Update on Research on Alcohol Use Disorders
National Institute on Alcohol Abuse and Alcoholism (NIAAA)

George F. Koob, Ph.D.
Director
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

Alcohol

- Prenatal Alcohol Exposure
- Underage /Binge Drinking
- Organ Damage
- Alcohol Dependence
- Medication Interactions
Key NIAAA Initiatives and Programs

Early Diagnosis Fetal Alcohol Spectrum Disorder

NADIA (Neurobiology of Adolescent Drinking in Adulthood)

N-CANDA: (National Consortium on Alcohol and Neurodevelopment in Adolescence)

ABCD: Adolescent Brain and Cognitive Development National Longitudinal Study

College Alcohol Intervention Matrix

Biosensor Initiative

Post-traumatic Stress Disorder Comorbidity
Fetal Alcohol Syndrome Disorder (FASD) Facial Features Correlate with CNS Deficits

Negative correlations between brain volume and lipometer scores after controlling for scan location, age, sex, and ICV in subjects with FASD. (N=52)

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
There was a 67% Increase In Hospitalizations Related To Alcohol Overdoses In 18-24 Year Olds Between 1999-2008

Neural Circuits Controlling Impulsivity and Compulsivity

Executive Dysfunction
- impulsivity
- compulsivity
- impaired decision making

Significance: Adolescent voluntary binge drinking reduces the density of myelinated axons in the medial prefrontal cortex and has long-lasting effects on prefrontal white matter. (Vargas WM, Bengston L, Gilpin NW, Whitcomb BW, and Richardson HN. J. Neuroscience. 34(44):14777-14782; 2014.)

Adolescent alcohol decreases myelinated fiber density in the medial prefrontal cortex and predicts poor T-maze performance 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
- Serves as a prototype study for ABCD longitudinal study
**Sex Differences**
- Total Gray Matter Volume
- Age 12-22
- Sex Differences
  - Male: $t(110) = 2.4, p = 0.02$
  - Female: $t(110) = 0.6, p = 0.5$
  - Male: $t(110) = 0.4, p = 0.6$

**Sex Similarities**
- Total Cortical Thickness
- Age 12-22
- Sex Similarities
  - $t(110) = 1.3, p = 0.05$
  - $t(110) = 1.0, p = 0.3$
  - $t(110) = 1.0, p = 0.3$

**Neuropsychological Testing**
- 8 functional domains
  - 25 tests
  - >1000 measures
  
  - **Stroop Match-to-Sample**
    - response inhibition
    - bottom-up → top-down control

**Harmonize Measurement across Sites**
- Fractional Anisotropy (FA)
- Correction factor applied to reduce scanner variance

**Stroop testing "on land"**
- (N=621)

**Stroop testing in the scanner**
- (N=268)

**Baseline**
- 788
- 1 year follow-up
- 303
- >1000 clinical and descriptive measures

**Sample as of September 2014**
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 substance 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 – CollegeAIM
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.

• The CollegeAIM will be released first as a written tool with an online presence. A searchable online tool is envisioned as a second step.
Putting it all together: Why preventing adolescent drinking is so important

• Adolescent brain does not fully develop until age 25

• Short-term, alcohol use in adolescents super activates the incentive salience system (locks in cues associated with drinking)

• Short-term, alcohol use disrupts the frontal lobes (decision making and impulse control), hippocampus (memory), amygdala (fear and anxiety) and brainstem (vital reflexes)

• Long-term, alcohol misuse 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: CollegeAIM, SBI
Alcohol Biosensors

RFA-AA-15-007 - STTR (R41/R42)
RFA-AA-15-008 - SBIR (R43/R44)

• To design and produce a wearable device to monitor blood alcohol levels in real time.

• Device must be unobtrusive.

• Device must be an accurate measure of BAC, have data storage, and provide secure transmission to smart phone or other device.

• Device will be useful in research, clinical, and treatment settings and for individual health monitoring.

Application Due Date: April 7, 2015  Earliest Funding Date: September 1, 2015
PTSD and Alcohol

- PTSD is prevalent among military personnel, veterans, and victims of violence, including sexual assault.
- AUD frequently co-occurs with PTSD and their co-occurrence complicates treatment for both conditions.
- PTSD increases risk for AUD; conversely, chronic alcohol use may increase the risk for PTSD.
- NIAAA will be expanding research on the neurobiological mechanisms that underlie co-occurring PTSD and AUD to improve the treatment of affected individuals.
- In November 2014, NIAAA held a scientific workshop on “PTSD, the Amygdala, and Alcohol Use Disorders” in conjunction with the Society for Neuroscience annual meeting.
Thank You!

Special Thanks
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health

Vivian Faden
Ralph Hingson
Bob Huebner
Keith Lamirande
Antonio Noronha
Patricia Powell
Kenneth Warren
Aaron White
Bridget Williams-Simmons