Overview of Developmental Research on Alcohol Misuse

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Alcohol Issues Across the Lifespan

- NIAAA supports research to study how alcohol can affect health and well-being at various stages of life.

Lifespan Transcending Themes
- Neurobiology
- Metabolism
- Genetics
- Epigenetics
- Epidemiology
- Health Services Research

- Prenatal Alcohol Exposure
- Underage/Binge Drinking
- Organ Damage
- Alcohol Dependence
- Medication Interactions
- Alcoholic Family Environment
Outline of the Talk

1. Neurocircuitry of Addiction
2. The Scope of the Problem: The Societal Cost of Underage Drinking
3. The Adolescent Brain: A Moving Target
4. The Scope of the Problem: The Brain Cost of Underage Drinking
5. New NIAAA Initiatives Basic Science: NADIA, N-CANDA, ABCD
6. New NIAAA Initiatives Prevention: AIM, SBI, NADIA, N-CANDA, ABCD
Conceptual Framework for Neurobiological Bases of the Transition to Excessive Drinking
1. Addiction is an incentive salience disorder.

2. Addiction is a reward deficit disorder.

3. Addiction is a stress surfeit disorder.

4. Addiction is an executive function disorder.
Binge Drinking is Decreasing Among 8th, 10th and 12th Graders in US

Binge = 5+ drinks at a time at least once in a two week period

Significant decline for all grade levels

Many young drinkers binge when they drink

But, Youth Drink Less Frequently Than Adults, But Drink More Per Occasion

Drinking Days per Month and Number of Drinks per Occasion for Youth (12–20), Young Adults (21–25), and Adults (≥26)

SAMHSA, CBHSQ, NSDUH, special data analysis 2012 (2011 NSDUH data)
And, There was a 67% Increase In Hospitalizations Related To Alcohol Overdoses In 18-24 Year Olds Between 1999-2008

Negative Consequences of Binge Drinking

- Nearly 1 million high school students and nearly 2 million 12-20 year olds consume 5 or more drinks 6 or more times per month. They are much more likely to:

  - Ride with a drinking driver
  - Drive after Drinking
  - Never wear safety belts
  - Carry weapons/guns
  - Be bullied
  - Be injured in a fight
  - Be injured in a suicide attempt
  - Be forced to have sex
  - Have had sex with 6 or more partners
  - Have unprotected sex
  - Use Marijuana/cocaine
  - Ever have injected drugs

Youth Behavior Survey, 2009
Alcohol Can Be Deadly

Excessive alcohol and/or other CNS depressants can shut down brainstem areas involved in vital reflexes like breathing, gagging, and heart rate and cause death.

Alcohol
• Suppresses respiratory areas and other vital reflex centers
• Causes death

Behavioral Effects of Alcohol Related to Blood Alcohol Level in mg%
Alcohol has a **very** small therapeutic index (TD$_{50}$/ED$_{50}$)
A toxic dose not much higher than a moderately intoxicating dose
Average and median BAC among 693 people who died from alcohol poisoning was 0.36%. (Jones and Holmgren, 2003)

Potentially fatal alcohol overdoses: How much alcohol?

If ED$_{50}$ = ~.05%
And TD$_{50}$ = ~.35%
Then TI = ~7

10 drinks in 2 hrs for a 140 lb female

13 drinks in 2 hrs for a 160 lb male

BAC = 0.32
BAC = 0.43
BAC = 0.44
BAC = 0.48
Those who first used alcohol at age 14 or younger were more than 7 times as likely to be classified with alcohol dependence or abuse than those who had their first drink at age 21 or older (15.2 vs. 2.1 percent)

From: NSDUH 2012 (www.samhsa.gov/data)
Annualized rate of change in cortical anatomy

Area

Thickness

Volume

Age in years

4
6
8
10
12
14
16
18
20

n = 637
308 females
329 males

Tim Brown, Josh Kuperman, Terry Jernigan, and Anders Dale for the PING Study
Frontal Lobe Changes During Adolescence

- Planning, decision-making, impulse control, memory, language, processing social cues
- Gray matter goes down, white matter goes up, overall size stays about the same

Subcortical Drive Contributes to Risk Taking

Strong emotional drive during adolescence combined with still developing executive circuits leads to risk taking.

“According to the model, the adolescent is biased by functionally mature subcortical relative to less mature cortical circuitry” Casey and Jones, 2010

Subcortical Drive Contributes to Stress Reactivity
Triadic Model: Amygdala, Striatal and Prefrontal Cortical Interactions Across Development

Adapted from: Casey and Jones (2010)
Adolescent Alcohol Abusers Show Strong Reactions
To Alcohol-related Cues Reflecting Strong
Associative Learning

Functional magnetic resonance imaging (fMRI) results during alcoholic beverage picture trials relative to non-alcoholic beverage picture trials

Greater activation in AUD subjects (red color) in the ventral anterior cingulate and subcallosal, prefrontal, orbital, and limbic regions, areas previously associated with reward and drug craving.

AUD group (N = 15) 6 girls 9 boys average age of 16, DSM abuse or dependence

Control group (N = 15) 6 girls 9 boys average age 16, low levels of previous use

Use of Alcohol Goes Up, Cognitive Functioning Goes Down

As the number of drinks consumed per day goes up, performance on tests of attention, executive function and memory go down. More days smoking marijuana per month equals poorer memory.

**SUBJECTS:** 48 adolescents (ages 12 to 18), recruited in 3 groups: a healthy control group (HC, n = 15), a group diagnosed with substance abuse or dependence (SUD, n = 19), and a group with a family history positive for alcohol use disorder (AUD) but no personal substance use disorder (FHP, n = 14).

**RESULTS:** More drinks per drinking day predicted poorer performance on Attention and Executive Function composites, and more frequent use of marijuana was associated with poorer Memory performance. In separate analyses, adolescents in the SUD group had lower scores on Attention, Memory, and Processing Speed composites, and FHP adolescents had poorer Visuospatial Ability.

Neurobiology of Adolescent Drinking at NIAAA -
Key Programs

NADIA (Neurobiology of Adolescent Drinking in Adulthood)

N-CANDA: (National Consortium on Alcohol and Neurodevelopment in Adolescence)
NADIA consortium preclinical studies support the hypothesis that adolescent binge drinking disrupts brain development altering adult neurobiology and behavior.

- Adolescent binge drinking increases expression of adult brain proinflammatory innate immune genes.

- Adolescent binge drinking reduces adult behavioral flexibility, i.e. adults have difficulty learning new rewards and show increased risky behavior as indicated by increased efforts for immediate unlikely rewards over greater delayed rewards.

- Adolescent binge drinking decreases adult forebrain cholinergic neurons.

- Adolescent binge drinking increases adult negative emotions through altered neuronal histone acetylation.

- Adolescent alcohol abuse retains many adolescent-like phenotypes into adulthood including cognitive disruption
NADIA
Neurobiology of Adolescent Drinking in Adulthood
Among the Objectives:

- Study effects of alcohol exposure on trajectory of adolescent brain development in the context of development
- Examine dose, duration, and timing effects of alcohol exposure
- Determine what structural and functional anomalies are the result of alcohol exposure and what predates, and may predict, heavy alcohol use
- Identify neuroimaging and/or neurocognitive brain markers that predict onset of AUD and other psychopathology
Adolescent Brain and Cognitive Development (ABCD) National Longitudinal Study

- Given the prevalence of substance use among adolescents and the changing policy climate, there is an urgency to better understand the short- and long-term effects of alcohol, tobacco, marijuana and other substances on the developing brain

- Study intends to:
  - Assess the impact of sporadic vs regular drug use on the developing brain
  - Explore gateway interactions
  - Identify neurodevelopmental pathways that link adolescent SUD and mental illnesses
  - Assess effect of multiple substances in combination

- Large representative cohort (~ 10,000) youth followed over a 10-year period, beginning before drug use into early adulthood

- Outcome measures--substance use, academic achievement, IQ, cognition

- Estimated to cost $30 million/year for 10 years.
College Drinking Initiative

*College Alcohol Intervention Matrix – Coming Soon*

- In response to a request from NIAAA’s College Presidents Working Group, NIAAA engaged top researchers in the field to develop an interactive, user-friendly, print and online “decision support system” to help colleges and universities select appropriate strategies to meet their alcohol intervention goals.

- The tool will allow college presidents and staff to review the strategies they are currently using as well as explore others that may serve them better.

- Users will be able to search for strategies according to intervention level (e.g., individual, group, campus-wide, community) and evaluate other factors such as effectiveness, barriers and costs, affecting implementation.

- We envision that much like online shopping applications, the online tool will allow users to select a set of strategies for side-by-side comparisons.
Screening & Brief Intervention for Youth

NIAAA Alcohol Screening Guide

- A brief, easy to score, empirically-based screen for risk, alcohol use, and problems that overcomes time constraints and other common barriers to youth alcohol screening.

- It is based on just two questions – one about friends’ drinking and the other about personal drinking frequency. Analysis of data from more than 160,000 youth indicated these questions had the greatest predictive power.

- The Guide is endorsed by the American Academy of Pediatrics.

- A Medscape course provides training on using the guide – CME credit is available – to date over 24,000 clinicians have been Medscape certified.
NIAAA Resources
(niaaa.nih.gov)
Putting it all together:
Why preventing adolescent drinking is so important

- Adolescent brain does not fully develop until age 25
- Short-term, alcohol in adolescents super activates the incentive salience system (locks in cues associated with drinking)
- Short-term, alcohol disrupts the frontal lobes (decision making and impulse control), hippocampus (memory), amygdala (fear and anxiety) and brainstem (vital reflexes)
- Long-term, alcohol can alter the trajectory of adolescent brain development and cause lingering cognitive deficits – NIAAA studies underway to understand vulnerability and resilience factors in adolescent brain development
- Joint NIAAA, NIDA, NCI, and NICHD initiative (ABCD) will be key to understanding impact of alcohol and drugs on the adolescent brain
- NIAAA is significantly invested in prevention of underage drinking: AIM, SBI
Thank You!

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Screening & Brief Intervention for Adults

Updated in 2007

• An evidence-based guide for primary health care practitioners to provide screening for their adult patients, provide brief intervention for risk drinkers, diagnose DSM-IV alcohol use disorders and provide treatment or referral to specialty treatment services.

• The Guide makes it is easier for clinicians to address alcohol use with their patients.

• The Guide provides up-to-date information on the latest evidence-based practices, including medications.