BINGES, BLACKOUTS AND BRAIN DEVELOPMENT

Why delaying the onset of drinking is so important

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Alcohol use by young people is a global concern

**Britain's 'chronic' teenage binge-drinking problem highlighted by European poll**

The survey of 36 countries found the UK had the third-highest number of 15 and 16-year-olds with an alcohol problem. 

Professor Martin Plant, the University of the West of England academic who led the research, said, "The UK retains its unenviable position in relation to both binge-drinking, intoxication and alcohol-related problems among teenagers.

**Australia battles rise in alcohol abuse**

**Alcohol increasingly has Australia in its poisonous grip.**

One in eight Australians drink at dangerous levels. The effects on long-term health are likely to be catastrophic.

Australia has always had a boozy reputation but excessive drinking is on the rise.

Doctors are warning of a surge in chronic diseases such as cirrhosis of the liver and cancers as well as brain disorders in the next 20 years.

"Unfortunately Australia has a massive alcohol drinking problem," said Associate Professor Gordian Fulde from Sydney’s St Vincent’s Hospital.
Past month use of alcohol decreasing among 8th, 10th and 12th graders in US

Significant decline in past month use for all grade levels

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

Interestingly, decline in binge drinking mainly for males – levels for females not declining much

Significant decline in binge drinking for 12th grade males but not females between 1992-2012

US teens (15-16 years old) less likely to drink in a year than teens across Europe

US teens (15-16 years old) less likely to get drunk in a year than teens across Europe

So what’s the big deal? Despite progress many in US start drinking as teens

Current, Binge, and Heavy Alcohol Use among Persons Aged 12 to 20, by Gender: 2012

- **Current**
  - Male: 25%
  - Female: 24%

- **Binge**
  - Male: 17%
  - Female: 14%

- **Heavy**
  - Male: 5%
  - Female: 3%

Each year almost 3 million people under 18 start drinking

Teens drink less often than adults but more per occasion

SAMHSA Report to Congress on Prevention and Reduction of Underage Drinking, May 2011
And earlier onset of use increases risk for abuse and dependence later in life

Source: NSDUH 2012 -- www.samhsa.gov/data/

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)
As age of onset goes down, risk of alcohol dependence goes up

<table>
<thead>
<tr>
<th>AGE</th>
<th>FHP (%)</th>
<th>FHN (%)</th>
</tr>
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<tbody>
<tr>
<td>≤ 13</td>
<td>57</td>
<td>26</td>
</tr>
<tr>
<td>14-15</td>
<td>48</td>
<td>32</td>
</tr>
<tr>
<td>16-17</td>
<td>35</td>
<td>21</td>
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<tr>
<td>18-19</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>20</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>≥ 21</td>
<td>16</td>
<td>7</td>
</tr>
</tbody>
</table>

FHP = Family history positive for alcoholism, FHN = Family history negative for alcoholism
Starting early predicts a range of negative outcomes

- Injuring other people after drinking
  - Hingson & Zha, Pediatrics, 2009
- Violent behavior, including predatory violence
  - Blitstein et al., Health Educ Behav, 2005; Ellickson, et al., Pediatrics, 2003
- Suicide
  - Swahn et al., Pediatrics, 2008; Bossarte & Swahn, Addict Behav, 2011
- Dating violence/victimization
  - Ramisetty-Mikler et al., J Sch Health, 2006
- Criminal behavior
- Prescription drug misuse
  - Hermos et al., J. Addict Med., 2008
- Unplanned and unprotected sex after drinking
  - Hingson et al., Pediatrics, 2003
- Abuse/dependence/addiction
  - Hingson et al., Archives Pediatric Adolesc Med, 2006
- Brain damage/altered brain development with heavy use
  - Squeglia et al., Clin EEG Neuroci, 2010

Important to delay the onset of drinking!

Source: Hingson et al., Age of drinking onset and injuries, motor vehicle crashes and physical fights after drinking and when not drinking. Alc Clin Exp Res, 33(5), 783-790, 2009
Key questions:

• **WHY** does alcohol use tend to begin in adolescence?
• **WHERE** in the brain does alcohol produce its effects?
• **WHAT** are the short- and long-term risks?
• **HOW** can we delay the onset of use?
Adolescent brain changes underlie many typical teen behaviors

“Teenage brains. Beautiful brains. Moody. Impulsive. Maddening. Why do teenagers act the way they do? Viewed through the eyes of evolution, their most exasperating traits may be the key to success as adults.”

David Dobbs
National Geographic
October, 2011

Overall size of brain changes little during adolescence

- Brain reaches adult size before age 10 and size changes little during the second decade of life
- *However*, there are widespread changes in wiring and in levels of *gray matter* and *white matter*

Experience driven changes in wiring occur within and between circuits

Pruning and fine tuning

Improved speed and efficiency

Frontal lobe changes during adolescence

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

Ball W et al with the Brain Development Cooperative Group (2012). Total and regional brain volumes in a population-based normative sample from 4 to 18 years: the NIH MRI Study of Normal Brain Development. *Cerebral Cortex, 22*(1):1-12.
According to the model, the adolescent is biased by functionally mature subcortical relative to less mature cortical circuitry” Casey and Jones, 2010

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

Adolescence is risky business

Sensation seeking increases in mid-teens

Alcohol and drug use often begins here

% Past month alcohol use (NSDUH 2012)

- Current Use (Not Binge)
- Binge Use (Not Heavy)
- Heavy Alcohol Use

Romer et al (2010)
Prevention Science, 11, 319-30.
% Past month drug use (NSDUH 2012)

- Psychotherapeutics
- Marijuana

Romer et al (2010)
Prevention Science, 11, 319-30.
Alcohol increased reaction time and false alarm errors in a dose-dependent manner in a Go/No-Go task (N = 51, mean age 24.5). FMRI analyses showed alcohol decreased activity in anterior cingulate, lateral prefrontal cortex, insula and parietal lobe regions during false alarm responses to No-Go stimuli.

Heavy drinking during adolescence associated with reduced frontal lobe volume

Binge drinking during adolescence linked to disrupted white matter tracts connecting brain areas

Binge drinking teens (N = 14, age 16-19, average 15 drinks per month) with no history of alcohol use disorders had lower FA than controls (N = 14, age 16-19) in 18 white matter areas including the corpus callosum (above). Lower FA in 6 areas was linked to significantly greater lifetime hangover symptoms and/or higher estimated peak blood alcohol concentrations.

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 DPDD 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.

Cognitive impairments in alcohol dependent teens three weeks into inpatient treatment

Cognitive deficits from heavy drinking in teens even after 1 month sobriety?

CVLT-II short and long delay verbal memory z-scores by heavy episodic drinking youth (HED) and controls (CON). Average number of days since last heavy episodic drinking episode in HED youth was 5.56 days at Time 1, 19.52 days at Time 2, and 32.81 days at Time 3. **HED evidenced poorer recall than CON at all time points.**

Are differences at Timepoint 1 due to the heavy drinking or might they predate the onset of heavy drinking?

Different trajectories of verbal attention/working memory (WISC-R/WAIS-R arithmetic) across 10-years after adolescents leave inpatient treatment based up drinking habits after treatment

Does frontal lobe activity at baseline predict transition to heavy drinking in teens?

Differences in BOLD response during no-go trials at baseline between adolescents who transitioned into heavy alcohol use (TU; n=21) versus controls (CON; n=17). Areas in blue indicate where future users had significantly less BOLD response during inhibition (no-go) trials relative to baseline than non-users (p<.01, clusters >864 μl). In no region did TU show more no-go response than CON.

Future heavy drinkers showed less BOLD response at baseline in several brain regions during response inhibition, but more BOLD response at follow-up after initiation of heavy drinking, compared to nondrinking controls.

Alcohol suppresses activity in the amygdala

- The amygdala is involved in forming emotional responses, particularly negative, to stimuli (i.e., fear and anxiety)
- The amygdala is hyper-reactive in adolescents, perhaps making alcohol more reinforcing because it dampens fear and anxiety

Hippocampus creates autobiographical memories and is suppressed by alcohol

Birth of new neurons in the hippocampus peaks during adolescence

Alcohol can produce amnesia – a.k.a., “Blackouts”
Example of a blackout
'Drunk and naked' in Cancun

By Gary Strauss, USA TODAY

CANCUN, Mexico — Shane Mahmood woke from a booze-induced fog with a half-inch stainless steel ring pierced through his lower lip.

Shane Mahmood doesn't remember getting his lip pierced.

"I don't know how I got it or if it hurt when I did," says Mahmood, who was partying at disco La Boom with University of Washington pals when the predawn procedure apparently occurred. "I just remember beer and tequila before waking up and seeing it in the mirror."
Alcohol-induced memory blackouts are common among recent HS grads and college students.

Prevalence of blackouts in a sample of U.S. college students (n = 772) (White et al., 2002)

- **LIFETIME**
  - 51%
  - 20% of all drinkers had 4+ lifetime blackouts

- **YEAR**
  - 40%

- **2 WKS**
  - 9%

Similarly, 12% of college bound recent high school graduates blacked out in a 2-week period over the summer before freshman year (White and Swartzwelder, 2009).

### TABLE 6

<table>
<thead>
<tr>
<th>Alcohol-related problem</th>
<th>Prevalence in %</th>
<th>Change over time</th>
<th>Test for linear time trend p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1993&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1997&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1999&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Miss a class</td>
<td>26.9</td>
<td>31.1</td>
<td>29.9</td>
</tr>
<tr>
<td>Get behind in school work</td>
<td>20.5</td>
<td>24.1</td>
<td>24.1</td>
</tr>
<tr>
<td>Do something you regret</td>
<td>32.1</td>
<td>37.0</td>
<td>36.1</td>
</tr>
<tr>
<td>Forget where you were or what you did</td>
<td>24.7</td>
<td>27.4</td>
<td>27.1</td>
</tr>
<tr>
<td>Argue with friends</td>
<td>19.6</td>
<td>24.0</td>
<td>22.5</td>
</tr>
<tr>
<td>Engage in unplanned sexual activities</td>
<td>19.2</td>
<td>23.3</td>
<td>21.6</td>
</tr>
<tr>
<td>Not use protection when you had sex</td>
<td>9.8</td>
<td>11.2</td>
<td>10.3</td>
</tr>
<tr>
<td>Damage property</td>
<td>9.3</td>
<td>11.7</td>
<td>10.8</td>
</tr>
<tr>
<td>Get into trouble with the campus or local police</td>
<td>4.6</td>
<td>6.4</td>
<td>5.8</td>
</tr>
<tr>
<td>Get hurt or injured</td>
<td>9.3</td>
<td>12.0</td>
<td>12.4</td>
</tr>
<tr>
<td>Require medical treatment for an overdose</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Drove after drinking</td>
<td>26.6</td>
<td>29.5</td>
<td>28.8</td>
</tr>
<tr>
<td>Have ≥ 5 different alcohol-related problems</td>
<td>16.6</td>
<td>20.8</td>
<td>19.9</td>
</tr>
</tbody>
</table>

<sup>a</sup><sub>n = 12,708</sub>, <sup>b</sup><sub>n = 11,506</sub>, <sup>c</sup><sub>n = 10,825</sub>, <sup>d</sup><sub>n = 8,783</sub>.<sup>*</sup><sub>p < .05</sub>, **<sup>p < .01</sup>, ***<sup>p < .001</sup>.

An interview questionnaire was administered to subjects regarding a recent alcohol associated arrest with a documented BAC greater than 0.08 g/dL for either public intoxication, driving under the influence, or under age drinking.

The Association of Alcohol-Induced Blackouts and Grayouts to Blood Alcohol Concentrations

**FIG. 1** Probability of grayouts or blackouts as a function of the blood alcohol concentration (BAC) (g/dL) where probability $= 2.46 \times \text{BAC} + 0.02$ ($R^2 = 0.27$).

**FIG. 2** Probability of blackouts as a function of the blood alcohol concentration (BAC) (g/dL) where probability $= 2.21 \times \text{BAC} - 0.18$ ($R^2 = 0.54$).

50/50 chance of partial or complete blackout at 0.22% BAC
Left hippocampus smaller in heavy drinking teens

Source: Nagel et al., 2005; Medina et al., 2007

Smaller in heavy drinking youth

Source: White et al., 2002, American Journal of College Health

Right / Left

Control (n=16)  Alc (n=21)  MJ+Alc (n=26)

p < .01
The reward system helps shape behavior by providing reinforcement when something presumably good for survival is done (e.g., eating, drinking, bonding, sex, etc.) Both the VTA and NA also send signals to the frontal lobes increasing attention so the brain can learn about and repeat what triggered the reinforcement. Alcohol and other drugs activate the reward system, compelling the user to repeat the behavior. Teens might be more sensitive to reward than adults.
FIGURE. Ventral striatal activity to reward and association with risk-taking. Note: Ventral striatum (left) is activated with reward (middle) and correlated with risk-taking (right) (adapted from Galvan et al.6 and Galvan et al.16). Such findings could mean that adolescents are more motivated for reward and more reinforced by it.

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

Amount of brain activation in response to alcohol-related cues increases with drinking levels

Blood oxygen level-dependent (BOLD) response signal contrast in the right precuneus/posterior cingulate region during exposure to alcoholic beverage pictures relative to nonalcoholic beverage pictures plotted as a function of drinks consumed per month for adolescents with alcohol use disorder (n = 15).

Are strong associations between alcohol and cues part of why adolescents are at such high risk of developing dependence and of relapsing?

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
Five binge-drinking deaths 'just the tip of the iceberg'

By Robert Davis, USA TODAY

This month has been deadly for binge-drinking college students.

Five underclassmen in four states appear to have drunk themselves to death, police say, after friends sent their pals to bed assuming that they would "sleep it off."
Alcohol - Small margin of safety

- 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
How common is alcohol poisoning?

26 Teens Taken to Hospital for Alcohol Poisoning Ahead of Wiz Khalifa Concert at Jones Beach

Twenty-six teenagers between the ages of 14 and 18 were taken from Jones Beach to Nassau University Medical Center in various stages of Intoxication Thursday

Friday, Aug 3, 2012 | Updated 5:18 PM EDT
67% increase in hospitalizations related to alcohol overdoses in 18-24 year olds between 1999-2008

Where do underage drinkers drink?

- In a Car or Other Vehicle
- At Home
- At Someone Else's Home
- At a Park, on a Beach, or in a Parking Lot
- At a Restaurant, Bar, or Club
- At a Concert or Sports Game
- At School
- At Some Other Place

Percent

SAMHSA Report to Congress on Prevention and Reduction of Underage Drinking, May 2011
Common question: Should parents allow teens to drink at home?

• Several studies in the US and other countries suggest that allowing teens to drink at home, either with parents or supervised by parents, increases the odds that a teen will binge drink outside of the home.

SAMHSA’s underage drinking prevention PSA campaign helps parents and caregivers start talking to their children early—as early as nine years old—about the dangers of alcohol.

The chance that your child will use alcohol increases as they get older. About 10% of 12-year-olds say they have tried alcohol, but by age 15, that number jumps to 50%. The sooner you talk to your children about alcohol, the greater chance you have of influencing their decision not to drink. See the PSAs

http://www.samhsa.gov/underagedrinking/
Iowa Strengthening Families Program

Goals:
- Improve parent/child relations
- Strengthen family communication skills
- Increase child coping skills

Implementation:
- 7 sessions at school
- 13 hours total
- Parent and child separately and together

Randomized controlled trial with families of 6th graders:
• Iowa Strengthening Families Program (ISFP) (206 families)
• Control (221 families)

Life Time Drunkenness Through 6 Years Past Baseline:
Logistic Growth Curve

Putting it all together:
Why delaying the onset of drinking is so important

- Adolescent brain changes help drive us toward peers and out of the house – which helps us transition to independence – but can also increase risk of alcohol use and related harms.
- Short-term, alcohol disrupts the frontal lobes (decision making and impulse control), hippocampus (memory), amygdala (fear and anxiety) and brainstem (vital reflexes).
- Alcohol also activates the reward system (pleasure/reinforcement).
- These effects can make alcohol feel fun while greatly increasing the risk of negative consequences, including injury and death.
- Long-term, alcohol can alter the trajectory of adolescent brain development and cause lingering cognitive deficits.
- It remains unknown whether these deficits are permanent.
- Safest bet is to delay onset of drinking until brain development is complete.
NIAAA Resources
(niaaa.nih.gov)
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THANK YOU!