Physiology of the World’s Second-Most Popular Drug

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1. Cellular mechanism of ethanol effects

2. Effects of ethanol on the nervous system
Alcohol Structure

Methanol

\[ \text{H} - \text{C} - \text{OH} \]

Ethanol

\[ \text{H} - \text{C} - \text{C} - \text{OH} \]

Propanol

\[ \text{H} - \text{C} - \text{C} - \text{C} - \text{OH} \]
Alcohol Structure

**Methanol**: Ingestion $\rightarrow$ blindness

**Ethanol**: THE alcohol

**Propanol**: Most “other” alcohols are highly toxic to the body
Ethanol Structure

• Clear, colorless liquid, miscible with H2O and Organics

Carbon-Hydrogen chains dissolve in lipids (hydrophobic)

This end interacts and dissolves in water (hydrophilic)
Basic Structure of Body Cells

Our bodies are made of 75 trillion specialized cells
with phospholipid membranes, and aqueous
environments inside and out.
Cell membranes are essentially oily bubbles formed from a bilayer of phospholipid molecules.
Proteins are the machinery that determine the function of different cell types; they’re found floating free and within membranes.

- Ion channels (Na+, K+, Ca+2)
- Enzymes
- Receptors
- Signals
Basic Structure of Body Cells

Proteins are made of amino acid chains:

20 different amino acids have unique “R” groups:

- Some are hydrophilic
- Some are hydrophobic
Basic Structure of Body Cells

Proteins are made of amino acid chains:

The “R”-group sequence determines the complex folding and final shape of a protein.
Ethanols unique chemistry makes it a universal key that can interact with protein machinery of cells throughout the body.

\[
\text{H} \quad \text{C} = \text{C} - \text{OH}\quad \text{(hydrophilic)}
\]

\[
\text{H} \quad \text{H}
\]

\[
\text{H} \quad \text{H}
\]
Why Does Whiskey “Burn”?
Why Does Whiskey “Burn”? 

“TRPv1 (Vanillin1) receptor” (mouth, throat)
Why Does Whiskey “Burn”?  

Heat, capsaicin…
Why Does Whiskey “Burn”?

Heat, capsaicin….and Ethanol!

Nerve signal to brain

“HOT!!”
Why Do People Drink Alcohol?
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Euphoria/Mood elevation
Increase social confidence
Anti-anxiety (“to relax”)
Aphrodesiac
Escape from problems
To fit in with friends/family
Why Do People Drink Alcohol?

- Euphoria/Mood elevation
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- Escape from problems
- To fit in with friends/family

Because of great advertising?
Why Do People Drink Alcohol?

Because of great advertising?
Why Do People Drink Too Much?
This happens a LOT......but why?
Why Do People Drink Too Much?

Ethanol affects synapses

Neuron signals and networks (x 100 billion!)
Why Do People Drink Too Much?

Ethanol affects synapses

Neuron signals and networks (x 100 billion!)

Synapses, Neurotransmitters and Receptors
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)
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.

As the dose goes up, your intelligence goes down……
Man eats underwear to beat breathalyzer

By D'ARCY RICKARD of The Advocate

STETTLER — An 18-year-old Stettler man tried to eat his underwear in the hope that the cotton fabric would absorb alcohol before he took a breathalyzer test, provincial court heard this week.

David Zurfluh was subsequently acquitted of a charge of impaired driving because he blew .08, the legal limit.

But the testimony broke up people in Judge David MacNaughton’s provincial court here Thursday afternoon.

Mr. Zurfluh was collared by RCMP Const. Bill Robinson after he ran from his vehicle, which had been seen weaving down the highway.

While sitting in the back of the patrol car, Mr. Zurfluh tried to eat his shorts, Const. Robinson told the court.

Mr. Zurfluh said he ripped the crotch out of his shorts, stuffed the fabric in his mouth and then spit it out.

A class of law students from William E. Hay Composite High, in court as observers,

was removed by the teacher when testimony unhinged the proceedings. The Grade 11 and 12 students had difficulty maintaining composure.

“People were leaving the courtroom with tears in their eyes, trying not to laugh,” said RCMP Const. Peter McFarlane.
Other Neurotransmitters: Ethanol stimulates brain “reward” centers in a specific way....
Glut + Glut + GABA — Glut — GABA

Mood/Pleasure

Serotonin
Dopamine

….which can explain why:
Short-term: Drinking leads to more drinking
Chronically: Addiction
Both related to “Rising Phase Effect”
Rising Phase Effect

Moderate Dose and Rate

Elevated Dopamine: Reward/Euphoria

Depressed Dopamine: Craving/Dependence

Blood Alcohol Content

Time

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

Binge Drinking

Blood Alcohol Content

Time

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

Binge Drinking
Optimized Drinking

Blood Alcohol Content

Time

Increasing Dose/Side Effects
Moderate Dose/Effects
If drinking a little makes you happy, does drinking a lot make you really, REALLY happy? (or depressed, or angry or horny?)
Global depression model explaining situational dependence of alcohol’s effect on mood and behavior:

ALCOHOL MYOPIA
“Alcohol Myopia” Can Explain Variable Neural Effects

The basic idea:

Ethanol globally suppresses cognition, reducing the mental focus of an individual to immediate internal thoughts or external stimuli.
“Alcohol Myopia” Can Explain Variable Neural Effects

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

Example: Study demonstrating that ethanol is NOT a good anti-anxiety drug....
Alcohol, Anxiety, and Public Speaking

Volunteer subjects invited to a party

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

\textit{What I dislike most about my body and physical appearance}

\begin{tabular}{|c|c|}
\hline
ANXIETY & ANXIETY \\
\hline
Sit and think & \\
\hline
Easy slide sorting task & \\
\hline
Moderate difficulty slide sorting task & \\
\hline
Complicated slide sorting task & \\
\hline
\end{tabular}
Alcohol, Anxiety, and Public Speaking

![Graph showing the effects of alcohol on stress in public speaking scenarios. The graph compares Placebo Subjects and Alcohol Subjects under different conditions of slide demand.](image-url)
Myopia can boost your self-esteem!

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.

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

The last time the Alcoholic-Beverage-Consumer Confidence Index spiked this dramatically was exactly one week earlier during the same time period.

Several market sectors reflected the spike, with beverage consumers’ confidence surging in dancing, aptitude for bar trivia, and ability to drive. Young women showed a 47 percent increase in dancing on the bar and a 31 percent increase in the maudlin conversations about relationships and troubles. In severe cases, however, this spike can trigger a depression.

Alcoholic 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 all of a sudden, I spilt my drink all over her and she came over and made a joke about it. It was really funny and we started talking.”

from: The Onion
How Does Alcohol Affect Memory?
Short-Term Memory ("Working memory") (RAM) → Long-Term Memory ("Learning") (Hard-drive)
Short-Term Memory \( \rightarrow \) Long-Term Memory

REM SLEEP

RECENT LEARNING RESEARCH
Alcohol affects neurotransmitters in a way that DOES make you go to “sleep” but…..
...but it is actually more like surgical anesthesia
...and may seem hilarious to your “friends”...
.....but.....
1. ETHANOL BLOCKS REM SLEEP
2. ETHANOL INHIBITS LTP

Long-term potentiation at glutamate synapses is a cellular correlate of memory formation.

Even at moderate doses, alcohol begins to inhibit LTP....
Inhibition of memory formation

Impaired long-term memory formation:
After a single drink, LTP is reduced 30%  
At BAC of 0.2%, LTP is reduced 80%  
Total amnesia/blackout can occur at higher levels...
COLUMBUS, OH—In an announcement that received wide attention throughout Wolverine’s tavern Tuesday, bar skanks Stephanie Fletcher and Jessica Keneally stated that they would share a passionate kiss at an unspecified time that evening.

“Steph and I are totally hot for each other,” Keneally said over the loud music to several unspecified bar patrons. “We’re going to make out. We don’t care who’s watching.”

According to eyewitnesses who looked up the second they walked in the door, the 22-year-old skanks arrived at the bar at approximately 10 p.m., dressed in their usual skank attire of low-cut tank tops paired with either low-rider jeans or a short skirt, and exposed, brightly colored thongs.

Afterdowning their third cosmo- politans, the two skanks stood up and began grinding to the R. Kelly song “I’m a Flirt,” which caused a nearby conversation about the Cleveland Indians to come to a sudden halt.

“Quit staring,” Keneally said to the approximately 25 male patrons in the immediate vicinity, all of whom were by that time involuntarily ogling the skank-ass pair. “Oh my God, you guys are such pervs.”

Fletcher would neither confirm nor deny that the kiss would involve tongue, saying that bargoers “would just have to wait.”

“Who knows what will go down,” Fletcher said as she reached into Keneally’s tight top and tweaked her left breast with her thumb and middle finger in front of seven rapt onlookers. “Possibly us.”

In previous months, Keneally and Fletcher have, either separately or...
THE COLLEGE STUDENT’S GRAND DELUSION...

Study from 5-11 pm ➔ Party from 11-2 am ➔ Long-Term Memory

REM SLEEP

LTP
Why Do Drunks Talk Loud, Fall Down, and Get the Bed Spins?
Global neural depression inhibits motor outputs and sensory inputs……
SIDE EFFECT: Depression of motor output and sensory input
1. Loss of coordination (see drunk driving stats)
SIDE EFFECT: Depression of motor output and sensory input

1. Loss of coordination (see drunk driving stats)
2. 8th Cranial Nerve especially sensitive
   ("Dude, turn it up!") (Field sobriety test) (Bed spins)
SOBRIETY TEST
Look at the photo above - if it looks right to you ...
You're Drunk
Calling alcohol a “Drug” doesn’t mean it is evil....
Calling alcohol a “Drug” doesn’t mean it is evil….

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Illegal</th>
<th>OTC</th>
</tr>
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<tbody>
<tr>
<td>Oxycontin</td>
<td>Cocaine</td>
<td>Tylenol</td>
</tr>
<tr>
<td>Prozac</td>
<td>Ecstasy</td>
<td>Nyquil</td>
</tr>
<tr>
<td>Valium</td>
<td>THC</td>
<td>Ipecac</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Heroin</td>
<td>Aspirin</td>
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</tbody>
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What do all “drugs” (and alcohol) have in common?
1. Sought-after effects
2. Unintended side-effects
3. The dose determines the effect/side-effect ratio
Calling alcohol a “Drug” doesn’t mean it is evil….

In moderate doses (<1-2 drinks/day), alcohol appears to cause no harm*, and much evidence suggests that it may have positive effects.

*EXCEPT in those who are pregnant, under 21, or susceptible to alcoholism.
Do you have feelings of inadequacy?

AN HONEST ALCOHOL AD