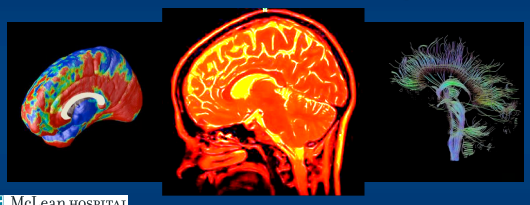
Riding the Rollercoaster:
Understanding the Impact of Substance Use on Teen Brain Development



McLean HOSPITAL
HARVARD MEDICAL SCHOOL AFFILIATE

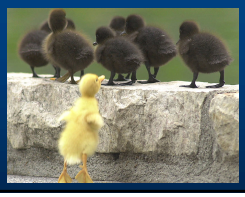
Marisa M. Silveri, Ph.D.
Director, Neurodevelopmental Laboratory on Addictions and Mental Health,
McLean Imaging Center, McLean Hospital
Associate Professor of Psychiatry, Harvard Medical School
Adjunct Assistant Professor of Psychiatry, Boston University School of Medicine

Poll Question

Which category best reflects your profession:

A. Prevention Specialist
B. Mental Health Specialist
C. Educator
D. Administrator
E. Other

Understanding the Teen Brain



New Experiences

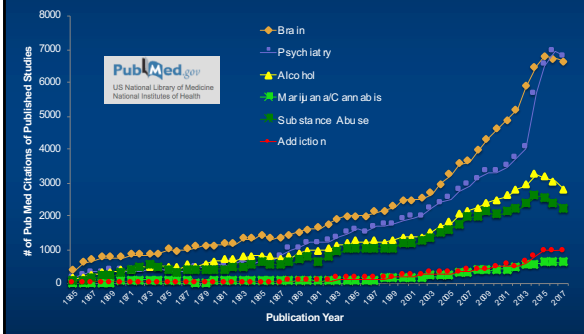
Making Good Decisions

Becoming Independent

FREEDOM!

Research Trends

Pub Med Search: Adolescence and …



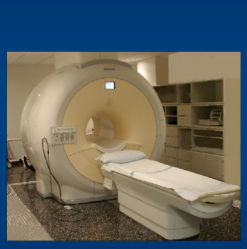
Poll Question

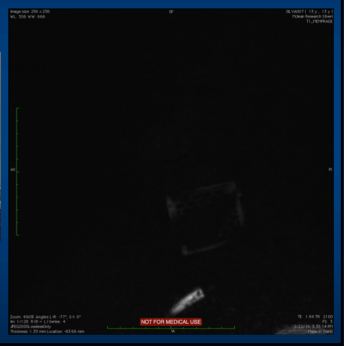
For your professional development:
What area do you identify as reflecting your greatest need for new information:

A. Substance Use/Addiction
B. Psychiatric Illness/Mental Health
C. Maintenance of Well-Being
D. Other

A Window into the Teen Brain

Magnetic Resonance Imaging (MRI)





The Developing Brain

- Brain size or weight of increases dramatically until age 5.
- Brain size plateaus, with no further changes in brain volume.
- Teen years: brain undergoes major, rapid remodeling.
- Emerging adults: brain changes detected between fall and spring semesters, in freshmen.

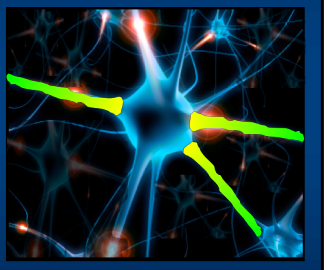
Brain Cells Under Construction

- Improving speed and efficiency of neuron communication:

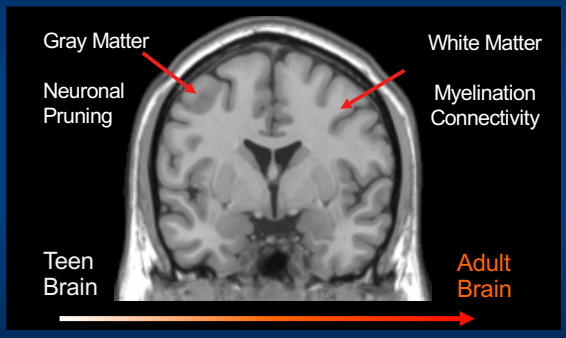
  myelination

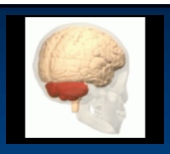
- Removing inefficient and unneeded neurons:

  pruning

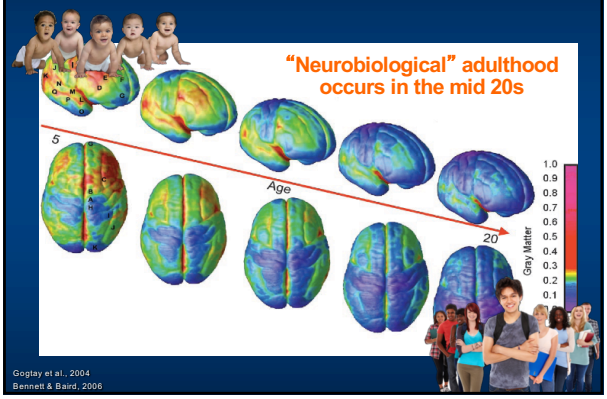


Same Size, Different Brain





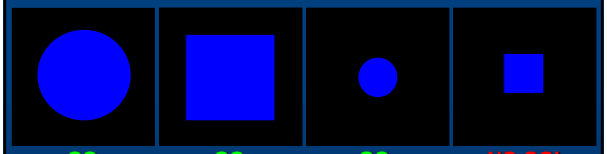
When is the Brain Adult?



Gogtay et al., 2004
Bennett & Baird, 2006

Response Inhibition/ Cognitive Control

Go No Go Task



GO GO GO NO GO!

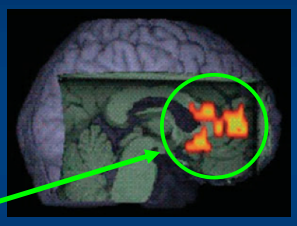
Teens & Cognitive Control

Go No Go Task

Greater brain response required to inhibit, "no go".

Mediated by the frontal lobe

Improves with age



Teens respond faster

Adults demonstrate better accuracy

Rubia et al., 2006

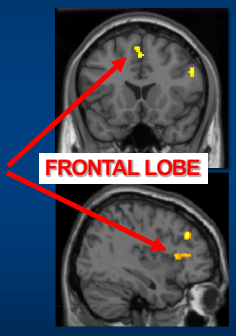
Why Was That So Hard?

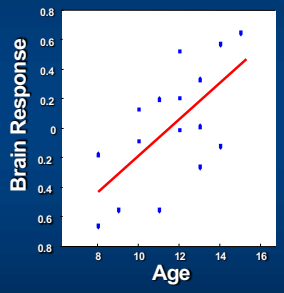
Msot plepoe can raed wodrs eevn wehn teh ltetres aer mxide. The biarn is eceexllnt at luaagnge and ridneag.

READING - AUTOMATIC
NAMING Colors - Less AUTOMATIC

Brain has to work harder to hold back
This is the frontal lobe working
Gets better with age

Teens & Cognitive Control



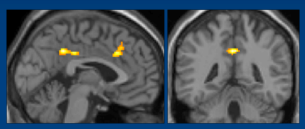


Yurgelun-Todd et al.

Teens & Cognitive Control

IN THE SAME TEEN AFTER 1 YEAR: BRAIN IS MORE EFFICIENT!

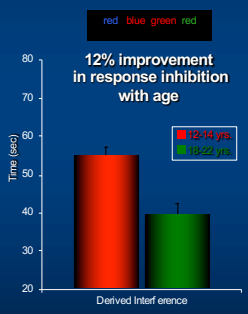
Year 2 > Year 1
13.7yrs. 12.6 yrs.
Region of the Frontal Lobe
Cingulate Gyrus

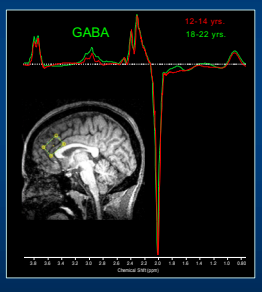


Year 2 > Year 1
13.7yrs. 12.6 yrs.
Region of the Frontal Lobe
Lateral Prefrontal Cortex

Developmental Brain Markers?

Measurable Inhibitory Neurotransmitter: GABA

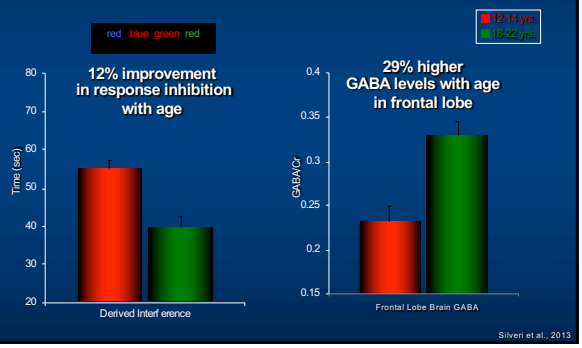




Silveri et al., 2013

Developmental Brain Markers?

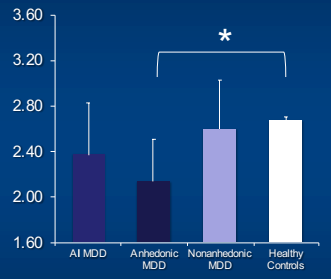
Measurable Inhibitory Neurotransmitter: **GABA**



Silveri et al., 2013

Adolescent Depression: Low GABA

- 20 medication-free adolescents with MDD
- 8+ wk episode duration
- 21 healthy controls
- MDD: lower ACC GABA (p=*.003*), greatest difference in anhedonic MDD



Anhedonia: reduced capacity to experience pleasure, core symptom of MDD that is prevalent and highly variable in adolescents with MDD.

Gabbay et al., 2012

Faced with Tough Choices?

What Should I Do After Class?
You Have a Math Test Tomorrow

Quick Response
Hang Out with Friends

Think It Out for a Minute
Study for Tomorrow's Test

Fail Test

Get an A on the Test

WHAT WERE YOU THINKING?????

Faced with Tough Choices?

What Should I Do After Class?
You Have a Math Test Tomorrow

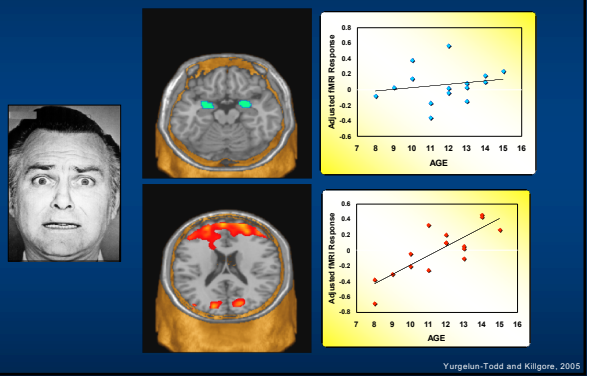
Quick Response
Hang Out with Friends

Amygdala

Fail Test

WHAT WERE YOU THINKING?????

Viewing Pictures of Fearful Faces

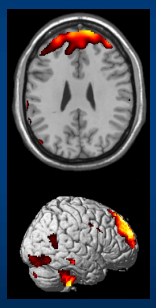


Yurgelun-Todd and Killgore, 2005

Viewing Pictures of Food

Teen

Adult



Killgore and Yurgelun-Todd, 2005

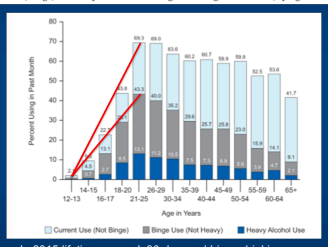
In the Face of Tough Choices

- Frontal lobe provides inhibitory control over the more rapid amygdala responses.
- Brain developmental changes help improve cognitive control, which is coming online as teens are faced making difficult decisions and navigating emotional responsiveness.
- Brain changes are ongoing as teens are initiating alcohol and marijuana use.

Public Health Concerns: 2016

- Alcohol, marijuana and prescription pain meds

Current, Binge, and Heavy Alcohol Use among Persons Aged 12 or Older, by Age: 2013



- In 2015 lifetime, annual, 30-day, and binge drinking measures of alcohol use were at historic lows in grades 10 and 12, and at or very close to historic lows in 8th grade, since 1975

Substance Abuse and Mental Health Services Administration, 2013

Age of First Use	Risk of Alcoholism
13	47%
14	45%
15	38%
16	32%
17	28%
18	17%
19	15%
20	11%
21	9%

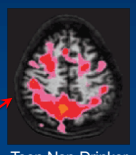
- **Earlier onset of alcohol use remains a strong predictor of increased risk of developing an alcohol use disorder later in life**

Adolescents More Affected

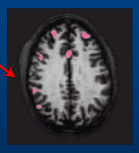
Teens who consistently use alcohol perform worse on memory tasks by 10%, and show less brain activity during memory tasks.

Identify when targets appear in same location

Brain activates when repeat target appears in repeat location location



Teen Non-Drinker



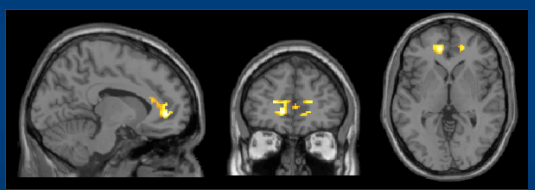
Teen Drinker

Tapert et al., 2004

Role of Familial Alcoholism

red blue green red

Brain Activity: FH+ Teens > FH- Teens

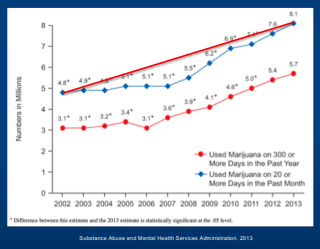


Teens with a family history of alcoholism activate more frontal lobe regions during response inhibition prior to the initiation of alcohol use.

Silveri et al., 2011

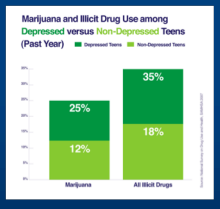
Public Health Concern: 2016

Daily or Almost Daily Marijuana Use in the Past Year and Past Month
Persons Aged 12 or Older: 2002-2013



Substance Abuse and Mental Health Services Administration, 2013

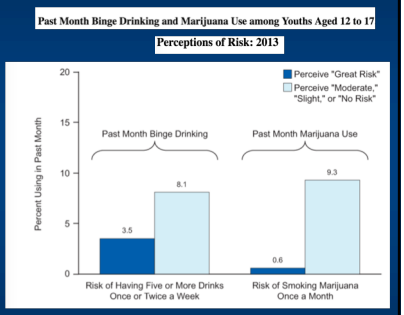
- **Significant increases in marijuana use have been reported, almost a doubling in the past ten years.**



- **Along with greater use is higher levels of depression in teen marijuana users.**

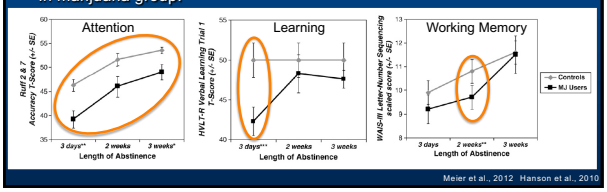
Public Health Concern: 2016

- Relative decreases in binge drinking and increases in marijuana use are influenced changes perceptions of harm by teens.
- Teens are reporting binge drinking as more risky, whereas teens are reporting marijuana as less risky.



Adolescents & Emerging Adults: Marijuana Use Associated with Poorer Cognition

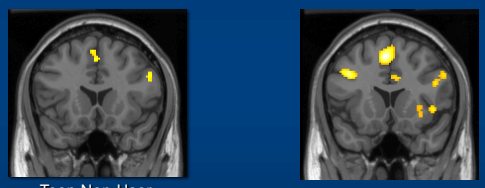
- 1,037 individuals followed from birth to age 38
- Cannabis use ascertained at ages 18, 21, 26, 32, and 38
- Neuropsychological testing was conducted at age 13, and again at age 38
- More persistent use was associated with greater decline, and stopping use did not fully restore functioning
- 40 adolescents, ages 15-19; 19 marijuana, 21 non-users
- In marijuana group:



Meier et al., 2012 Hanson et al., 2010

Marijuana Use Affects Cognitive Control

red blue green red



Teen Non-User | Teen Marijuana User

More neurons recruited to perform task at same level

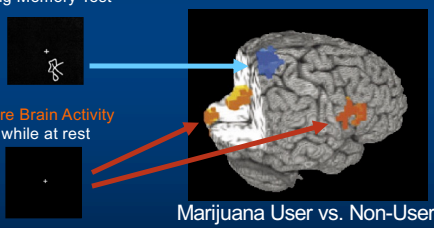
Yurgelun-Todd et al.

Marijuana Use Affects Memory

Identify when targets appear in same location

Brain activates when repeat target appears in repeat location

Less Brain Activity during Memory Test

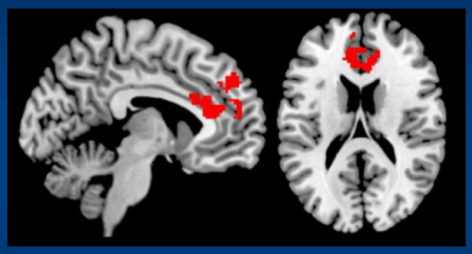


More Brain Activity while at rest

Marijuana User vs. Non-User

Schweinsburg et al., 2008

Marijuana Use Affects Reward Circuit

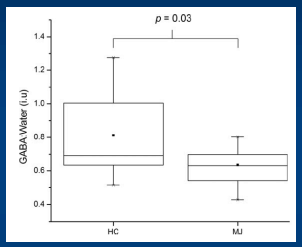


Disrupted brain circuitry may result in poor regulation of motivation, including difficulty enhancing positive affect, pursuing goals or focusing on future reward

Lichenstein et al. 2017

Adolescent Marijuana Use: Low GABA

- adolescent marijuana (MJ) users
- age-matched non-using controls
- MJ: lower ACC GABA (p=.03), *trend towards predicting total MJ use*



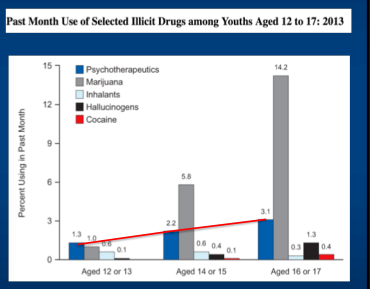
- Important neurochemical necessary for response inhibition, rapidly matures in the adolescent frontal lobe.
- Low GABA levels observed in depression, anxiety, alcohol and marijuana dependence.

Prescot et al., 2013

Public Health Concerns: 2016

- Alcohol, marijuana and **prescription pain meds**

- 22% of first time illicit drug users start with controlled medications (e.g. Vicodin®, OxyContin®, Adderall®), second to marijuana. **The rise in prescription drug abuse appears highly related to access via friends and family.**
- Adolescents prescribed opioids or who used nonmedically had more substance abuse and psychological symptoms than youth who had never received a prescription for an opioid analgesic.



Substance Abuse and Mental Health Services Administration, 2013

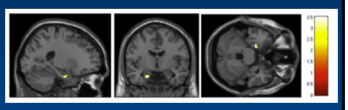
Prescription Drugs: Brain Effects

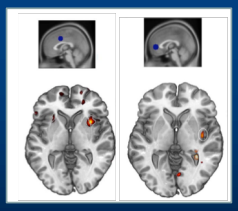
- There is very limited data available on the effects of prescription drugs on the human adolescent brain.
- One study conducted in animals showed that adolescents exhibit greater sensitivity than adults to the rewarding effects of oxycodone, which was indicated as an increased release of dopamine at the lowest dose tested.
- **Greater sensitivity could lead to greater use.**
- **Adolescent exposure to the active ingredient in marijuana (THC) recently was shown to be associated with enhanced sensitivity to heroin.**

Szutorisz et al., 2014 Zhang et al., 2014

Prescription Drugs: Brain Effects

- Heroin acutely reduced left amygdala response to fearful faces. Amygdala activity was related to anxiety, stress hormones, and heroin craving.

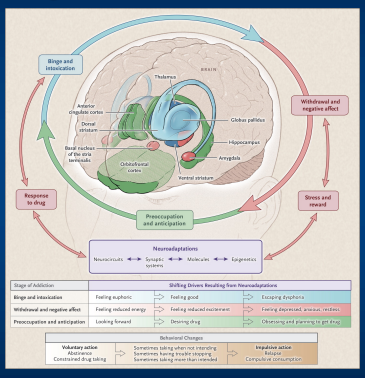




- Drug users claim to use oxycodone to dampen physical and emotional pain.
- Oxycodone attenuates connectivity of the frontal lobe with other important brain areas, which may impair the perception and appraisal of internal pain states.
- **Alterations in these neural pathways may underlie the pathophysiology of drug abuse.**

Schmidt et al., 2014
Gorka et al., 2014

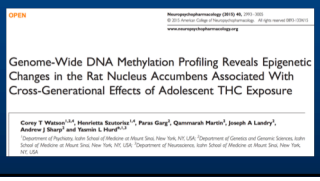
Cycle of Addiction



Volkow ND et al., N Engl J Med 2016;374:363-371.

Where is Science Headed…

Adolescent alcohol exposure can alter genes



Parental exposure to drugs can transcend generations

Poll Question

What information presented during this keynote do you envision will have the biggest impact on your work:

A. **Understanding Brain Development**
B. **Impact of Alcohol on Brain Function**
C. **Impact of Marijuana on Brain Function**
D. **Impact of Opioids on Brain Function**
E. **Overlap between Substance Use and Mental Health**

Second Decade of Life:

Period of Opportunities & Vulnerabilities

Google News Alert

"adolescent", "adolescence", "teen", "teenager"

10/21/08

Party a Painful Reminder of Teen Drinking Dangers

~The Sun Chronicle

The *recent death of a 17 year old* is another bitter reminder that alcohol and young people do not mix, experts on teenage drinking said Monday.

They said drinking by teenagers brings on a whole host of possible problems ranging from driving accidents, unwanted pregnancies, illness & injury.

Google News Alert

"adolescent", "adolescence", "teen", "teenager"

Posted by scooter at 4:13PM on Monday, 3/31/08

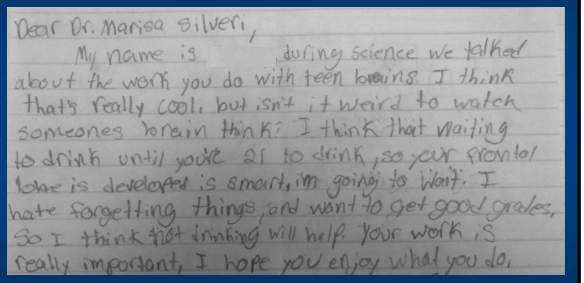
I had three close high school friends whose "cool" parents let them and others drink at home.

The ol' "it's better to know where they're at" motto.

Two of those kids are now raging alcoholics, and the third is dead (yes, alcohol related).

It's better to tell kids that drinking is a choice to be made when you turn 21. Until then, let "youth" be the only thing impairing your judgment.

In Their Own Words


Dear Dr. Marisa Silveri,
My name is ____ during science we talked about the work you do with teen brains. I think that's really cool, but isn't it weird to watch someones brain think? I think that waiting to drink until you're 21 to drink, so your frontal lobe is developed is smart, im going to wait. I hate forgetting things, and want to get good grades, so I think not drinking will help. Your work is really important, I hope you enjoy what you do.

In Their Own Words

Please set at least one goal and indicate how you plan to use what you learned today to put the plan into action.

- WAIT TO DRINK

Very rapid brain development in a short period of time, second decade of life

Biggest leaps in cognitive abilities occur between ages 10-18 years old

Time when emotions are strong/can be hard to manage

Teen brain more vulnerable to insults such as alcohol and drug use compared to the adult brain, which may be further elevated by family history

By sharing science, we can help teens protect the brain, which will lead to better decision making