Ethanol

The Physiology Behind the World’s Second Most Popular Drug

Kevin T. Strang, PhD
Department of Physiology
Alcohol Structure

H
H
H

H\(\text{C}\)\(\text{C}\)\(\text{C}\)\(\text{C}\)\(\text{C}\)-OH
H H H H

H\(\text{C}\)\(\text{C}\)-OH
H H H

H\(\text{C}\)-OH
H H

Methanol
Ethanol
Propanol
Alcohol Structure

Methanol: Ingestion → 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)
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
Proteins are made of amino acid chains:

Different amino acids have unique “R” groups:

- Some are hydrophilic
- Some are hydrophobic
Ethanol Interacts with Cell Proteins

Ethanol’s unique chemistry allows it to interact with protein machinery of cells throughout the body.

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

(hydrophilic)

(hydrophobic)
e.g., Ethanol can alter gating properties of many different types of ion channels...
Why Does Whiskey “Burn”? 
Why Does Whiskey “Burn”? 

“Vanillin Receptor 1” (mouth, throat)
Why Does Whiskey “Burn”? 

Heat, capsaicin....
Why Does Whiskey “Burn”?  

Heat, capsaicin….and ethanol!

Nerve signal to brain
Ethanol Affects All Body Systems

Cardiovascular

Gastrointestinal

Endocrine/Reproductive

Urinary

Today’s Focus: Nervous System
Why Do People Drink?

Mood elevation
Mild euphoria
Reduced social inhibitions
Anti-anxiety
Why Do People Drink?

Mood elevation
Mild euphoria
Reduced social inhibitions
Anti-anxiety

But the effects aren’t as predictable as other drugs and there are side effects......
Ethanol affects synapses

Neuron signals and networks (x 100 billion!)

Synapses, Neurotransmitters and Receptors
Normal cognition depends on a balance of excitatory and inhibitory synaptic activity:

- 50% of the brain’s synapses use Glutamate
- 40% use GABA (gamma-amino-butyric acid)
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.

Dose-dependent decline in cognitive ability……
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. 8\textsuperscript{th} Cranial Nerve especially sensitive
   ("Dude, turn it up!") (Field sobriety test) (Bed spins)
How Does Alcohol Affect Memory?
How Does Alcohol Affect Memory?

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

Even at moderate doses, alcohol begins to inhibit LTP....
ALCOHOL AND LEARNING

Short-Term Memory
("Working memory")
(RAM)

Long-Term Memory
("Learning")
(Hard-drive)

Assimilation
Short-Term Memory

Long-Term Memory

SLEEP

NEW LEARNING RESEARCH
WHAT IS LEARNING?

ETHANOL

Short-Term Memory

Long-Term Memory
WHAT IS LEARNING?

ETHANOL

Short-Term Memory

X

Long-Term Memory

SLEEP

THE GRAND DELUSION...
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
What Makes a Mean Drunk Mean? (or happy or horny or depressed?)
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.

Overall MOOD effects are dose and situation dependent.
"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.
The basic idea:

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:”
What I dislike most about my body and physical appearance

<table>
<thead>
<tr>
<th>ANXIETY</th>
<th>ANXIETY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sit and think</td>
<td>Moderate difficulty slide sorting task</td>
</tr>
<tr>
<td>Easy slide sorting task</td>
<td>Complicated slide sorting task</td>
</tr>
</tbody>
</table>
Alcohol, Anxiety, and Public Speaking

The graph illustrates the changes in stress levels among placebo and alcohol subjects in different slide conditions: No Slides, Low Demand Slides, Moderate Demand Slides, and High Demand Slides. The stress decreases are measured on the y-axis, with positive values indicating an increase in stress and negative values indicating a decrease in stress.

- Placebo Subjects:
  - No Slides: Minimal stress increase
  - Low Demand Slides: Moderate stress increase
  - Moderate Demand Slides: Significant stress increase
  - High Demand Slides: Very high stress increase

- Alcohol Subjects:
  - No Slides: Minimal stress decrease
  - Low Demand Slides: Moderate stress decrease
  - Moderate Demand Slides: Significant stress decrease
  - High Demand Slides: Very high stress decrease

The graph shows that alcohol subjects tend to experience a greater stress decrease compared to placebo subjects, especially in high-demand slide conditions.
Myopia CAN boost 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.

“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.”

“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 soaring in dancing, aptitude for bar trivia, and ability to drive. Young women showed a 47 percent increase in dancing confidence. A 28 percent increase in the enjoyment of loud rock concerts.

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

from: The Onion
Why is it So Hard to Have Just One?
Other Neurotransmitters: Ethanol stimulates brain “reward” centers.
Glut 

GABA 

Glut + 

+ 

GABA 

Mood/Pleasure

Serotonin
Dopamine

THIS EXPLAINS:

Short-term: Drinking leads to more drinking
Chronically: Addiction
Both related to “Rising Phase Effect”
Rising Phase Effect

Moderate Dose and Rate

Blood Alcohol Content vs Time

Elevated Dopamine: Reward/Euphoria

Depressed Dopamine: Craving/Dependence

Increasing Dose/Side Effects

Moderate Dose/Effects
Rising Phase Effect

- Binge Drinking
  - Increasing Dose/Side Effects
  - Moderate Dose/Effects

**Axes:**
- Blood Alcohol Content
- Time
Rising Phase Effect

Blood Alcohol Content

Time

Binge Drinking
Optimized Drinking

Increasing Dose/Side Effects
Moderate Dose/Effects
WHY DO BEER AND BRATS MAKE A GREAT TEAM?
WHY DO BEER AND BRATS MAKE A GREAT TEAM?

Fatty foods are best at delaying the emptying of the stomach (enterogastric reflex)

Reduces the rate of rise of blood alcohol 3-fold!

Always eat before/during alcohol consumption!
How Does the GI System Save Lives?
How Does the GI System Save Lives?

Normally:

- Stretch
- Bacteriotoxin
- Excess acid

**Stomach Wall Receptors**

**Brainstem**

**Vomit**
How Does the GI System Save Lives?

- stretch
- bacteriotoxin
- excess acid

High ethanol concentrations stimulate stomach wall receptors 2 ways:
- direct
- indirect

resulting in...

brainstem
“Drug” isn’t a four-letter-word....

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Illegal</th>
<th>OTC</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

What do all “drugs” (and ethanol) have in common?
1. Sought-after effects
2. Unintended side-effects
3. The dose determines the effect/side-effect ratio
Think of alcohol as a “drug”

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 under 21, pregnant, or susceptible to alcoholism.
Moderate **doses** seem to be **good** for you.....