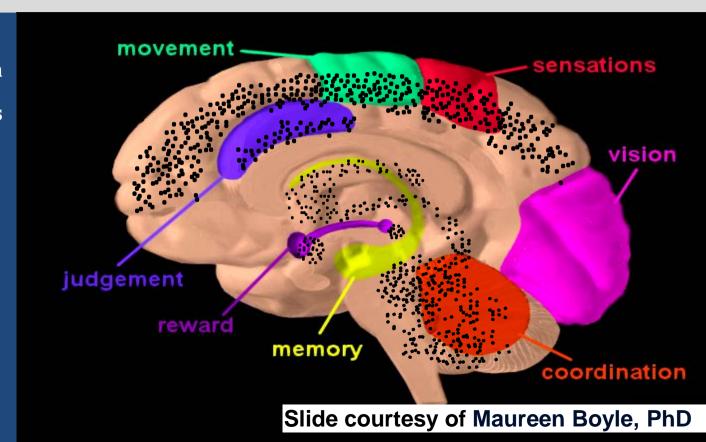
Implications of Brain Development for <u>Drug</u> <u>Abuse Vulnerability</u>

# 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





## Eight Adverse Health Effects of Chronic Cannabis 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

Some Adverse Health Effects of Chronic Cannabis Use More Pronounced with Youth Onset (Volkow et al., 2014)

#### "Low Level of Confidence"

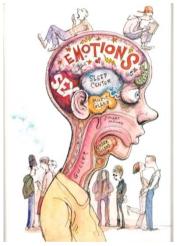
Lung cancer

#### "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



## The Dunedin Study (New Zealand) (N=1,037)



## **Assessment ages**

Slide courtesy of Sion Kim, MD; Source: Meier et al. PNAS, 2012



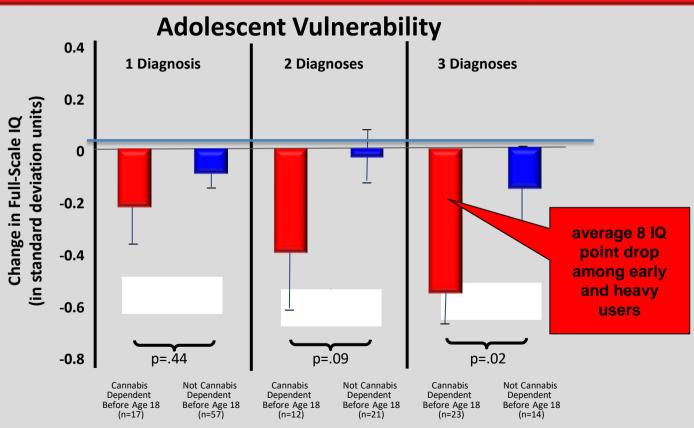
## The Dunedin Study (New Zealand) (N=1,037)



## **Assessment ages**

Slide courtesy of Sion Kim, MD; Source: Meier et al. PNAS, 2012

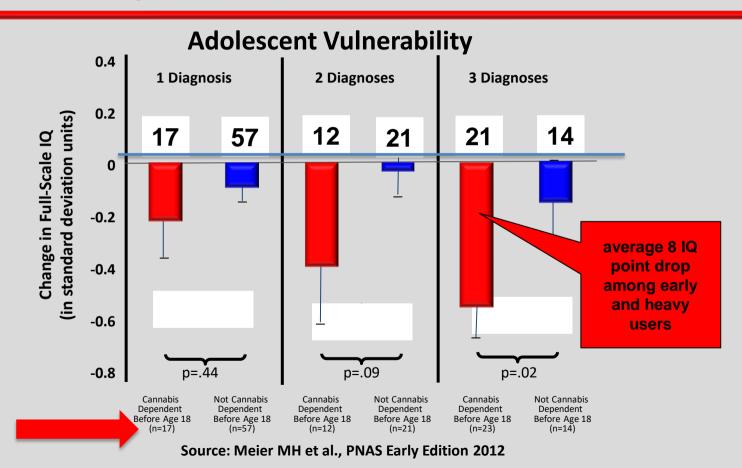
## Marijuana and Cognitive Development



NIH National Institute on Drug Abuse

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

## Sample Sizes Far from Ideal!!



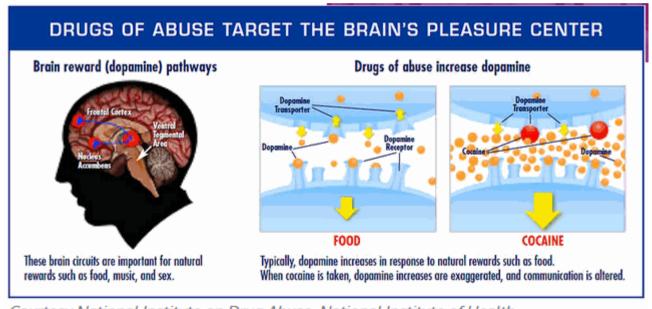
National Institute on Drug Abuse

# WHY?

- 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
      - novelty
- Less than optimal..
- 5. control of emotions
  - 6. consideration of negative consequences
- Greater tendency to...
  - 7. be attentive to social information
    - take risks

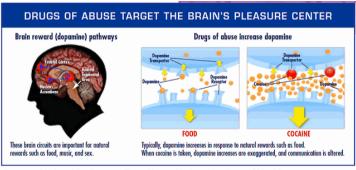


2. Adolescent pleasure centers in the brain may be more sensitive to the acute effects of drugs than pleasure centers in the adult brain.



Courtesy National Institute on Drug Abuse, National Institute of Health

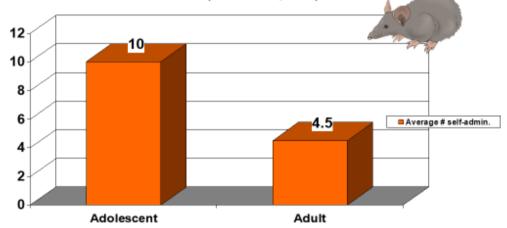
- 2. Adolescent pleasure centers in the brain may be more sensitive to the acute effects of drugs than pleasure centers in the adult brain. (Chambers, Taylor and Potenza, 2003)
- Evidence that dopamine activity is more "robust" during adolescence.
- If dopamine production is more pronounced or "robust" during adolescence, risk of drug abuse could be heightened
- > sensitivity to initial drug effects
- > motivation to continue use
- > difficulty to reduce use



Courtesy National Institute on Drug Abuse, National Institute of Health

### 3. Early Use May Create a Biological Priming or Gateway Effect





Age of Rates When First Exposed to Nicotine. All Data Collected When Rats were Adults.

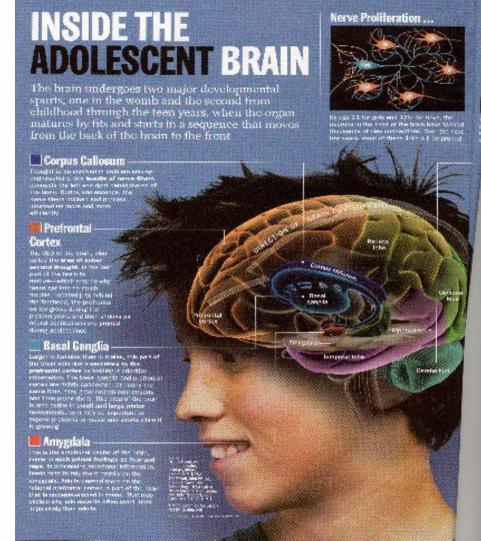
#### Nicotine Gateway Effects on Adolescent Substance Use

Michelle Ren, MS\* Shahrdad Lotfipour, PhD† \*University of California, Irvine, Department of Pharmaceutical Sciences, Irvine, California
\*University of California, Irvine, Department of Emergency Medicine and Pharmaceutical
Sciences, Irvine, California

Section Editor: Tony Zitek MD

- Literature suggests: Disruption of nicotinic acetylcholine receptors (nAChR) development with early nicotine use may alter the release of reward-related neurotransmitters, and thus increase the likelihood of future drug seeking behaviors, including drugs other than nicotine.
- There is a "large collection of clinical and preclinical evidence that adolescent nicotine exposure influences long-term molecular, biochemical, and functional changes in the brain that encourage subsequent drug abuse."

## ii. Brain development and behavioral disorders

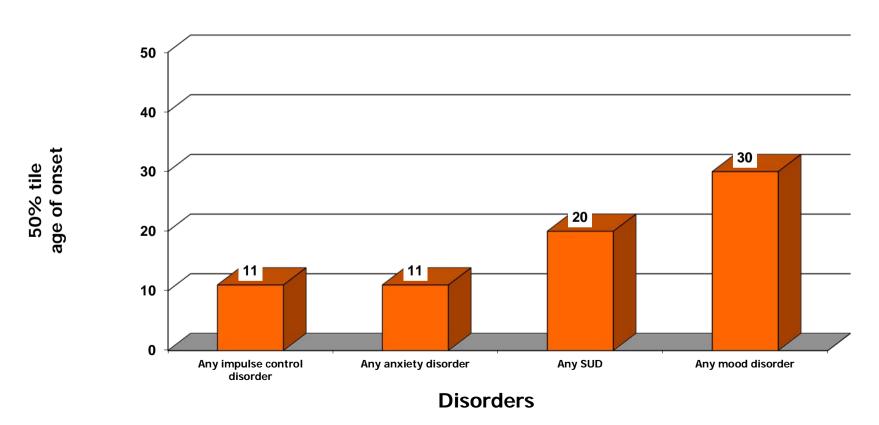


## Adolescence and Behavioral Disorders

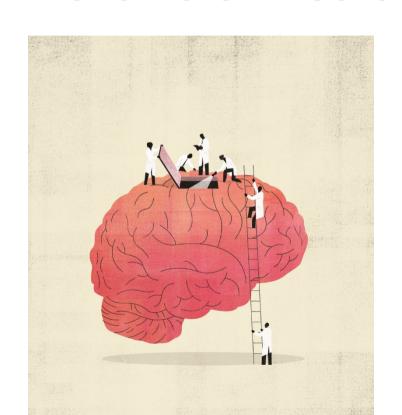
- Alterations in neurodevelopment have been linked to several adolescent-onset mental and behavioral disorders (Charney et al., 2013):
  - ADHD
  - Affective Disorders
  - Anxiety Disorders
  - Autism
  - Obsessive-Compulsive Disorders
  - PTSD
  - Schizophrenia



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



## Adolescent Use of *Marijuana* and Behavioral Disorders





#### 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 Reservice of Preeman, 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)

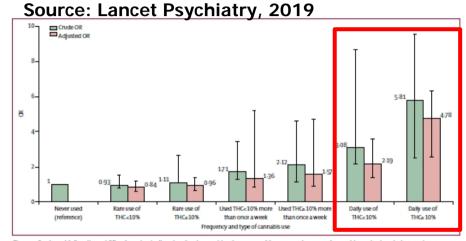


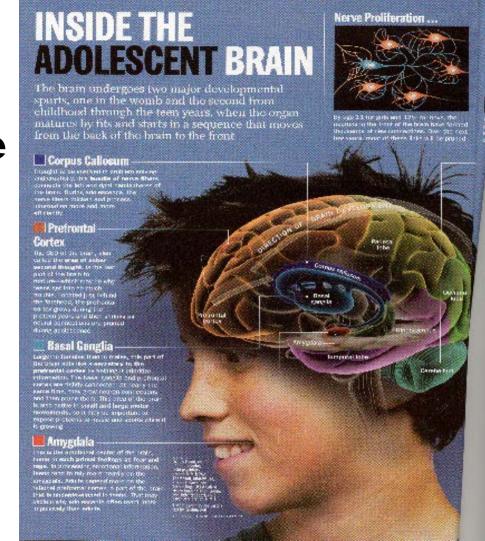
Figure 1: Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample Crude ORs are adjusted only for age gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and use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

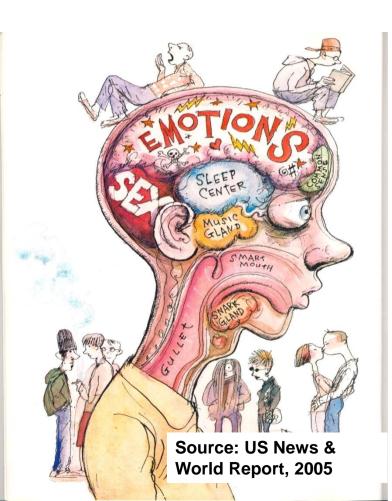
## Cautionary Notes

 Reverse causation (selfmedication).



 Early drug use may be a marker of underlying genetic risk and not causative, or only partially causative. iii. Impact of early experiences on the developing brain and subsequent health and wellbeing

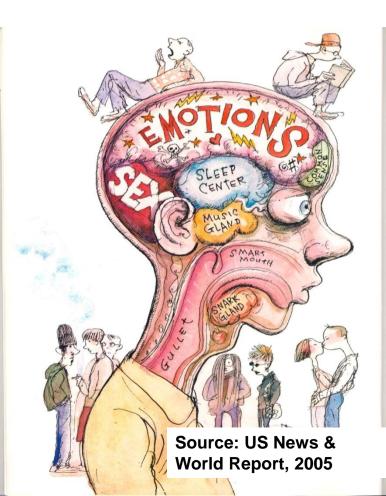




## A Developing Brain

- > 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)



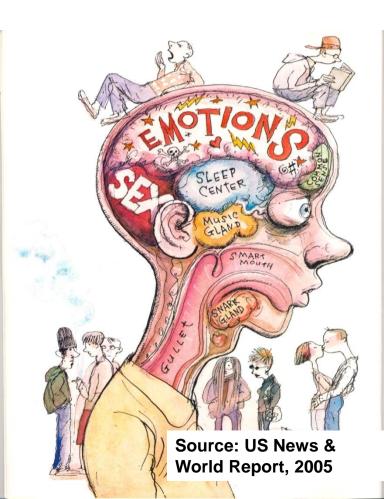
## A Developing Brain

> Impact from Environment?

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

"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."





## 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."

## Early experiences can alter brain development in positive ways





https://www.cdc.gov/ncbddd/childdevelopment/early-brain-development.html

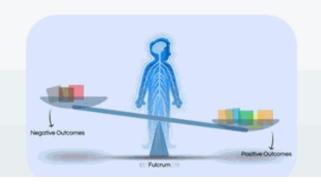
"Nurturing and responsive care for the child's body and mind is the key to supporting healthy brain development."

## Early experiences can alter brain development in positive ways





## https://developingchild.harvard.edu/



The science of early childhood is a source of new ideas that could be used to develop more effective policies & services focused on the early years of life.

Browse Key Concepts | Browse Deep Dives



## 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>

\*Department of Psychiatry, Washington University in St. Louis, St. Louis, MO 63110; \*Department of Psychological & Brain Sciences, Washington University in St. Louis, MO 63130; and \*Department of Radiology, Washington University in St. Louis, St. Louis, MO 63130; and \*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
  - mental illness; diminished level of functioning
  - increased use of a health services, including mental health services

## 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
    - prefrontal cortex activation to emotional faces



## 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.....
  - 1. altered hormonal changes; and
  - abnormal development of connections between regions of the brain that control fear and stress responses

## Brain development, depression and suicidality



- Some experts have warned that the rate of adolescents who have seriously considered committing suicide is increasing at an alarming rate.
- Suicide was the 10th most common cause of death among Americans of all ages in 2017,
  - Yet it was the second leading cause of death among young Americans in the U.S. age 15 to 24 (Curtin & Heron, 2019).

## Brain development, depression and suicidality



In my home state of Minnesota, a recent state-wide student health survey indicated that 13% of 11<sup>th</sup> grade students reported "seriously considered suicide".

Source: https://www.mprnews.org/story/2019/10/17/survey-finds-mn-students-feel-less-safe-less-healthy

- Suicide rates vary across tribes and communities, but AI/AN people overall face a disproportionate burden of suicide.
  - In 2017, the age-adjusted suicide rate was 51% (males) and 80% (females) higher compared to the general population (https://www.cdc.gov/nchs/products/index.htm).

## Implications of Brain Development for Adolescent Behavior (Winters et al., 1995)

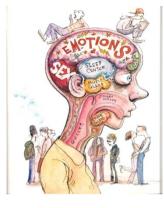


- Preference for ....
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  - 3. activities with peers that trigger high intensity/arousal
  - 4. novelty
- Less than optimal...
  - 5. control of emotions
  - 6. consideration of negative consequences
- Greater tendency to...
  - 7. be overly attentive to social information
  - 8. take risks

Contributors for suicide ideation?

## Screening adolescents for depression

- Patient Health Questionnaire-9 (https://www.mdcalc.com/phq-9-patient-health-questionnaire-9)
  - Screening tool for depression
  - 9 questions, 1 of which screens for suicide thinking ("thoughts you would be better off dead, or thoughts of hurting yourself in some way?)



#### **Suicide Resource**



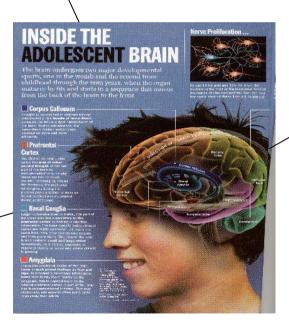
The National Council of Urban Indian Health (NCUIH), in partnership with the Action Alliance's AI/AN Task Force, put forward a resolution in 2015 to create an "Annual National American Indian and Alaska Native Hope for Life Day (Suicide Prevention Awareness Day).

That initiative involved the development of the National Hope for Life Day Toolkit. This resource seeks to help community leaders, grassroots organizers, and health care professionals working in AI/AN communities implement a community-wide Hope for Life Day.

Source: https://www.ncuih.org/krc/news?article\_id=293

# SEPTEMBER 10, 2019 American Indian/Alaska Native Hope for Life Day National Council of Urban Indian Health

## I. Brain development

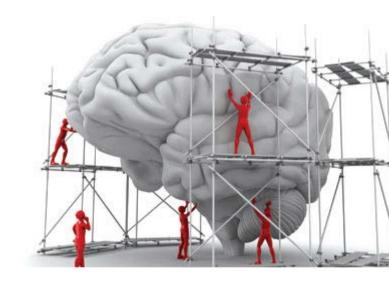


II. Developing brain, drug use and mental health

III. Youth Serving Workers

Brain Development: Implications for Youth Serving Workers & Educators

 Teach youth about brain development and its importance to health and personal growth



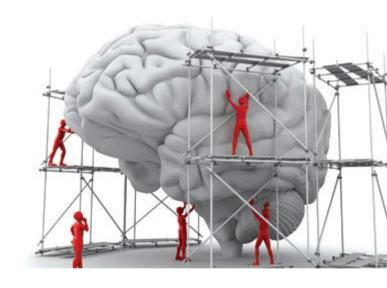
#### Implications of Brain Development for Adolescent Behavior

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- Greater tendency to...
  - 7. be overly attentive to social information
  - 8. take risks

- Teach "adaptive" decision making
  - taking risks that promote "personalgrowth"
  - "on second thought" skills
  - how to avoid peer pressure to engage in delinquency



Interested in a "teen brain" resource to help teach youth about brain development?

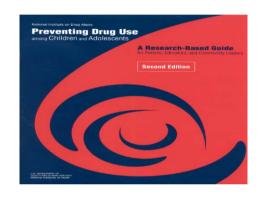


send me an e-mail:

winte001@umn.edu

### ii. Use evidenced-based prevention programs

- Keys to effective prevention are in the research literature
  - 1. National Institute on Drug Abuse https://www.drugabuse.gov
  - 2. Cochran literature review https://www.cochranelibrary.com/cdsr/about-cdsr
  - 3. ISSUP's prevention curriculum https://www.issup.net/training/universal-prevention-curriculum





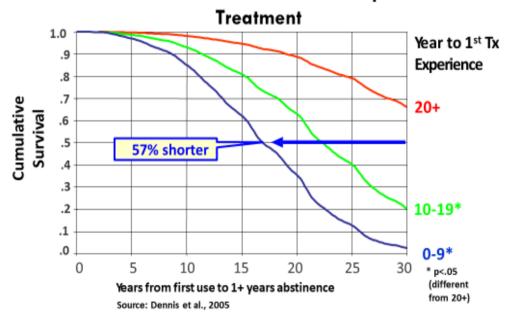
Trusted evidence. Informed decisions. Better health.



Brain Development: Implications for Service Providers

iii. Earlier the treatment, the better







## Brain Development: Implications for Service Providers

#### iv. Use evidenced-based treatment

Treatment: Recent literature summary and meta-analysis (Hogue et al., 2018; NIDA, 2014; Tanner-Smith et al., 2012)

Treatment "as usual" is no better than prevention education only or no treatment.

A wide range of more recent evidenced-based treatment do significantly better.

MET, CBT and family therapy



- V. Increase the "cannabis and vaping IQ" of adolescents
  - Sources of exercises and quizzes
    - Cannabis:
      - www.dfaf.org (Busting the Top Ten Myths of Marijuana)
    - Vaping:
      - Google "CDC educating kids on vaping" https://www.cdc.gov/tobacco/features/back-to-school/ecigarettes-talk-to-youth-about-risks/index.html

## Brain Development: Implications for Service Providers & Educators

### vi. 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.
- = Encourage 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

1.





MENTOR INTERNATIONAL'S SELECTION OF SUBSTANCE ABUSE PREVENTION RESOURCES FOR PARENTS





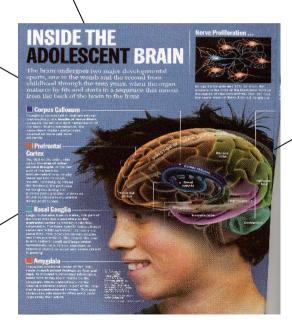
3. Prevent\_Intervene\_Get Treatment\_Recover

www.drugfree.org

#### I. Brain development

#### **IV. Summary**

III. Youth Serving Workers



II. 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.
- It is also a time when personal growth can be shaped in ways that are unique to adolescence



- 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 to strengthen parenting with brain development science



### Teen Brain Development Quiz

 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)

- What lifestyle choices during adolescence promote good brain development?
  - i. no drug use
  - ii. healthy lifestyle (good diet, exercise, sufficient sleep; active social life)
- 3. Which is more harmful to the developing brain?
  - a. Chronic, heavy use of marijuana?
  - b. Chronic, heavy drinking? Good question!!





## **THANK YOU**

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### **Questions and Discussion**

