The World’s Second Most-Popular Drug
(alcohol)

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Topics For The Evening

Why we drink alcohol, and how it works

Neural mechanisms underlying alcohol effects

Cultural/historical factors underlying our alcohol use
Why Do People Drink Alcohol?

Euphoria/Mood elevation
Increase social confidence
Relaxation/antianxiety
To sleep
Escape from problems
Culture/Ancestry
How Does Alcohol (Ethanol) Work?
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The human body is composed of ~75 trillion cells.
Our body cells are made mainly of fatty membranes and proteins. Proteins are the MACHINES that make cells function.
Protein folding/shape/function is partly a result of the sequence of fatty and water-soluble side chains.
Ethanol alters the folding and therefore the function of proteins.
Ethanol Affects All Body Systems

Cardiovascular

Gastrointestinal

Self-medication efforts aimed at the brain

Endocrine/Reproductive

Urinary

Nervous system
How Does Alcohol (Ethanol) Work?

Ethanol affects synapses

Neuron signals and networks (x 100 billion!)

Synapses, Neurotransmitters and Receptors
Ethanol affects multiple neurotransmitters

- Glutamate
- GABA (Gamma-Amino Butyric Acid)
- Endorphins
- Serotonin
- Dopamine
- Acetylcholine
- Glycine
- Adenosine
Ethanol affects multiple neurotransmitters

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- Acetylcholine
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Differential sensitivities of these systems to dose, time course, and context can make alcohol an unpredictable drug!
Neurotransmitters of pleasure centers:
Ethanol increases dopamine signaling in “reward” centers in a way that reinforces binge drinking
Euphoria

Rising Phase Effect

Blood Alcohol Content

Elevated Dopamine: Reward/Euphoria

Depressed Dopamine: Craving/Dependence

Time

Increasing Dose/Side Effects
Moderate Dose/Effects
Euphoria | Rising Phase Effect

Blood Alcohol Content | Time

Binge Drinking

Increasing Dose/Side Effects
Moderate Dose/Effects
Rising Phase Effect

Time

Blood Alcohol Content

Euphoria

Binge Drinking

Responsible Drinking

Increasing Dose/Side Effects

Moderate Dose/Effects
Dopamine tolerance time frames

*Acute* tolerance of reward center transmitter systems leads to excess drinking within one episode

*Chronic* tolerance leads to alcohol dependence (alcoholism).
Parts of the brain that regulate impulsive pleasure seeking behaviors don’t mature until the early 20’s, so binge drinking is inevitable in younger drinkers with access to alcohol....
…and of the people who binge drink by age fourteen, 50% will be alcoholic adults. Only 8% of people who don’t drink until age 21 become alcoholics.
According to the Centers for Disease Control:

17% of US adults had an episode of binge drinking in the previous month

50% of College-aged students binge drink, averaging nine drinks per episode.
Social confidence/relaxation
Normal thinking depends on a balance of excitatory and inhibitory synaptic activity:

- 50% of the brain’s synapses use Glutamate
- 40% use GABA (gamma-aminobutyric acid)
Normally:

Many brain circuits involving Glutamate/GABA are involved in determining how we respond to situations.

- empathy/compassion
- sense of justice/fairness
- basic personality
- understanding of cause/effect
- cultural learning
- biological drives, like sexual behaviors
- situational memories
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.
Global depression model explaining situational dependence of alcohol’s effect on mood and behavior:

ALCOHOL MYOPIA
As alcohol dose rises: ALCOHOL MYOPIA

Ethanol globally suppresses cognition, reducing the mental focus of an individual to immediate internal thoughts or external stimuli.

Behavior

- Social confidence/relaxation
- Empathy/compassion
- Basic personality
- Cultural learning
- Situational memories
- Sense of justice/fairness
- Understanding of cause/effect
- Biological drives, like sexual behaviors
Alcohol, Anxiety, and Public Speaking

<table>
<thead>
<tr>
<th>Alcohol drinks</th>
<th>Volunteer subjects invited to a party</th>
<th>Placebo drinks</th>
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</thead>
</table>

“In 15 minutes, you have to go on stage and give an impromptu speech:”

*What I dislike most about my body and physical appearance*

<table>
<thead>
<tr>
<th><strong>ANXIETY</strong></th>
<th><strong>ANXIETY</strong></th>
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<tbody>
<tr>
<td>Sit and think</td>
<td>Easy slide sorting task</td>
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<tr>
<td>Easy slide sorting task</td>
<td>Moderate difficulty slide sorting task</td>
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<tr>
<td>Moderate difficulty slide sorting task</td>
<td>Complicated slide sorting task</td>
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</tbody>
</table>
Alcohol, Anxiety, and Public Speaking
Alcohol myopia can boost self-confidence

from: The Onion
Alcohol myopia can boost self-confidence

I’m gonna date this asshole, because I think I can fix him!

Alcoholic Beverage Consumer Confidence Skyrockets

NEW YORK—Alcoholic-beverage-consumer confidence hit a record high Friday between the hours of 5 p.m. and 3 a.m., briefly reaching 105.3 points before dropping to 94.2 at last call.

"Weekend market conditions were extremely favorable for cash/beverage trading," said Byron Seidler of the Board of Alcohol Consumption and Expenditure. "Drinkers' confidence in the strength of the dollar, in their attractiveness to the opposite sex—even in their dart-playing abilities—rose sharply."

"You know the secret to getting women? Being a total asshole."

showed a 47 percent increase in dancing, bar trivia, and ability to drive. Young women maudlin conversations about relations troubles. In severe cases, however, these spikes can trigger a depression."

Alcohol consumer Kirk Britmer, Raleigh, NC offered a detailed analysis of his weekend's spending patterns.

"I noticed an attractive woman across the bar from me. At first, I was afraid to talk to her because she was with some friends and seemed like she was doing her own thing," Britmer said. "But then at one point, she gave up on me, and when she walked over..."
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.

As the dose goes up so may confidence, but appropriate decision-making is increasingly impaired....
Social confidence/anxiolytic

Just because it's a bad idea, doesn't mean it's not going to be a good time.
Social confidence/anxiolytic
Social confidence/anxiolytic
CDC: 38% of emergency room visits are alcohol-related
Effects on cognition are reversible in adults, but.....

.....people who binge drink starting by age 14 have smaller brains and reduced cognitive ability as adults, compared to those who didn’t drink before age 21.
Sleep/Escape from Problems
Alcohol affects neurotransmitters in a way that CAN make you get “sleepy” but.....
Sleep/Escape

…it isn’t really sleep, it’s more like surgical anesthesia
Short-Term Memory → LTP → Long-Term Memory

REM SLEEP

RECENT LEARNING RESEARCH
Short-Term Memory

REM SLEEP

+ LTP

Long-Term Memory

ALCOHOL IMPAIRS REM SLEEP SO IT INHIBITS MEMORY FORMATION
Inhibits formation of NEW memories not old, so escape from past problems isn’t possible; if anything, alcohol myopiaMagnifies them.

Alcohol abuse is a leading cause of depression.
Alcohol use is also a major cause of academic failure.
Why Do People Drink Alcohol?

Euphoria/Mood elevation
Increase social confidence
Anti-anxiety (relaxation)
To sleep
Escape from problems
Culture/Ancestry
Animal studies reveal genetic and developmental basis for variation of alcohol effects and preference
Fruitfly experiments create “Cheapdates”
Fruitfly experiments create “Cheapdates”

Hic....burp!
Fruitfly experiments create “Cheapdates”
Fruitfly experiments create “Cheapdates”

1. I can fix this guy!

2. Hic....burp!

3. I can fix this guy!

4.
Fruitfly experiments create “Cheapdates”

1. Hic....burp!
2. Hey, you want to--
3. I can fix this guy!
4. YES!
5. Cheap date
Mouse strains: Long-sleep, Short-sleep, Energetic, Cold, Hot, DT-prone, Resistant
Cross-breeding animals that willingly drink alcohol creates ancestors with a tendency to drink heavily.
Alcohol abuse can also be induced developmentally by exposing young animals to neglect/abuse

Drunk Monkeys (NIH)

discovermagazine.com/2002/jul/featdrunk
Some historians argue that most humans have been selected for alcohol preference and tolerance.
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First evidence of alcohol production, 8000 BC, after humans took up agriculture and established sedentary communities.

By 1000 BC, all over the world where humans had settled into towns, alcohol was consumed.

Most modern humans are descendants of these cultures.
Culture/Ancestry

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Culture/Ancestry

The Ghost Map

700 deaths in 2 weeks all around the Broad Street pump
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The Ghost Map

700 deaths in 2 weeks all around the Broad Street pump.

Not a single worker of the Lion Brewery died: they received an allotment of ale as part of their wages.
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Water in cities was inevitably tainted with sewage, resulting in epidemics of cholera and dysentery.
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Those who preferred alcohol to water (and could handle its toxicity) survived more often and had children that survived.
Some historians argue that most humans have been selected for alcohol preference and tolerance. Water in cities was inevitably tainted with sewage, resulting in epidemics of cholera and dysentery. Those who preferred alcohol to water (and could handle its toxicity) survived more often and had children that survived. Native Americans and Australian Aborigines were not exposed to alcohol until modern times.
People vary not only in synapse proteins that determine neural effects of alcohol, but also in detox enzyme expression.
When you say WiiiisConsin....
Now we have clean water, but......
Now we have clean water, but......

Health problems caused by alcohol cost over 6 billion dollars per year in Wisconsin.

Alcoholism is a leading cause of domestic violence, divorce, and 1 in 10 deaths.

An alcohol-related car crash happens every 2 minutes, and a fatal one every 30 minutes.
We’re #1!
Questions?
Moderate Doses Might Be Healthy

Figure 1: Alcohol consumption and relative risk of death over 12 years in American Cancer Society prospective study of 276,802 men aged 40–59
“Moderate” = 12 oz. beer, 5 oz. wine, 1.5 oz whiskey

Learn to limit yourself to having just one....