

## Addiction, Development and Beyond: New Behavioral Neuroscience Opportunities

UC San Diego

NIAAA  
National Institute on Alcohol  
Abuse and Alcoholism

NIDA  
NATIONAL INSTITUTE  
ON DRUG ABUSE  
The Science of Drug Abuse & Addiction

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## University of California, San Diego



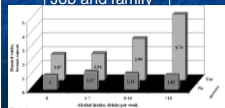
### Life span and excessive alcohol consumption

Prenatal  
Fetal Alcohol Syndrome



Photo courtesy of  
Teresa Kellerman

Adulthood  
Hypertension  
Breast cancer  
Liver disease  
Job and family

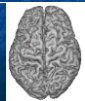


Rehm et al. PLoS One 2007

Teenage and Young Adulthood  
Binge drinking  
Drunk driving  
Unsafe sex

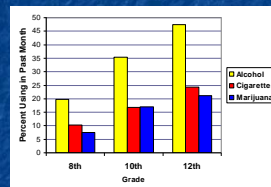


Maturity  
Brain damage  
Cognitive impairment



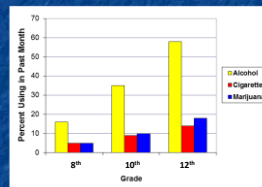
## Youth Substance Use

United States



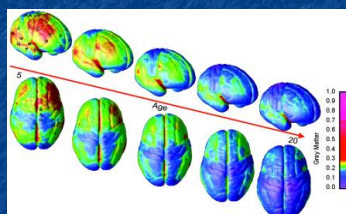
Source: Monitoring the Future, 2003

Australia



Source: Australian School Students Alcohol and Drug (ASSAD) survey (2011)

## Structure and Function Changes as Brain Maturation Continues into the Early to Mid 20s



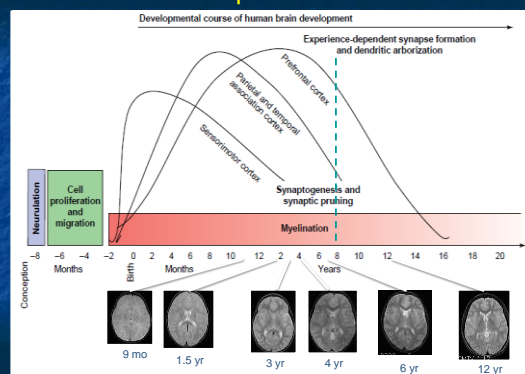
Maturation  
Sequence:

- Structures that Underlie Coordination & Affect First
- Planning, Long Term Consequence Evaluation and Inhibition More Slowly

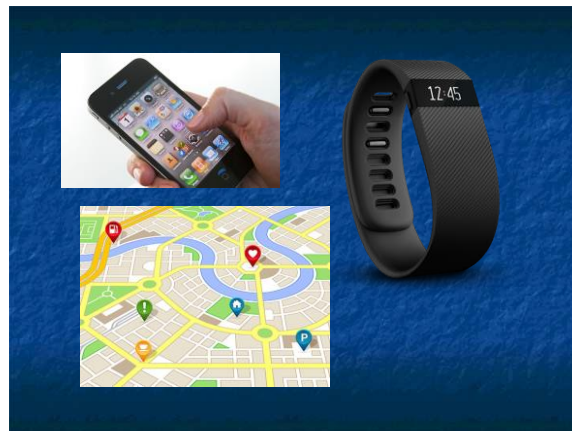
Gogtay, Nitin et al. (2004)

PNAS

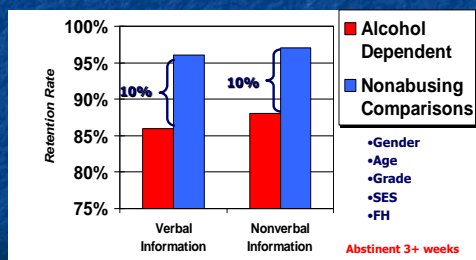
## Brain Development after Birth



Neuropsychology Review December 2012 cover



### AUD Teens Remember 10% Less Than Community Teens After 20 Minutes



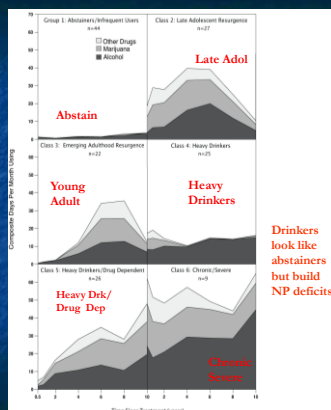
Brown et al. 2000

### 10 Year Alcohol/Drug Use Trajectories of Treated Youth

1. Abstainers-infrequent use (30%)
2. Late Adolescent Resurgence (18%)
3. Early 20's Resurgence (14%)
4. Heavy Drinkers –no drugs (16%)
5. Heavy Drinkers/Drug Dependent (16%)
6. Chronic Severe (6%)

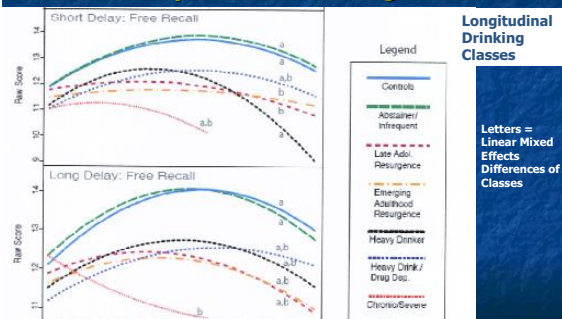
Anderson et al 2010

Long Term Course Varies Markedly :  
 Abstention, Regular use, Age Dependent Problems and Chronic Problems



Drinkers look like abstainers but build NP deficits

### Memory Performance over 10-Years: Concern for Heavy Drinkers and Drug Users



Hanson et al 2011



## Animal Studies of Adolescent Alcohol/Drug Exposure

- Reduced bone density
- Delay of puberty in females
- Brain changes
  - Frontal lobe damage (Spear, White)
  - Hippocampal volume (White, Spear)
  - Slower cellular repair (Crews)

## Neurobiological Studies of Alcohol/Drug Effects on Adolescent Animals

Adolescent animals are:

- **Less sensitive** to sedative effects
- **More sensitive** to disruption of memory, impairment of neurotransmission in hippocampus and cortex, and social facilitation
- **More impaired** spatial memory
  - reduced neurotransmitter release/uptake

## Alcohol Effects on Adolescent Animals: Binge Exposure

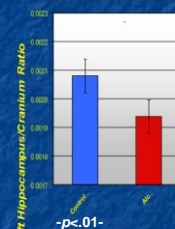
Long-lasting memory effects and damage to frontal-anterior cortical regions

- testing in adulthood shows poorer performance
- on autopsy cell abnormalities

Enhanced withdrawal and produces changes in cortex and hippocampus.

- loss of hippocampal and cortical cells
- slower to repair/regenerate neural cells

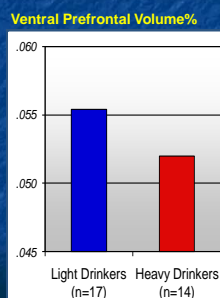
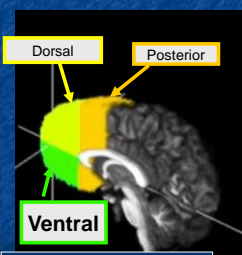
## Adolescent Alcohol Use and Reduced Left Hippocampal Volume



Nagel et al., 2005, PRN; Medina et al., 2007, NTT

Core to memory functioning/learning  
Develops during adolescence  
Intensity of Use Assoc with smaller vol

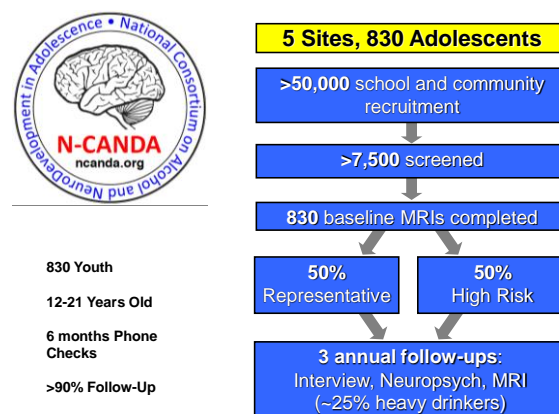
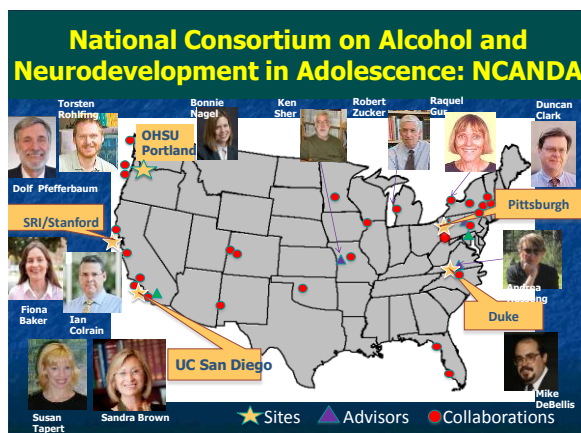
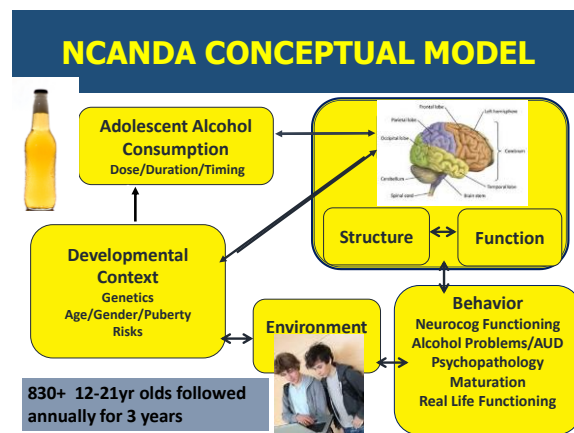
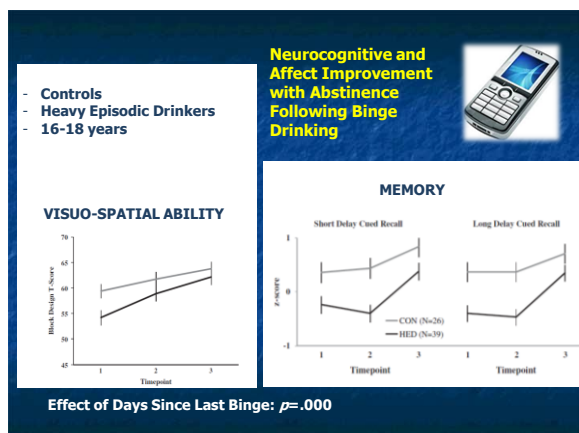
## Prefrontal Cortex Volume



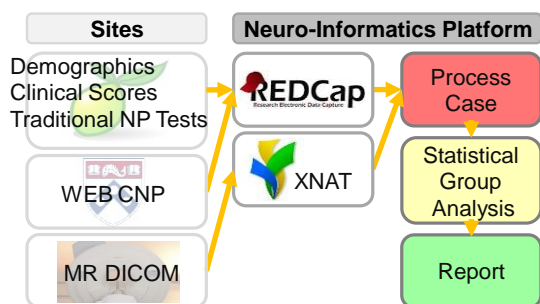
Develops during adolescence  
Plan, inhibit, decisions, new uses of old info  
Medina et al., 2009, ACER

## Adolescent Brain Development & Alcohol

1. Some risks before any alcohol use
  - Poorer inhibition at age 12-14
  - More frontal and parietal activation to perform memory tasks
  - White matter integrity predicts later binge drinking
2. Boys and Girls are different
  - Pubertal development & brain maturation differences
  - Girls appear to be more vulnerable or more impacted
  - Binge: girls > lower comprehension & interpretation of visual info  
boys > lower attention (10%)
  - Slow cumulative process
3. Alcohol affects vulnerable groups differently
  - FH < functional connectivity of frontal parietal regions, but not architecture
  - Lower responsivity = less change in brain response when exposed to alcohol



### NCANDA – Data Flow



Provide comprehensive report of measurements to scientists

### NCANDA Baseline MRI Findings

- Automated and individualized reviews of 831 MRIs (10% abnormalities)
- Showed similar age-related differences in regional cortical volumes and thickness (NCANDA and PING)
- Moderate/high alcohol drinking youth had smaller and thinner cortices in frontal, temporal, and cingulate regions.
- Youth who binged had thinner frontal and parietal cortices than no/low drinking youth.





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## NEWS RELEASES

Friday, September 25, 2015

### NIH launches landmark study on substance use and adolescent brain development

Thirteen grants awarded to look at cognitive and social development in approximately 10,000 children.

The National Institutes of Health today awarded 13 grants to research institutions around the country as part of a landmark study about the effects of adolescent substance use on the developing brain. The Adolescent Brain Cognitive Development (ABCD) Study will follow approximately 10,000 children beginning at ages 9 to 10, before they initiate drug use, through the period of highest risk for substance use and other mental health disorders. Scientists will track exposure to substances (including nicotine, alcohol, and marijuana), academic achievement, cognitive skills, mental health, and brain structure and function using advanced research methods.

"With advances in neuroimaging and other investigative tools, we will be able to look in greater detail at the impact of substance use on young people," said Nora D. Volkow, M.D., director of NIH's National Institute on Drug Abuse (NIDA). "Adolescents have access to high potency marijuana and greater varieties of nicotine delivery devices than previous generations. We want to know how that and other trends affect the trajectory of the developing brain."

**Adolescent Brain Cognitive Development**

**Institute/Center**  
National Institute on Drug Abuse (NIDA)  
National Institute on Alcohol Abuse and Alcoholism (NIAAA)

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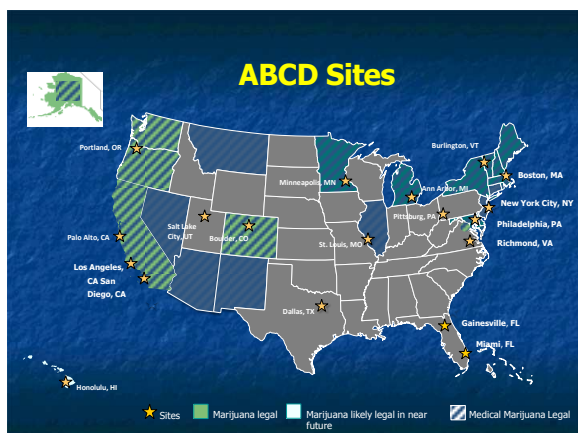
## ABCD

10,000 9-10 year olds



## Domains of Assessment

- Demographics and Background
- Substance Use
- Structural and Functional Neuroimaging
- Health and Mental Health
- Culture and Environment
- Biospecimens

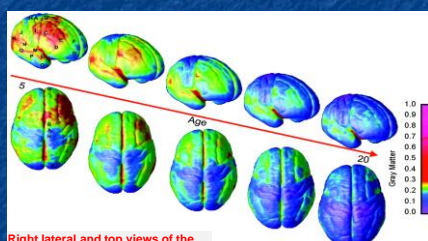


## Using Social Developmental Neuroscience to Inform Adolescent Alcohol Intervention

- Attention
- Memory
- Problem-solving
- Autonomy
- Social/Affect Influence
- Skill building



## Developmental Neuroscience and Behavioral Science suggests "SCAFFOLDING" approaches may Protect and Facilitate Skill Development as the Brain Matures (Dahl)

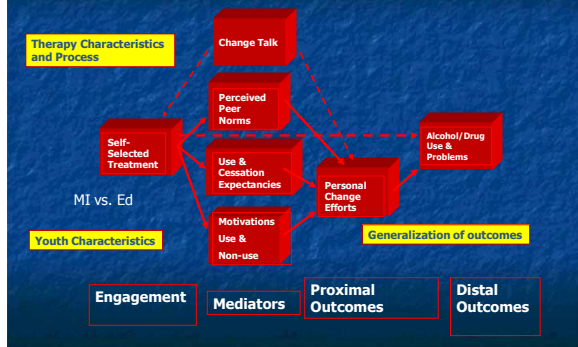


Right lateral and top views of the dynamic sequence of GM maturation over the cortical surface  
Gogtay, Nitin et al. (2004) PNAS  
Copyright ©2004 by the National Academy of Sciences

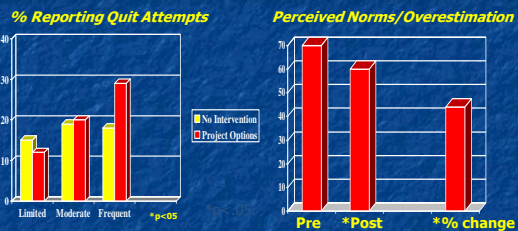
## Applying Developmental Neuroscience to Early Interventions: Project Options

1. Design a developmentally tailored intervention appealing to youth
  - Neurodevelopment Based
  - Motivational Enhancement
  - Perceived Norms, Expectancies, Motivations for Use
  - Cognitive Behavioral Self Regulation Skills
  - Focus on Youth Concerns
2. Market to attract youth with diversified alcohol involvement histories
  - Facilitators and Barriers
  - Multiple Formats and Topics
  - Market to Youth
3. Test intervention
  - Voluntary Engagement
  - Mediators and Proximal Outcomes
  - Distal Use Problem Outcomes
  - Change Mechanisms/Processes

## Project Options Multi-site Clinical Trial: What Group Process Methods Contribute to Change?



## Better Outcomes & Cognitive Mediators Change: Project Options vs No Intervention/Assessment Only



Fewer Binge Episodes  
Lower Average Drinks  
Fewer Alcohol Problems (1-3 Mo)

# Sessions, Trt Satisfaction & Alliance predict Early Quit Efforts & Reduced problems

Thank You  
QUESTIONS?

