

# 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**

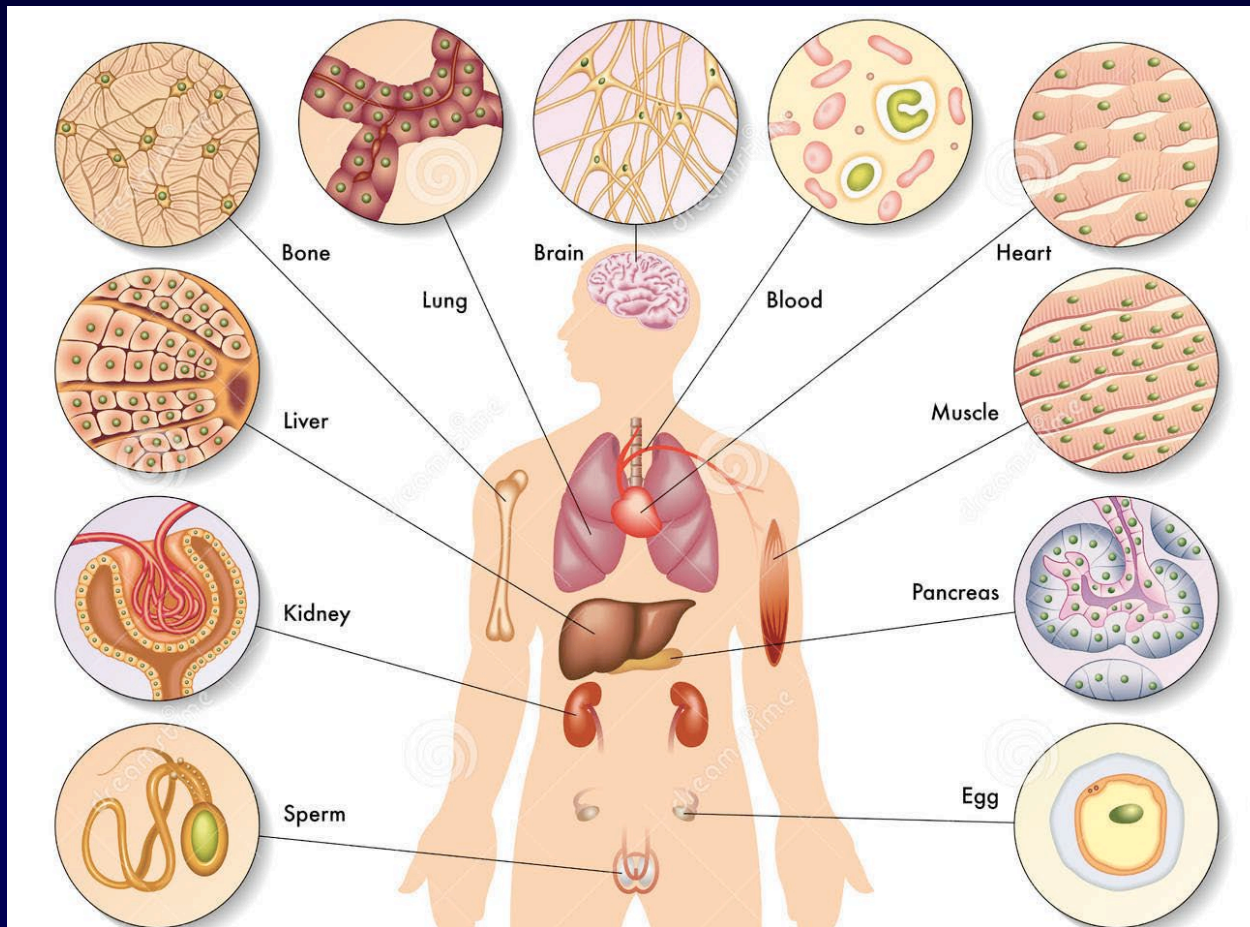
**To sleep**

**Escape from problems**

**Culture/Ancestry**

# How Does Alcohol (Ethanol) Work?

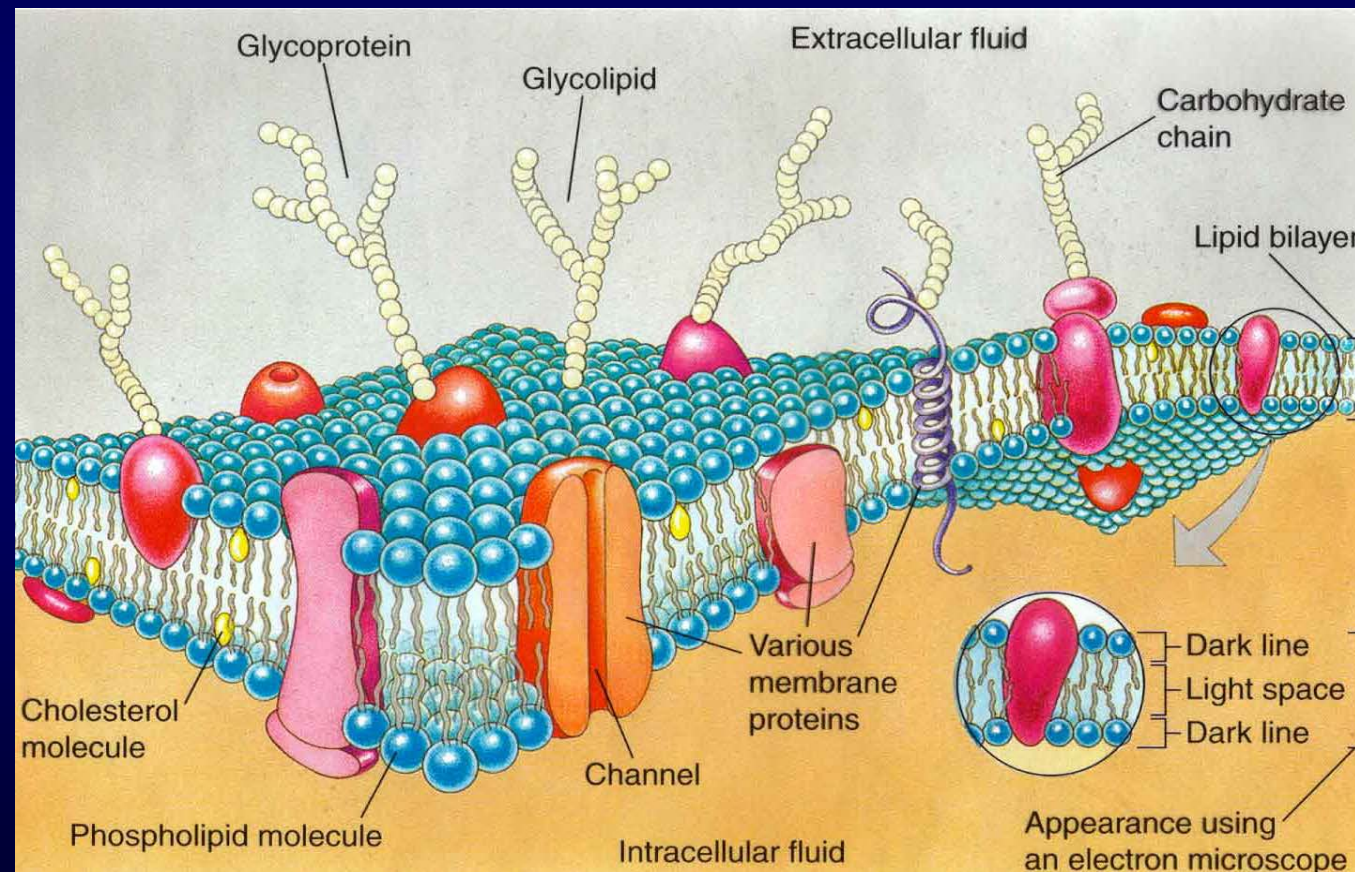
# How Does Alcohol (Ethanol) Work?



**The human body is composed of ~75 trillion cells**

# How Does Alcohol (Ethanol) Work?

**Our body cells are made mainly of fatty membranes and proteins. Proteins are the MACHINES that make cells function.**



## Protein machines

**Ion channels**  
( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{+2}$ )

**Enzymes**

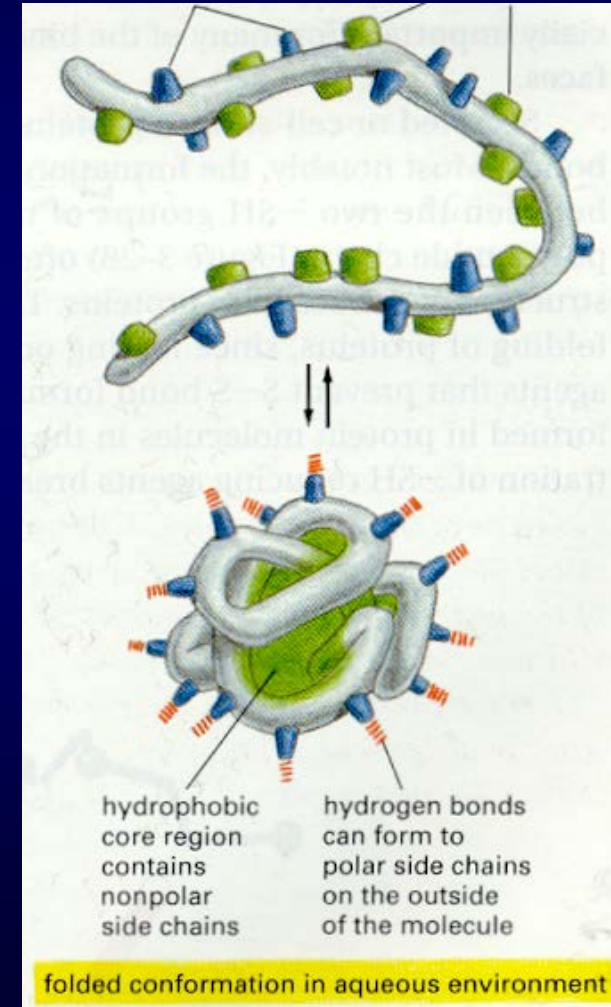
**Receptors**

**Signals**



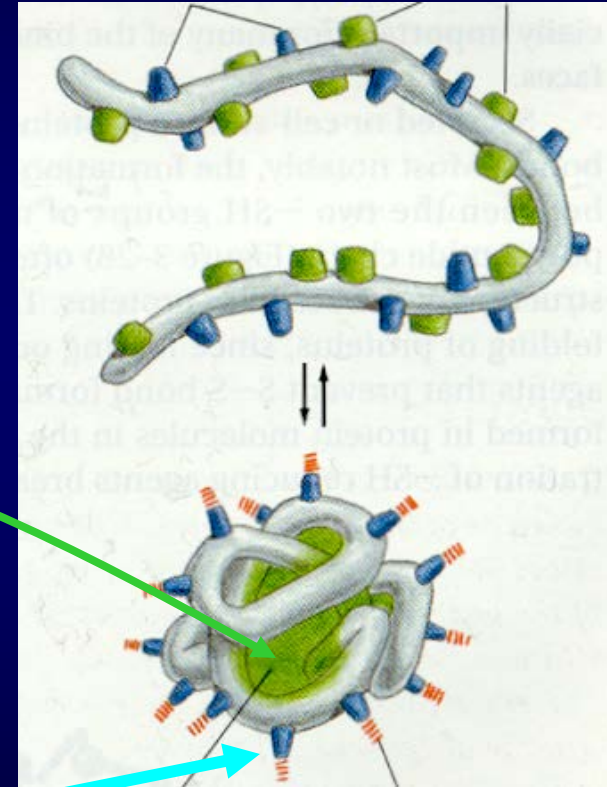
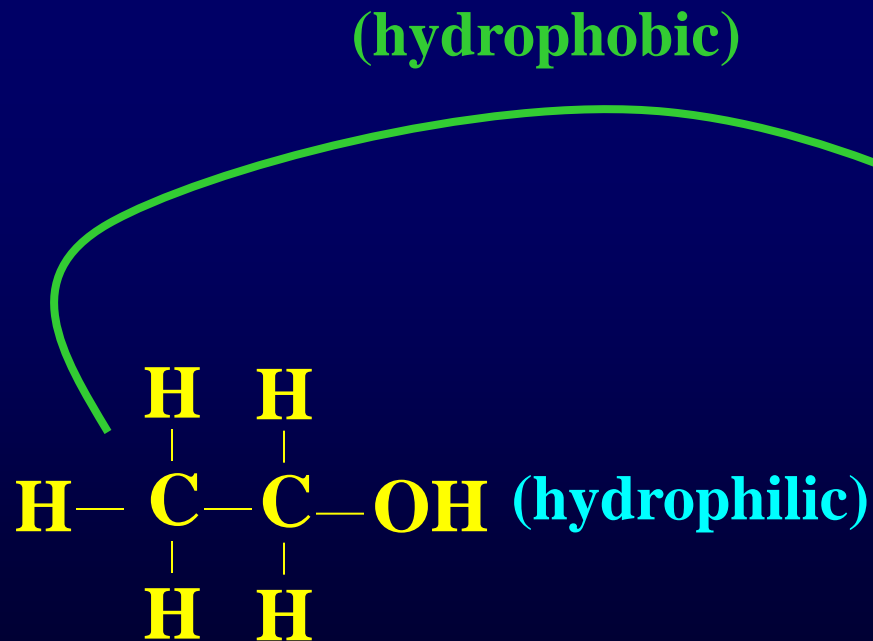
# How Does Alcohol (Ethanol) Work?

**Protein folding/shape/function is partly a result of the sequence of fatty and water-soluble side chains**



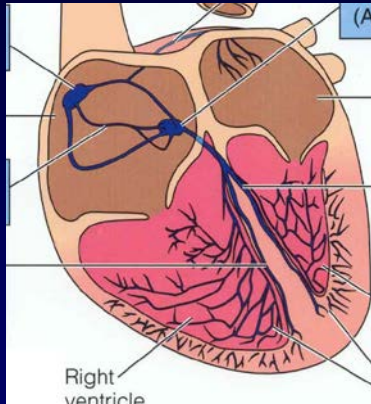
# How Does Alcohol (Ethanol) Work?

**Ethanol alters the folding and therefore the function of proteins**

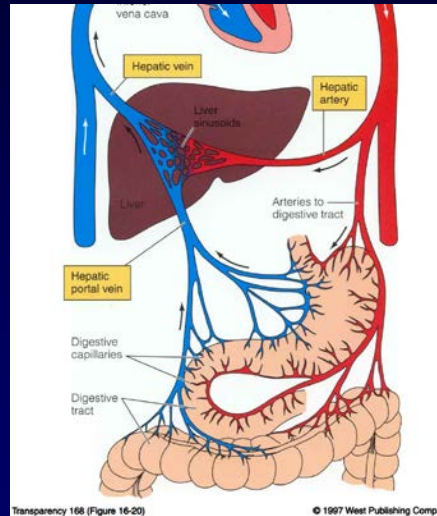




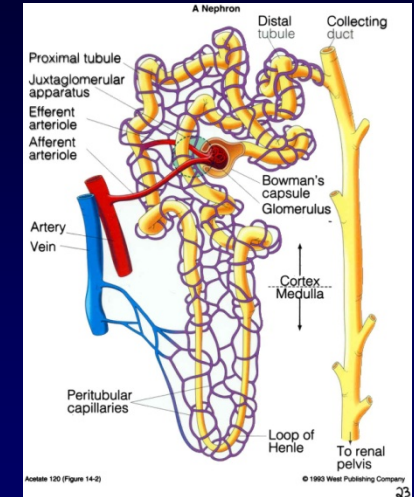
# Ethanol Affects All Body Systems



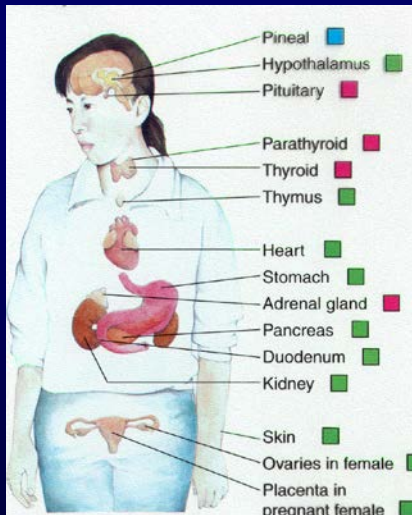
## Cardiovascular



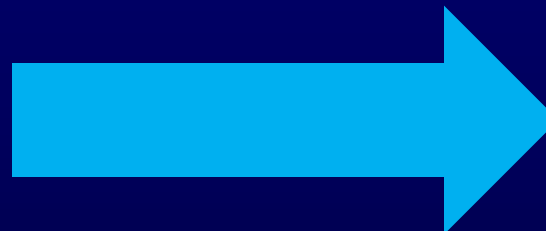
## Gastrointestinal



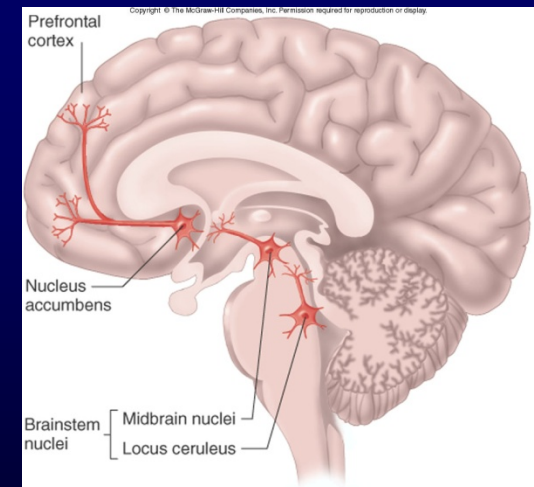
## Urinary



## Endocrine/ Reproductive



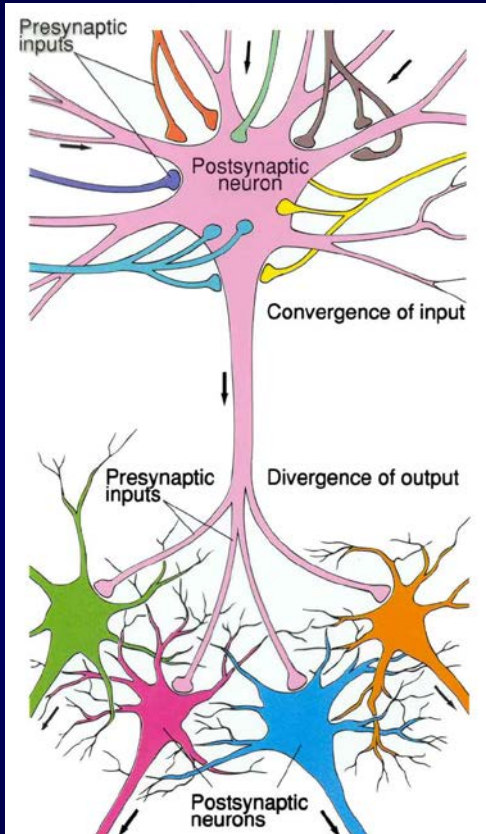
Self-medication  
efforts aimed  
at the brain



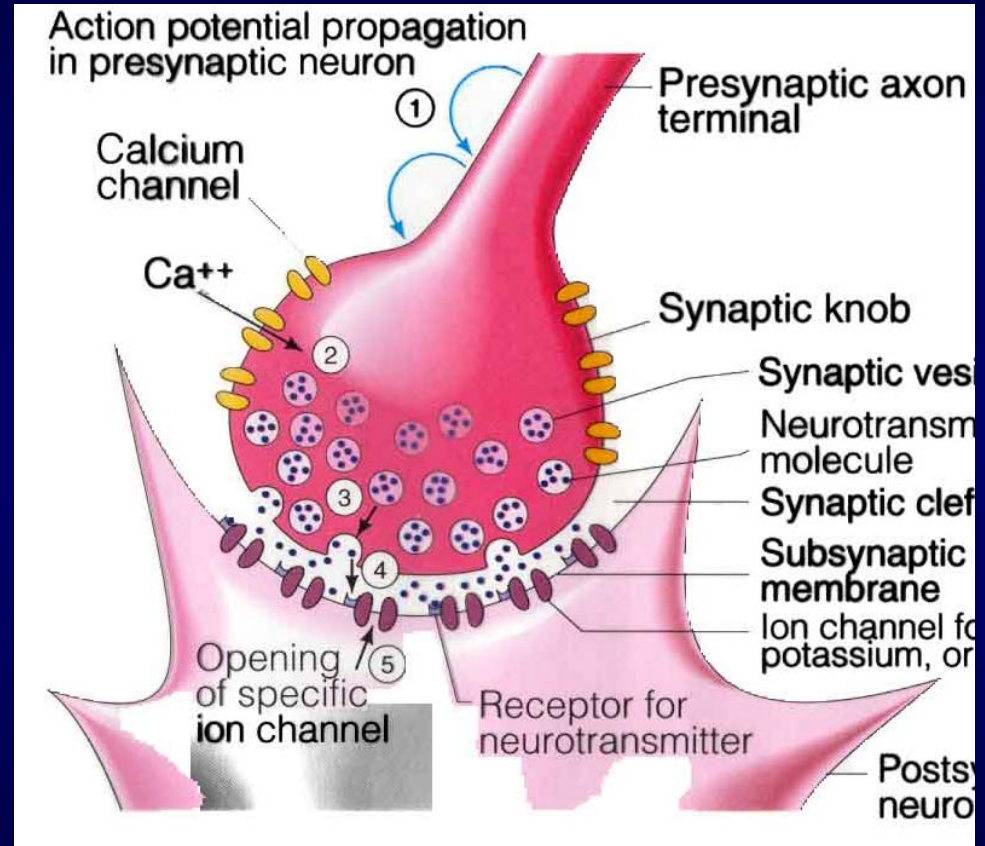
## Nervous system

# How Does Alcohol (Ethanol) Work?

## Ethanol affects synapses



**Neuron signals  
and networks**  
( x 100 billion!)



**Synapses, Neurotransmitters  
and Receptors**

# How Does Alcohol (Ethanol) Work?

## Ethanol affects multiple neurotransmitters

---

**Glutamate**

**GABA (Gamma-Amino Butyric Acid)**

**Endorphins**

**Serotonin**

**Dopamine**

**Acetylcholine**

**Glycine**

**Adenosine**

# Ethanol affects multiple neurotransmitters

---

**Glutamate**

**GABA (Gamma-Amino Butyric Acid)**

**Endorphins**

**Serotonin**

**Dopamine**

**Acetylcholine**

**Glycine**

**Adenosine**

**Differential sensitivities of these systems to dose, time course, and context can make alcohol an unpredictable drug!**

# Euphoria

1999

1999

1999

1999

1999

1999

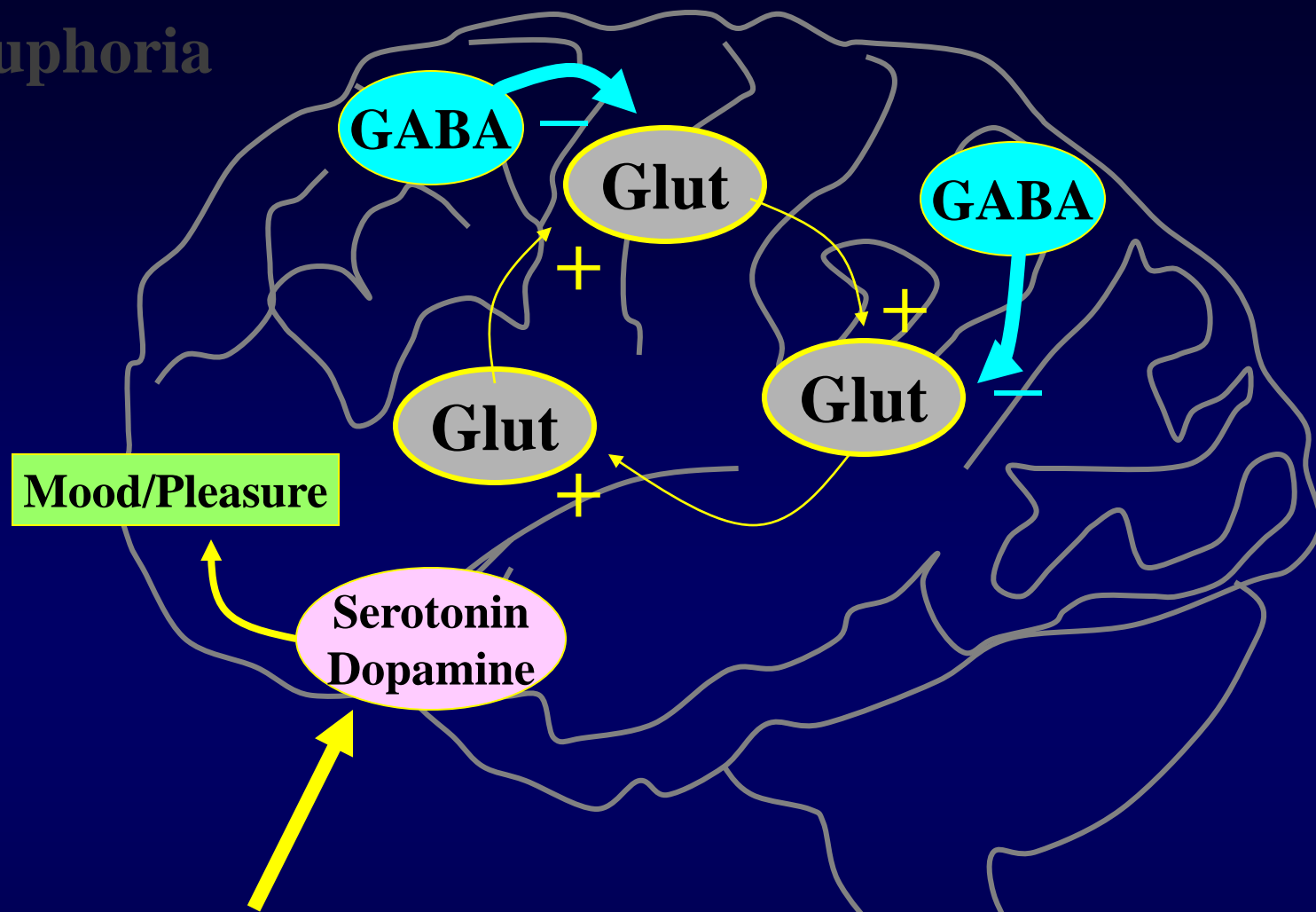
1999

1999

1999

1999

Euphoria



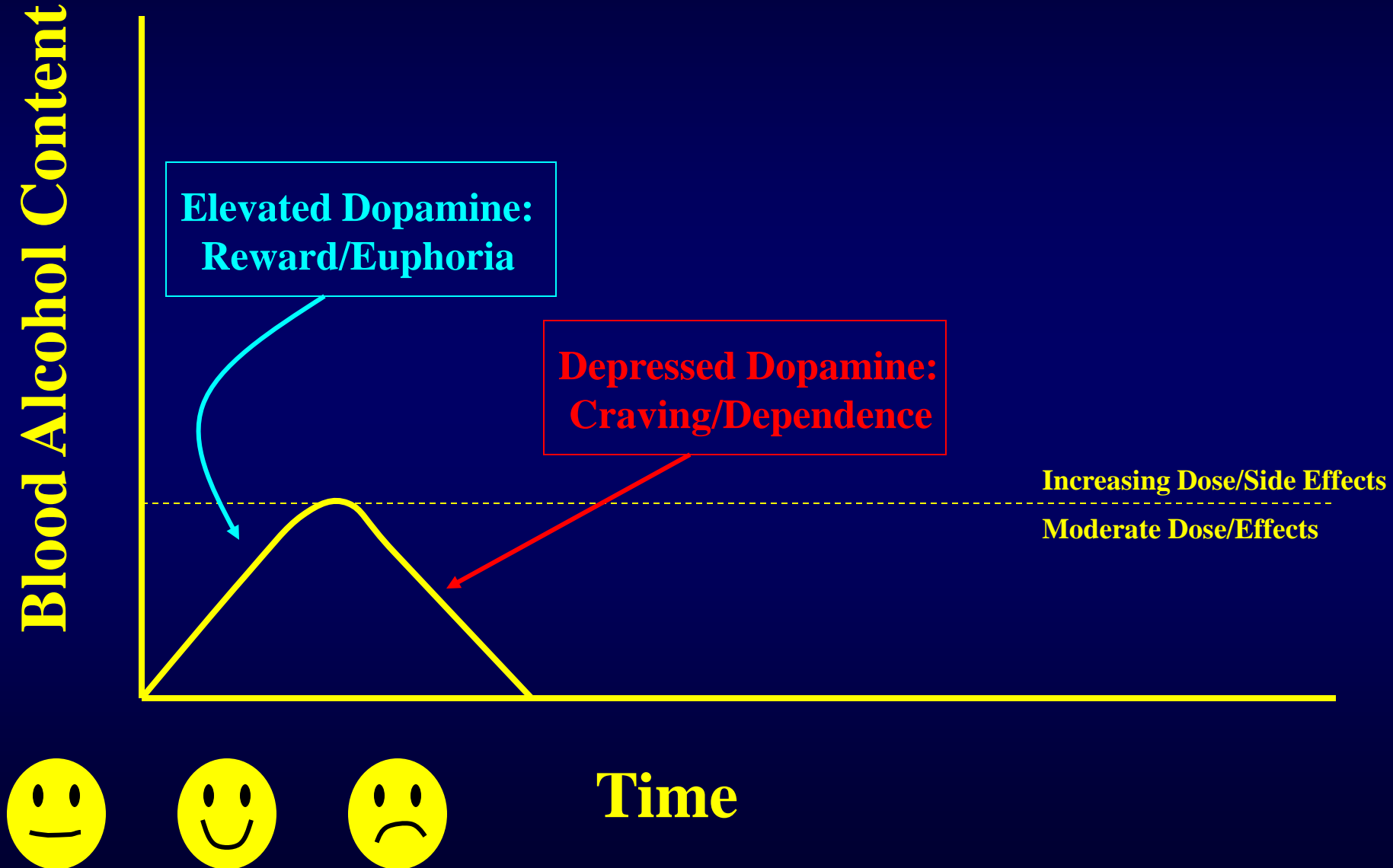
**Neurotransmitters of pleasure centers:**

**Ethanol increases dopamine signaling in “reward” centers in a way that reinforces binge drinking**



Euphoria

# Rising Phase Effect



**Euphoria**

**Rising Phase Effect**

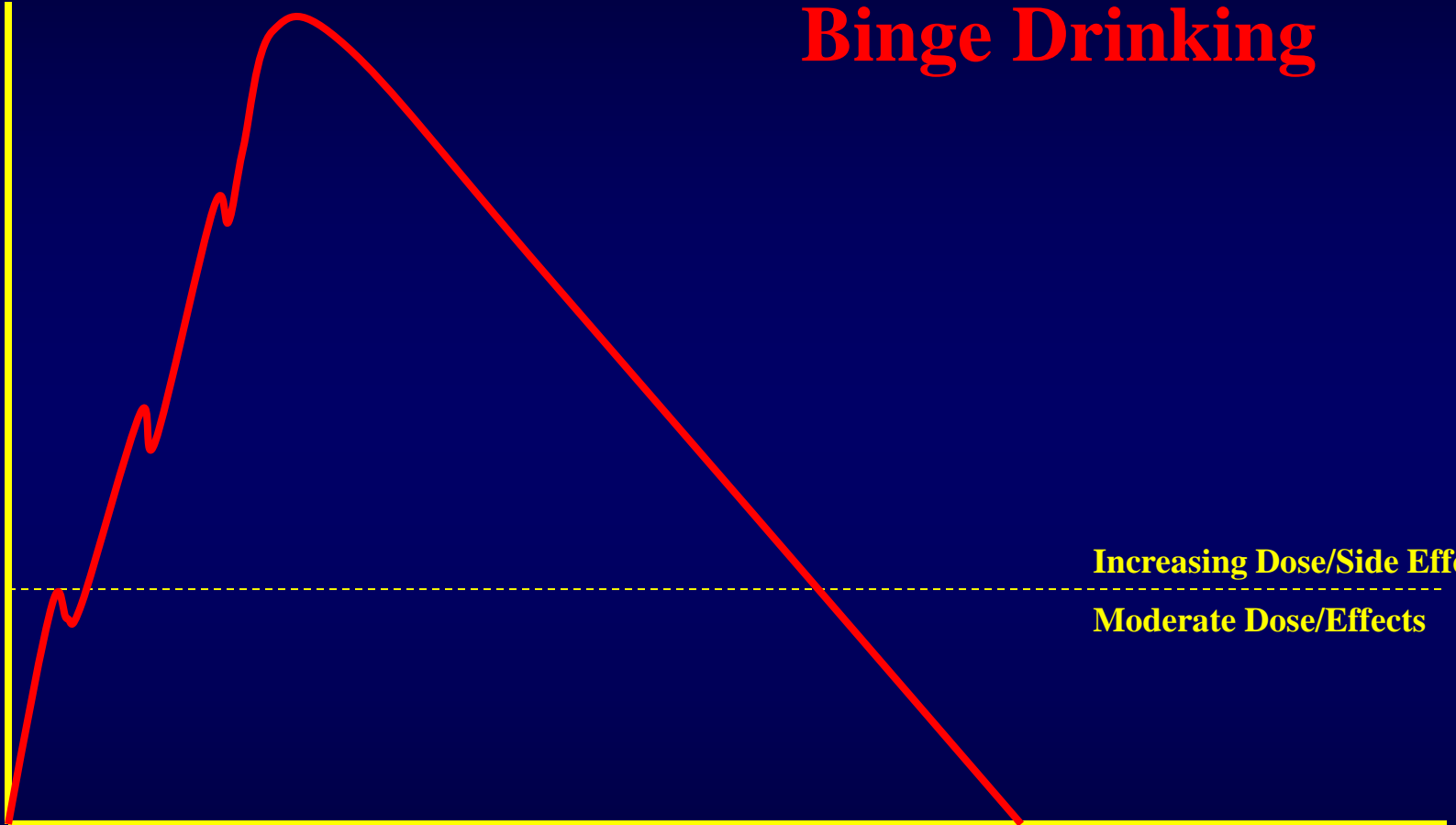
**Blood Alcohol Content**

**Binge Drinking**

**Increasing Dose/Side Effects**

**Moderate Dose/Effects**

**Time**



**Euphoria**

**Rising Phase Effect**

**Blood Alcohol Content**

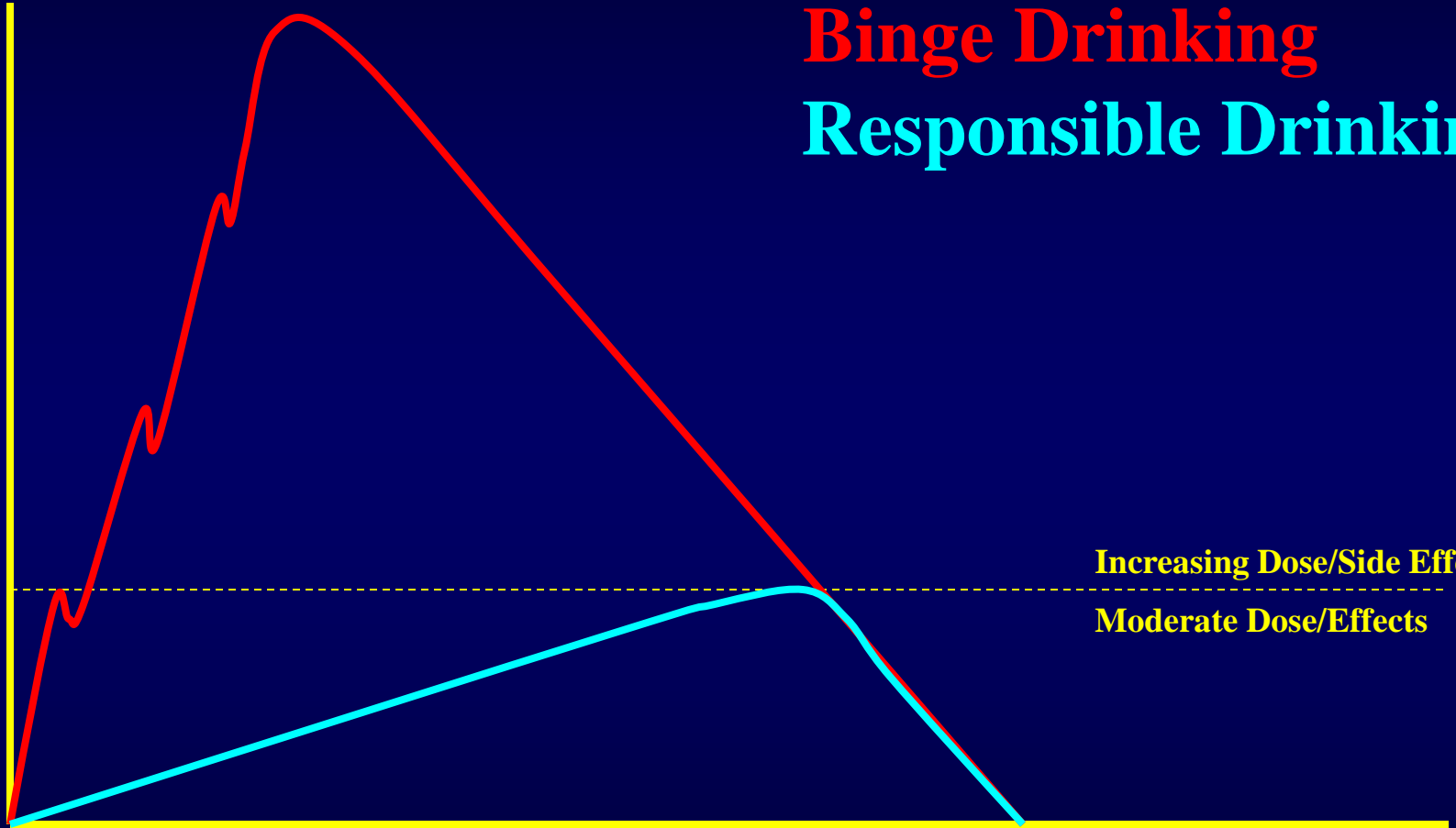
**Binge Drinking**

**Responsible Drinking**

**Increasing Dose/Side Effects**

**Moderate Dose/Effects**

**Time**



# Euphoria

## 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).

# Euphoria

**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....**



# Euphoria

**....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.**





# Euphoria

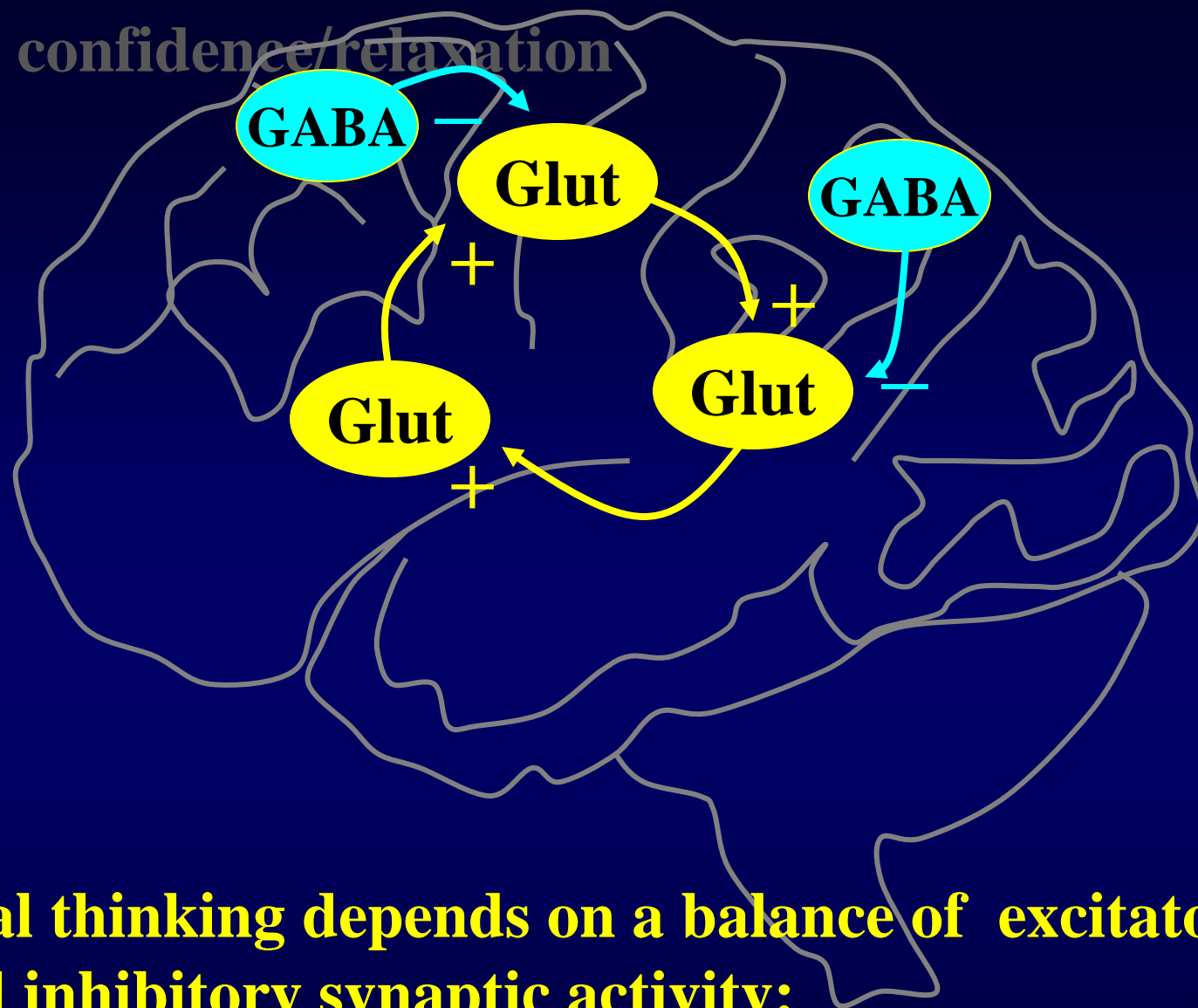
**According to the Centers for Disease Control:**

**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

Social confidence/relaxation



**Normal thinking depends on a balance of excitatory and inhibitory synaptic activity:**

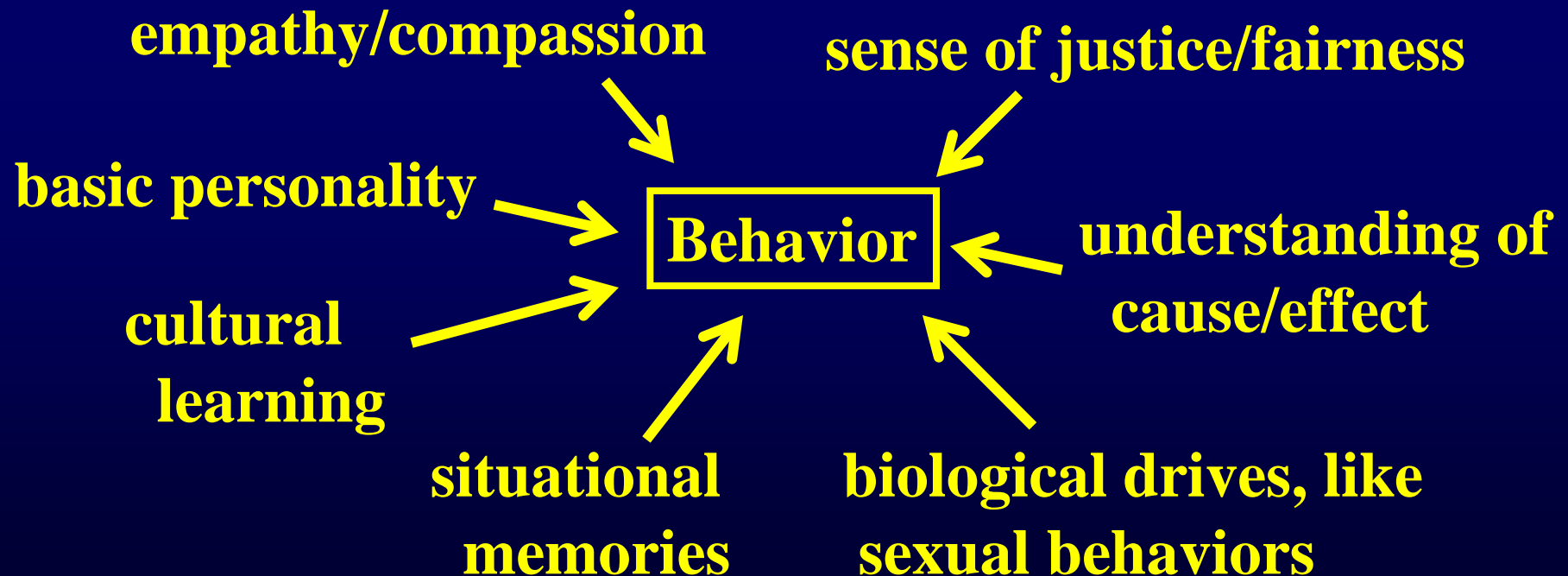
**→50% of the brain's synapses use Glutamate**

**→40% use GABA (gamma-amino-butyric acid)**

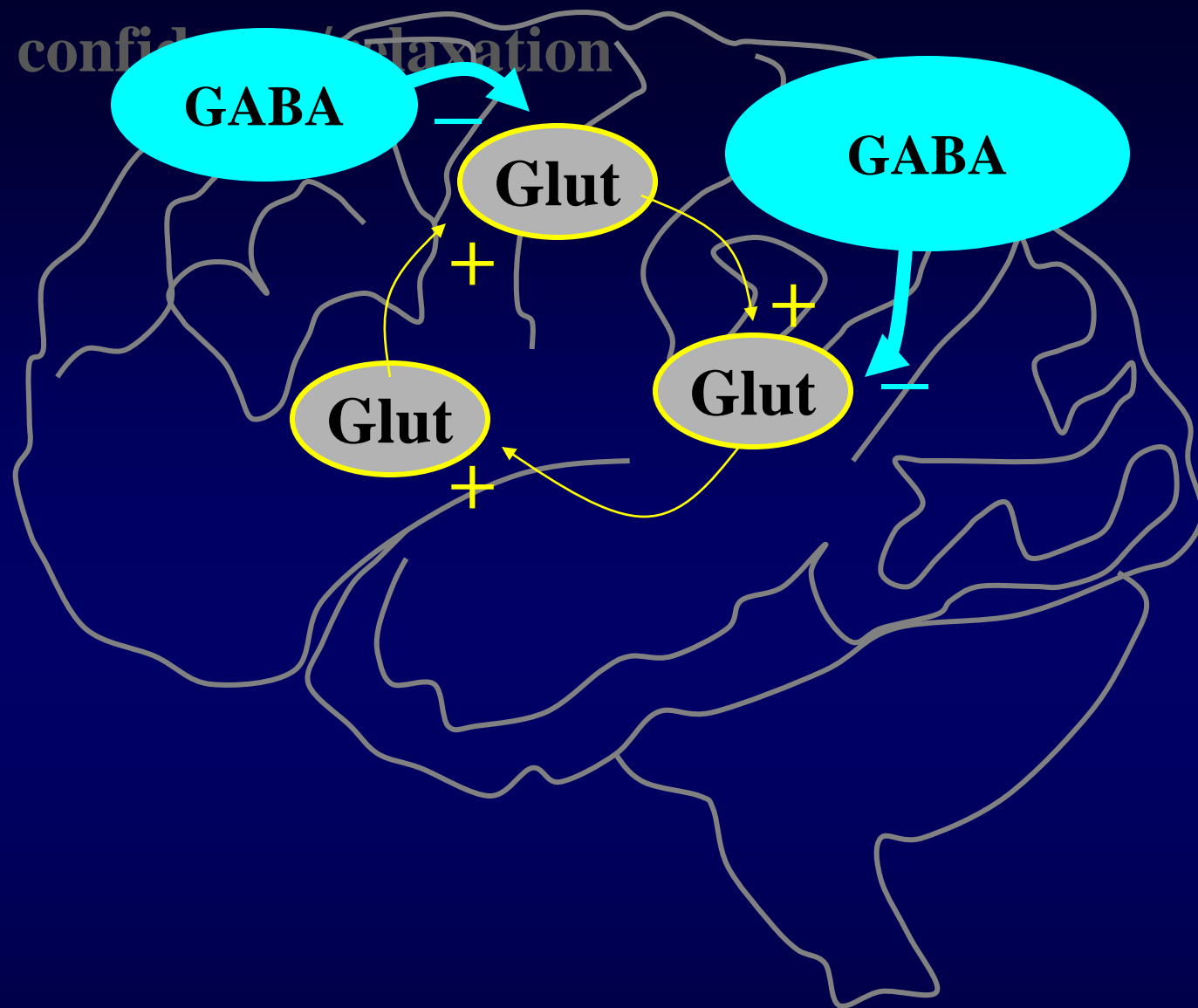
# Social confidence/relaxation

**Normally:**

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

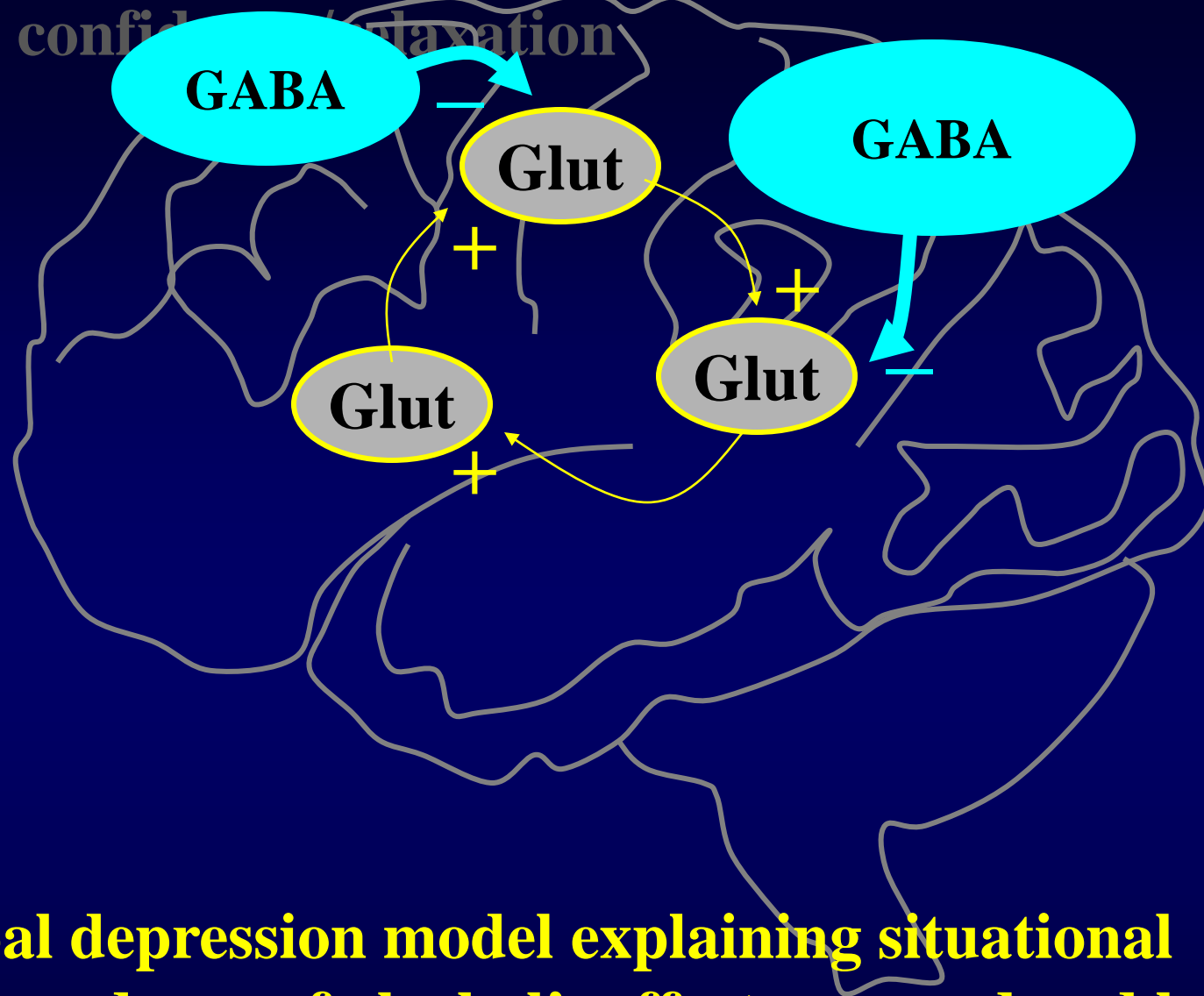


Social confidence / Relaxation



**Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.**

Social conflict / Relaxation



**Global depression model explaining situational dependence of alcohol's effect on mood and behavior:**

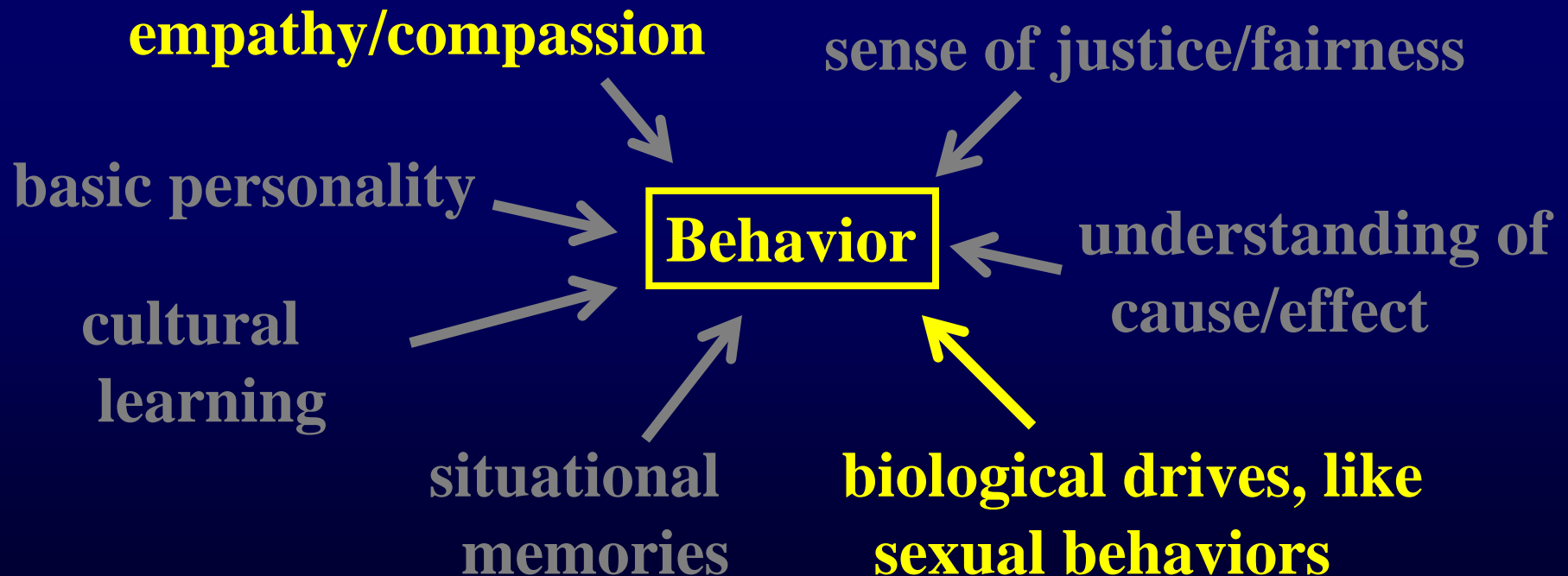
**ALCOHOL MYOPIA**



# Social confidence/relaxation

**As alcohol dose rises: ALCOHOL MYOPIA**

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



# Alcohol, Anxiety, and Public Speaking

Alcohol drinks

Volunteer subjects  
invited to a party

Placebo drinks

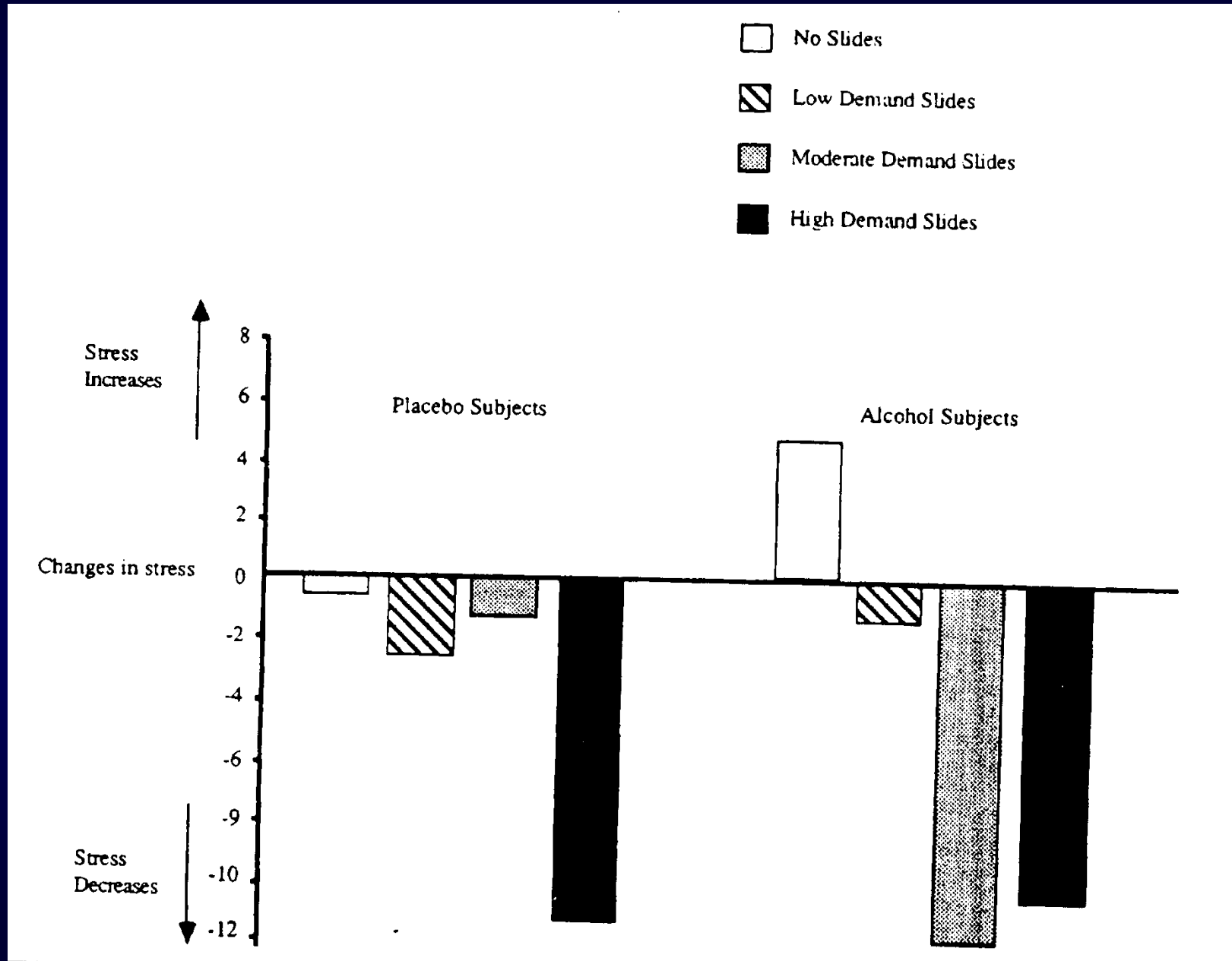
**“In 15 minutes, you have to go on stage and give an impromptu speech:”**  
*What I dislike most about my body and physical appearance*

**ANXIETY**

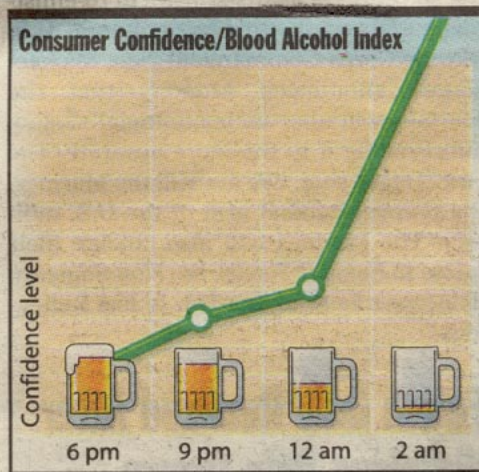
**ANXIETY**

	Sit and think	
	Easy slide sorting task	
	Moderate difficulty slide sorting task	
	Complicated slide sorting task	

# Alcohol, Anxiety, and Public Speaking



## Alcohol myopia can boost self-confidence

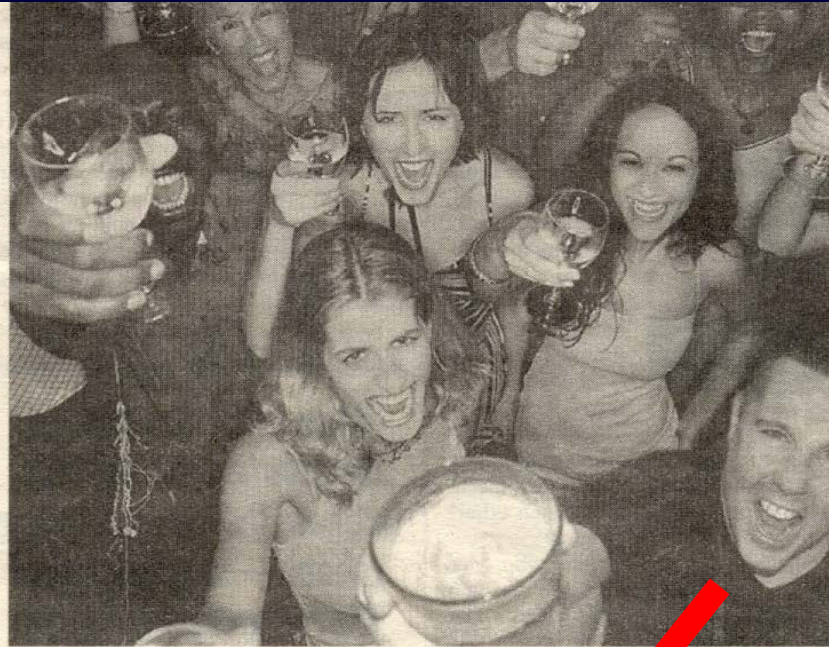


### Alcoholic-Beverage-Consumer Confidence Skyrockets

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.”

see CONFIDENCE page 9



Above: A group of alcohol consumers in Boston.

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

maudlin conversations about relationship troubles. In severe cases, however, the spikes 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 so many friends and seemed like she was doing her own thing,” Britmer said. “But then at 2 a.m., she came over to me and asked me to dance.”

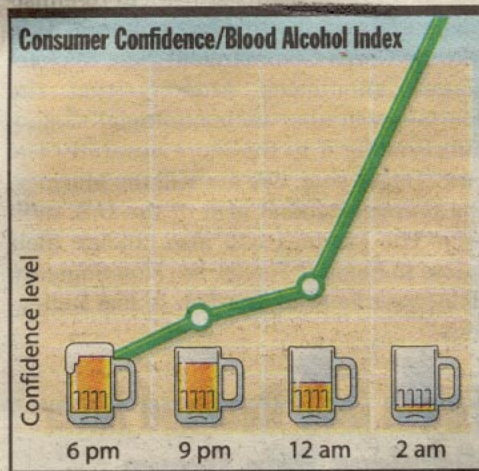
**“You know the secret to getting women? Being a total asshole.”**

showed a 47 percent increase in dancing

**from:  
The Onion**



## Alcohol myopia can boost self-confidence

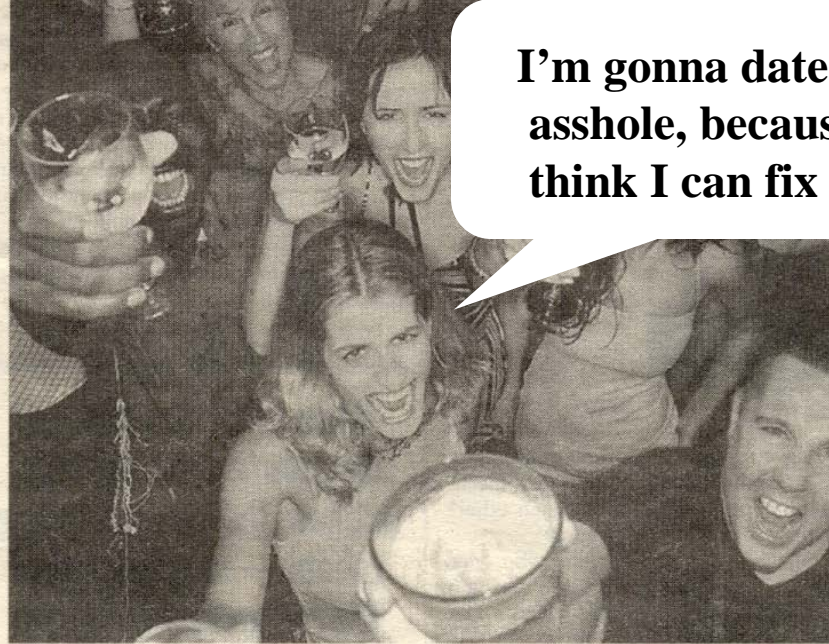


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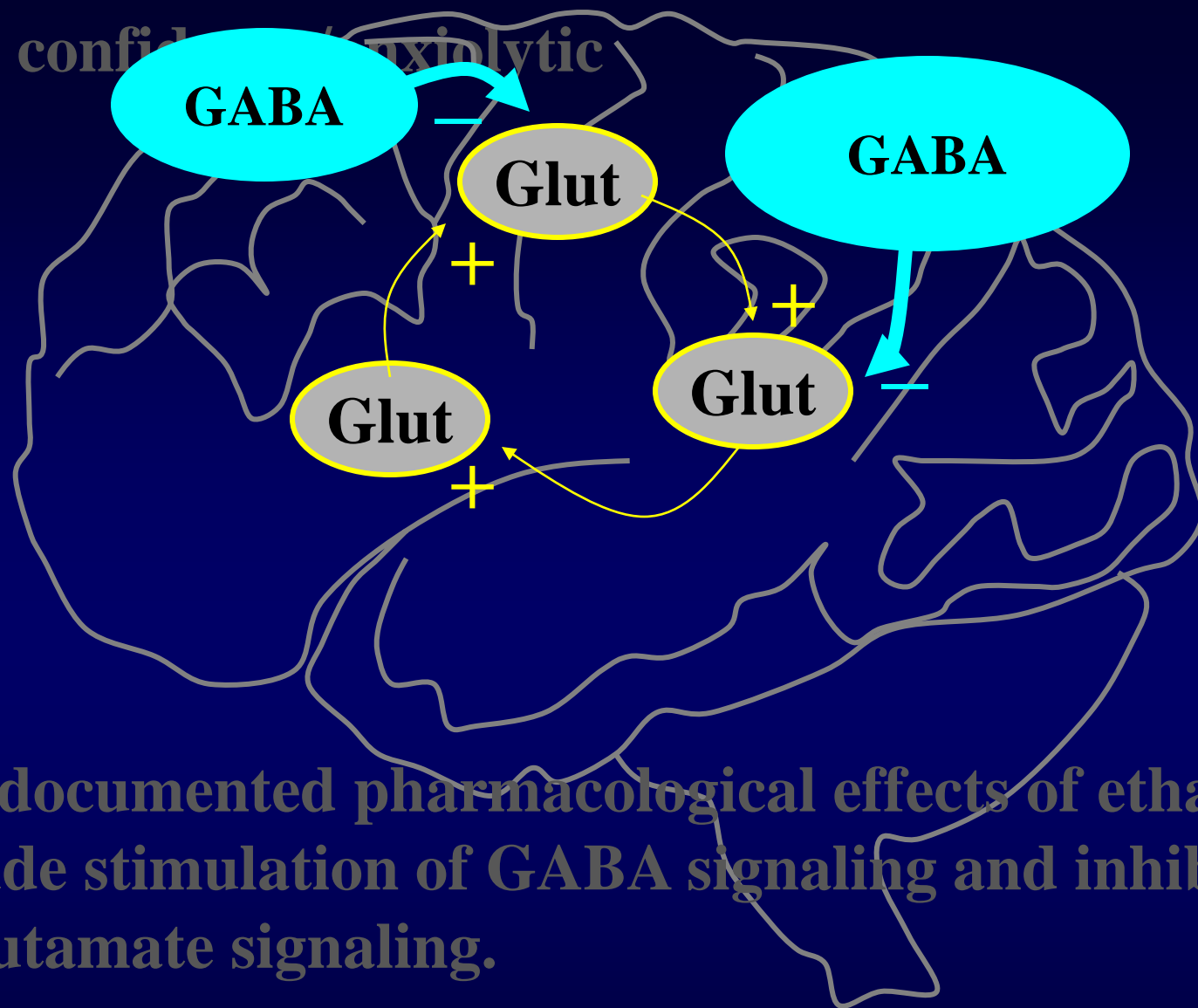
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Social confidence / anxiolytic

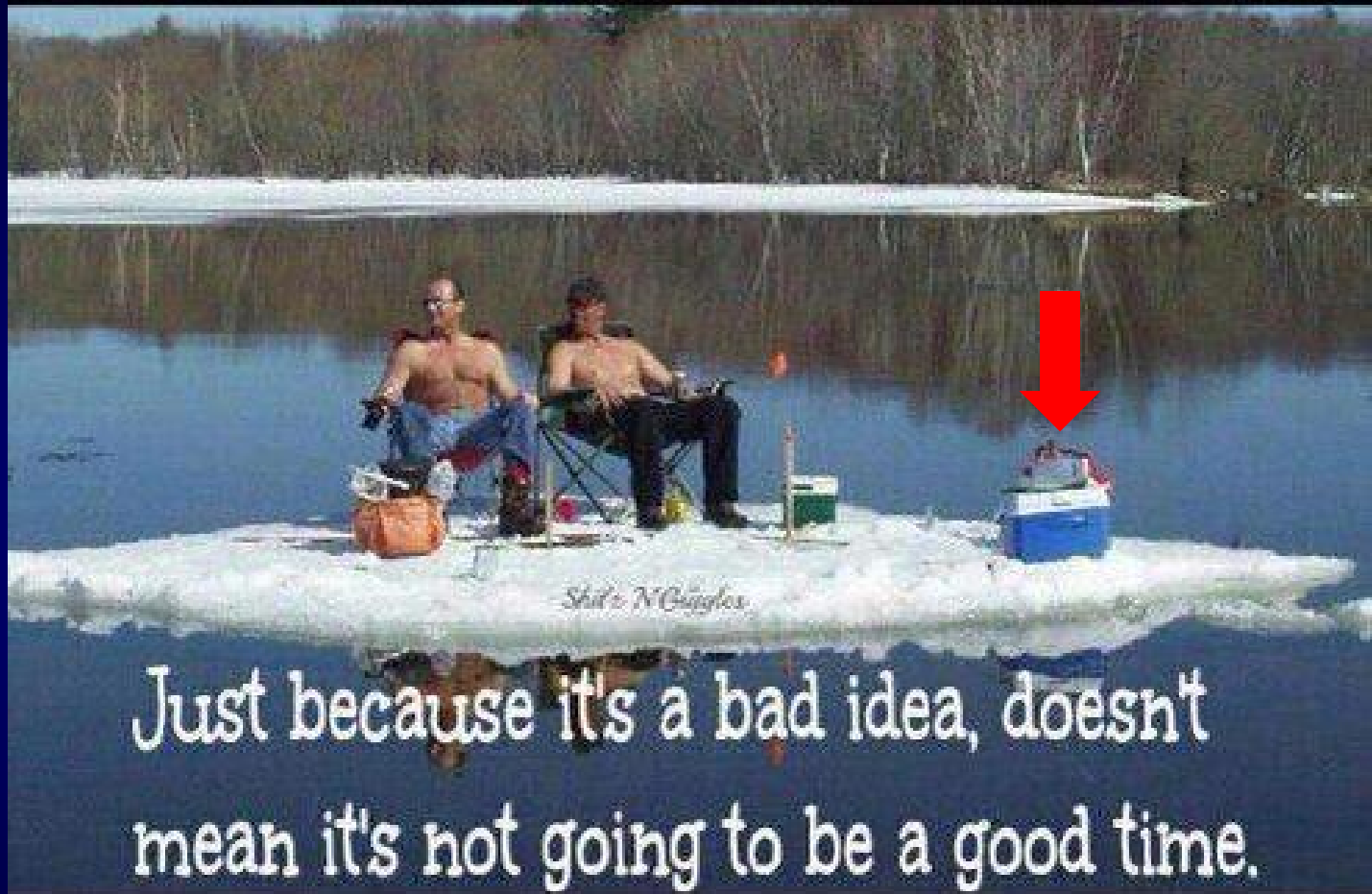


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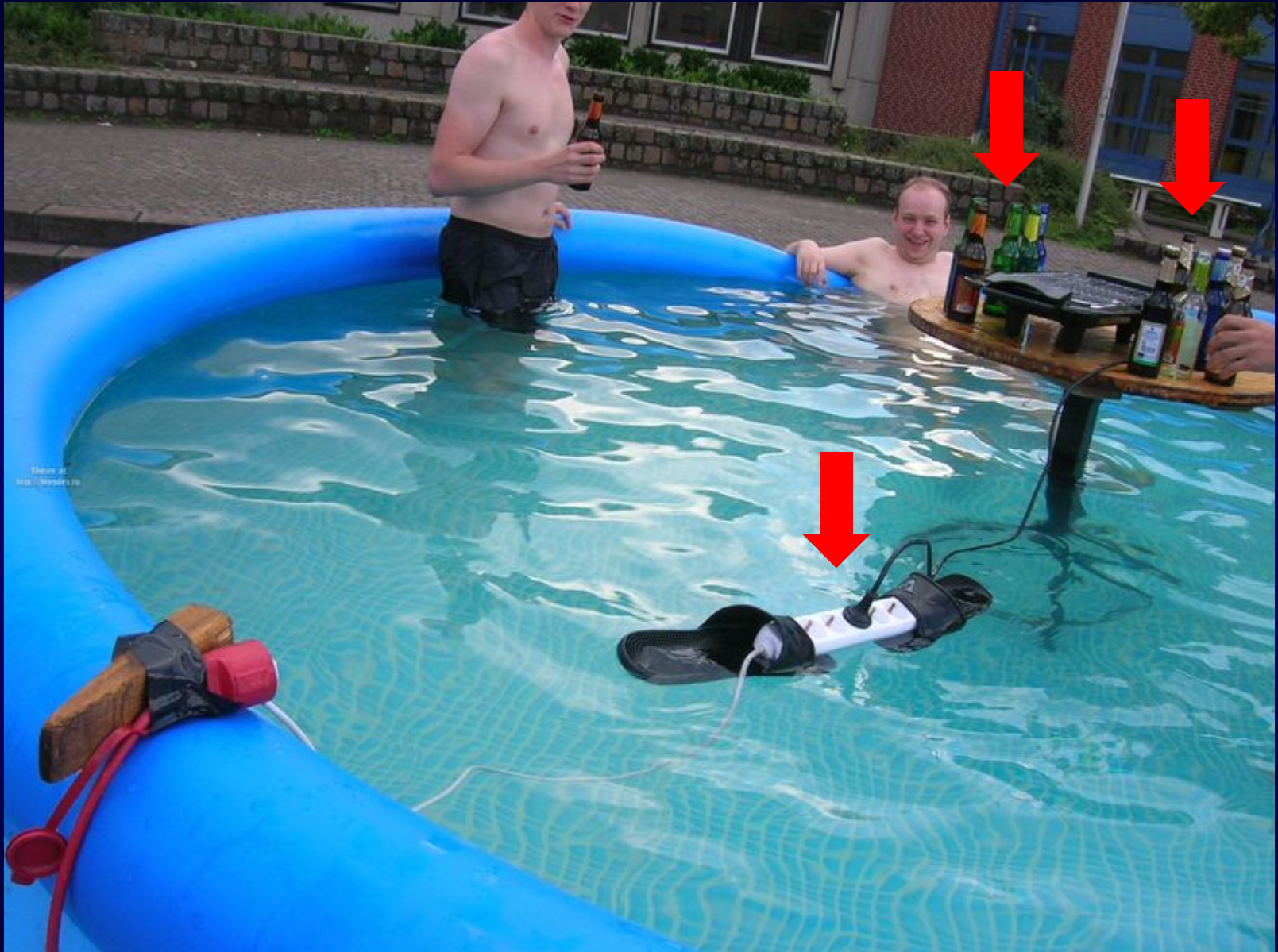
**As the dose goes up so may confidence, but appropriate decision-making is increasingly impaired....**



# Social confidence/anxiolytic



# Social confidence/anxiolytic





# Social confidence/anxiolytic



## Social confidence/anxiolytic



**CDC: 38% of emergency room visits are alcohol-related**

Social confidence/anxiolytic

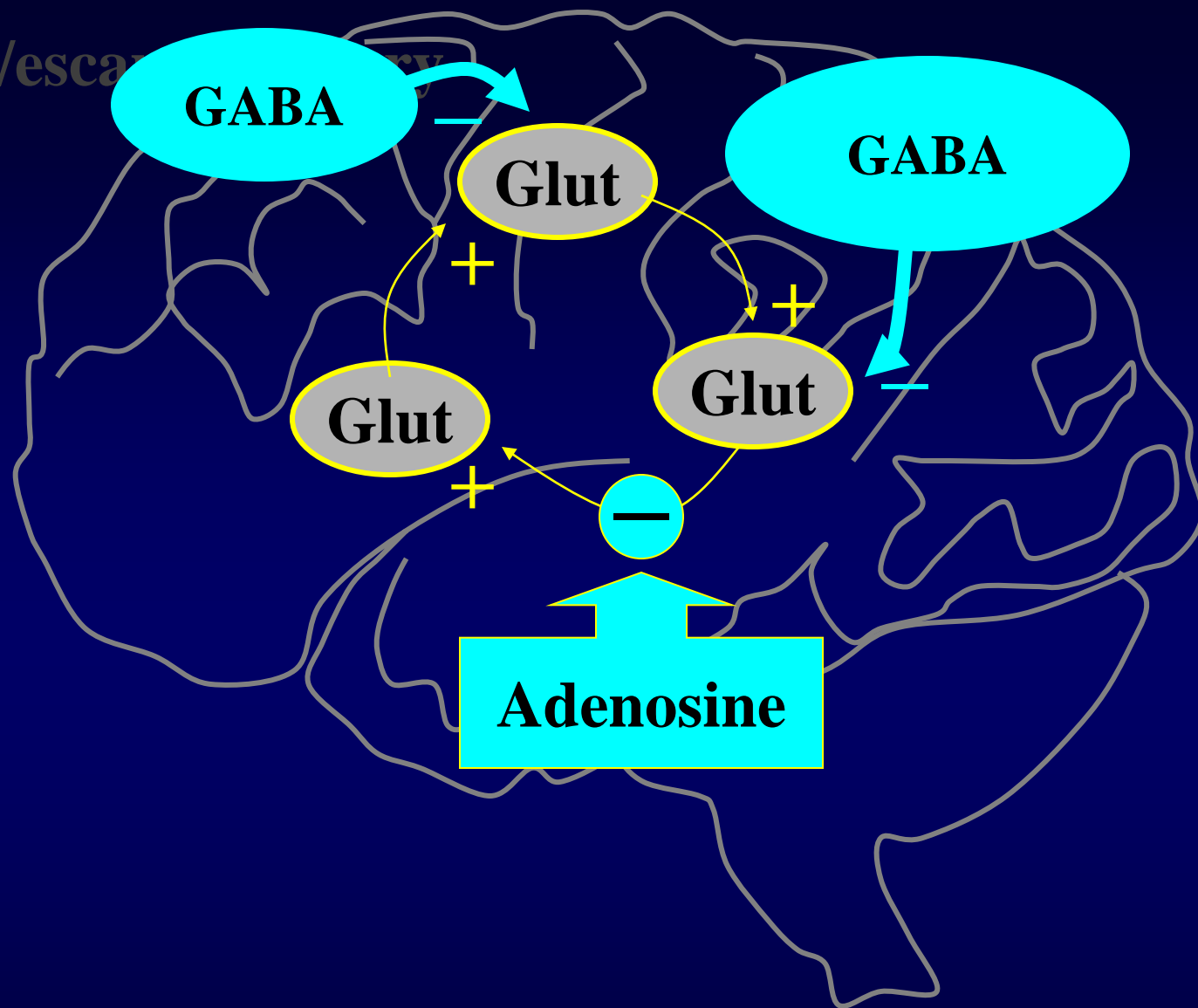
**Effects on cognition are reversible in adults, but.....**



**.....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

Sleep/escape



**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

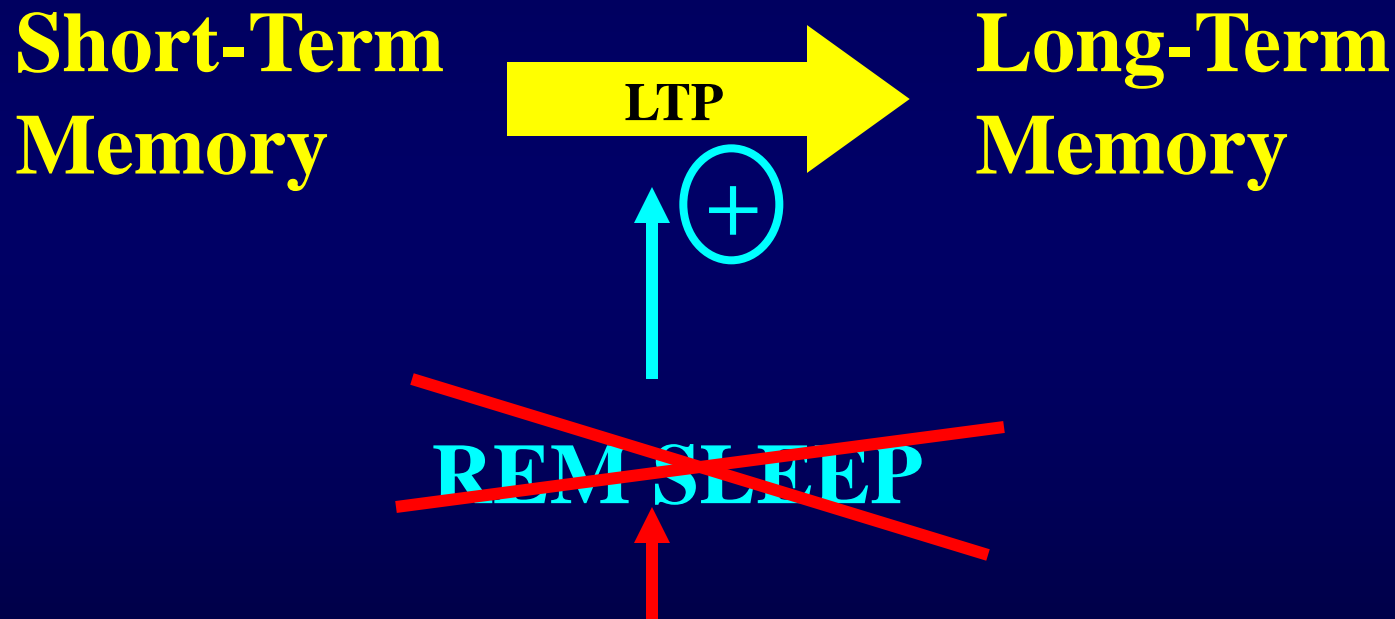


**Sleep/Escape**



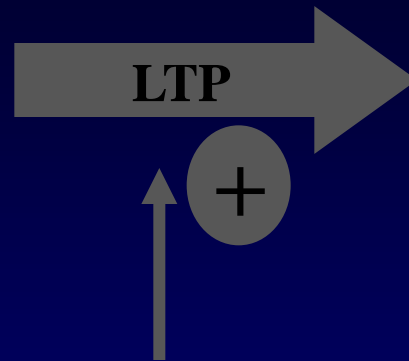
**RECENT LEARNING RESEARCH**

# Sleep/Escape



**ALCOHOL IMPAIRS REM SLEEP SO  
SO IT INHIBITS MEMORY FORMATION**

**Sleep/Escape  
Short-Term  
Memory**



**Long-Term  
Memory**

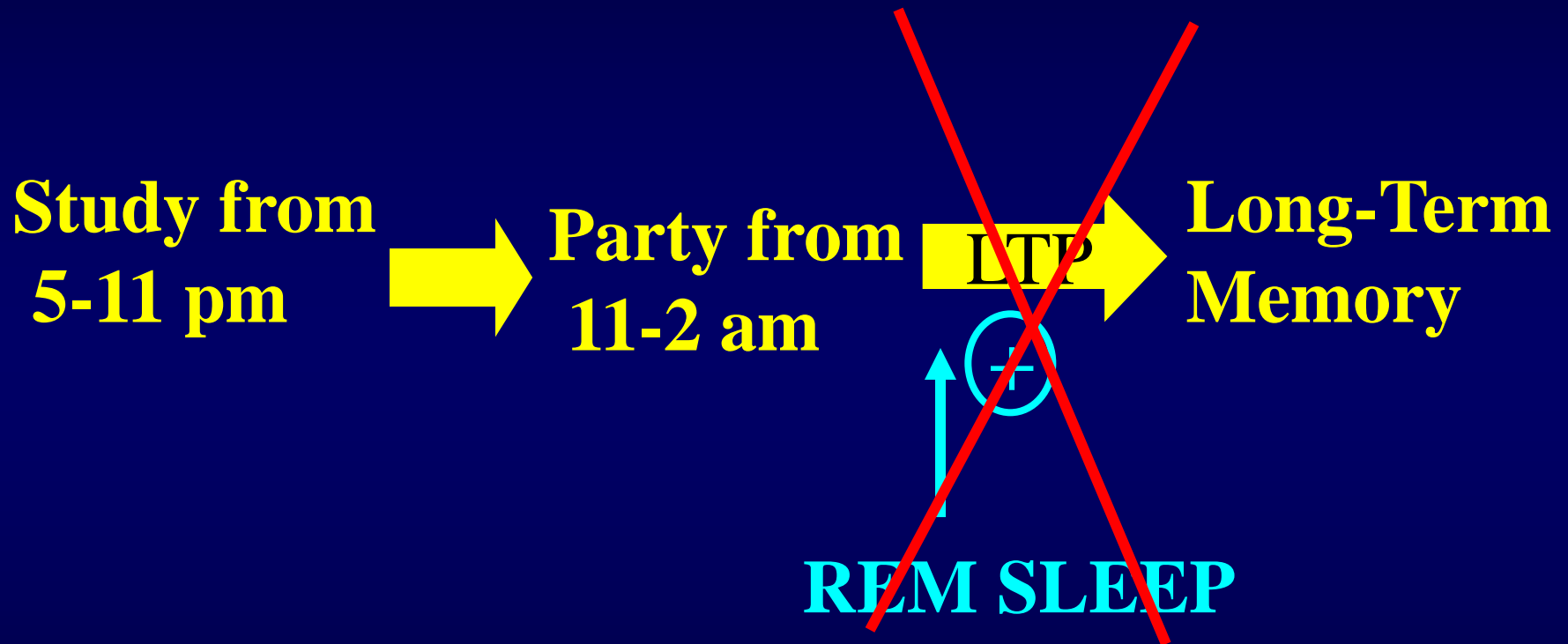


**Inhibits formation of NEW memories not old,  
so escape from past problems isn't possible;  
if anything, alcohol myopia MAGNFIES them**

**Alcohol abuse is a leading cause of depression**

# Sleep/Escape

**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**

# **Culture/Ancestry**

**Animal studies reveal genetic and developmental basis for variation of alcohol effects and preference**

# Fruitfly experiments create “Cheapdates”

1



## Fruitfly experiments create “Cheapdates”

1



2



Hic....burp!



## Fruitfly experiments create “Cheapdates”

3

1



2



Hic....burp!



I can fix  
this guy!

## Fruitfly experiments create “Cheapdates”

1



2



Hic....burp!

3



I can fix  
this guy!

4



## Fruitfly experiments create “Cheapdates”

3

1



2



Hic....burp!



I can fix  
this guy!

4



Hey, you  
want to--

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**



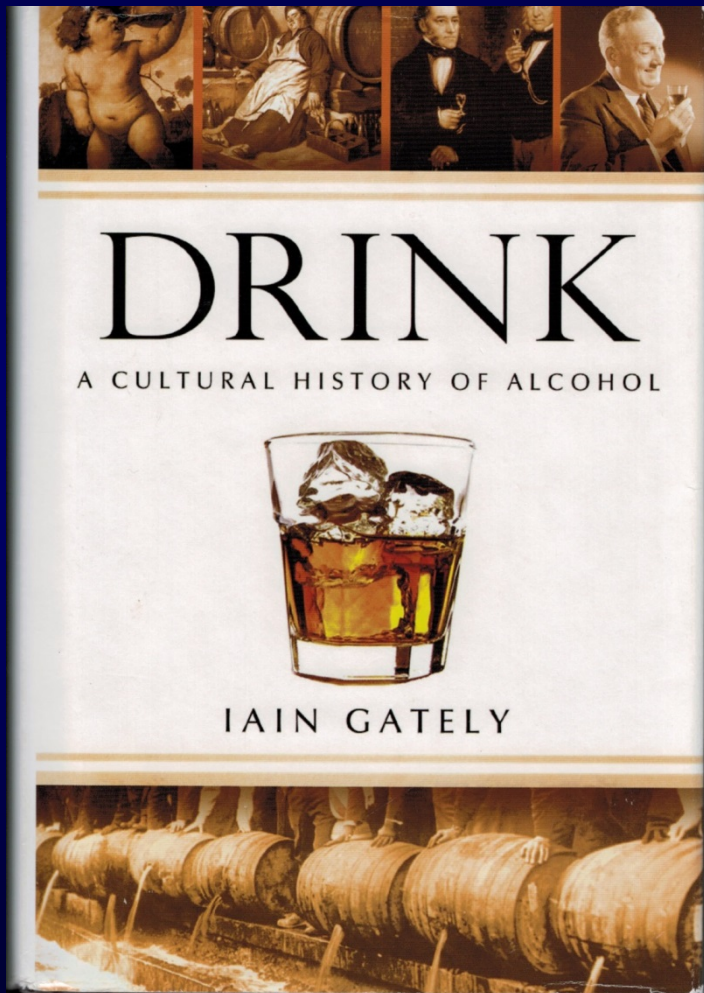
**Alcohol abuse can also be induced developmentally  
by exposing young animals to neglect/abuse**



**Drunk Monkeys (NIH)**

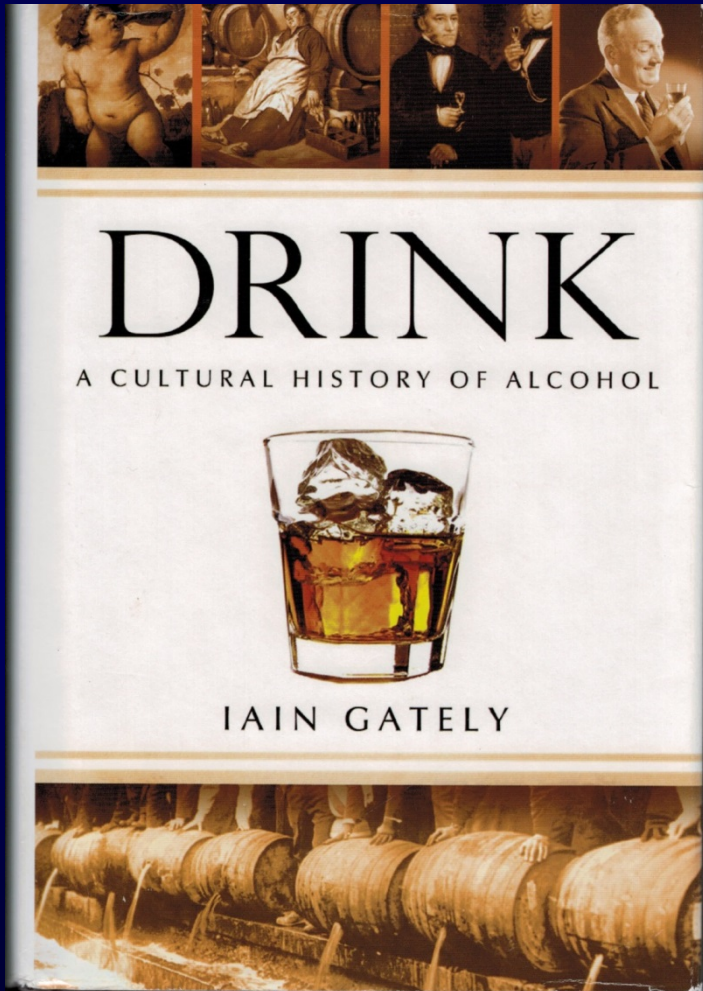
[discovermagazine.com/2002/jul/featdrunk](http://discovermagazine.com/2002/jul/featdrunk)

**Some historians argue that most humans have been selected for alcohol preference and tolerance**



# Culture/Ancestry

Some historians argue that most humans have been selected for alcohol preference and tolerance



**First evidence of alcohol production, 8000 BC, after humans took up agriculture and established sedentary communities**

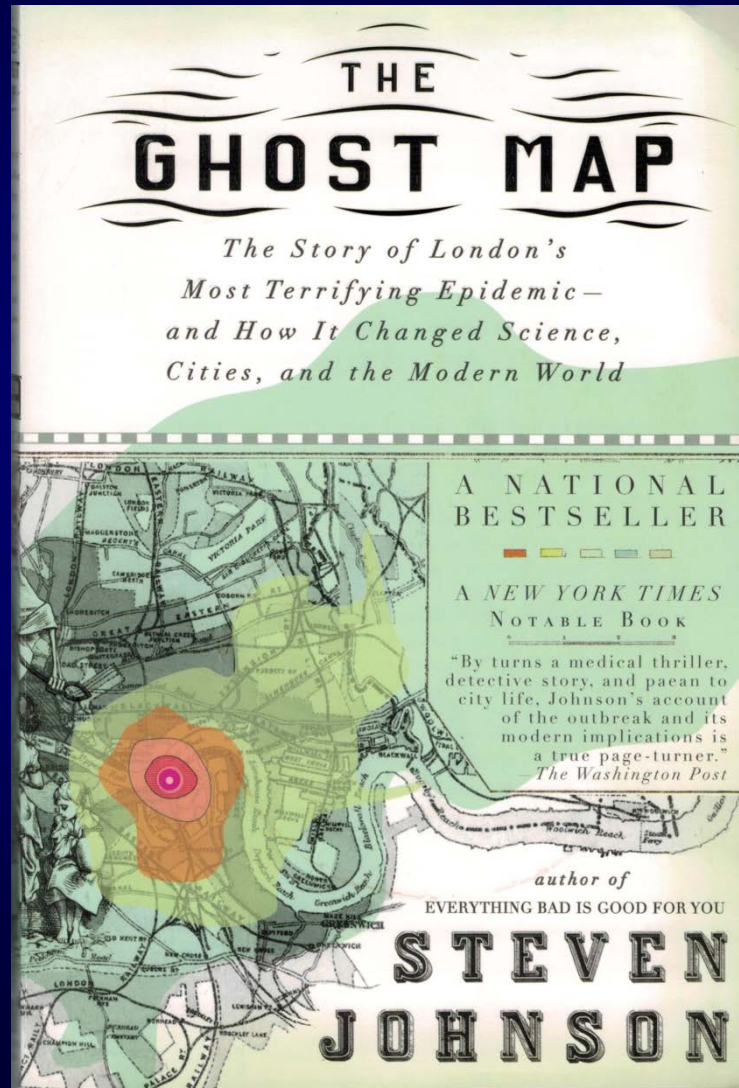
**By 1000 BC, all over the world where humans had settled into towns, alcohol was consumed**

**Most modern humans are descendants of these cultures**



# Culture/Ancestry

Some historians argue that most humans have been selected for alcohol preference and tolerance



# Culture/Ancestry

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## The Ghost Map



700 deaths in 2 weeks all around the Broad Street pump

# Culture/Ancestry

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## The Ghost Map



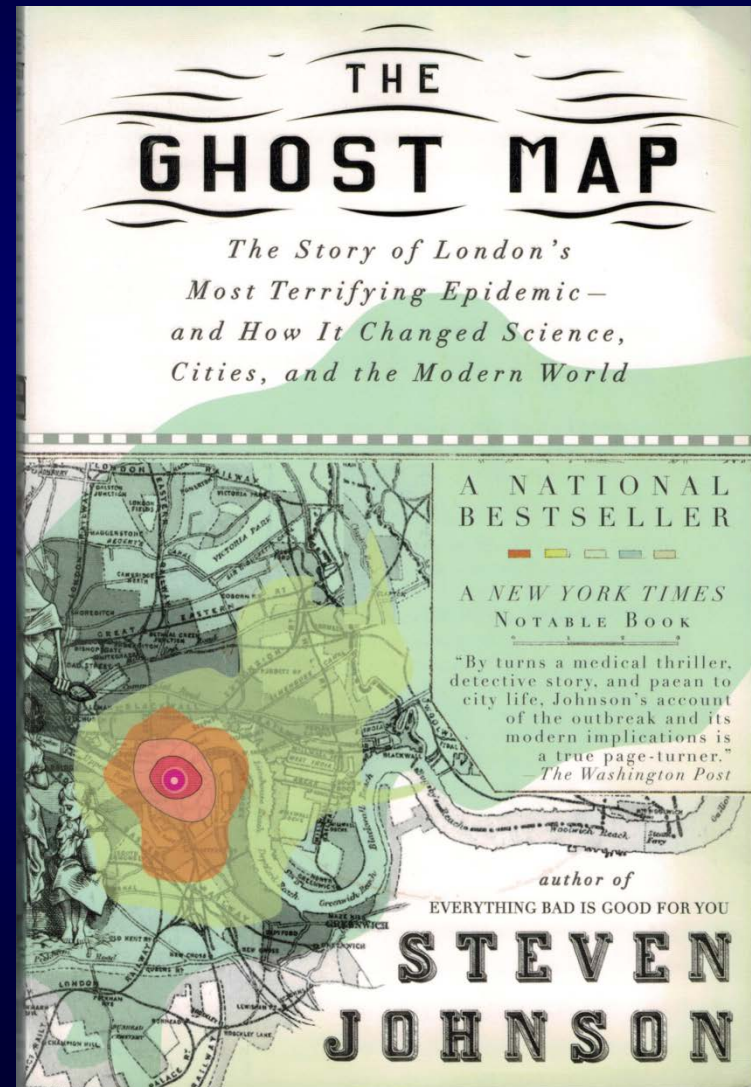
700 deaths in 2 weeks all around the Broad Street pump

Not a single worker of the Lion Brewery died: they received an allotment of ale as part of their wages

# Culture/Ancestry

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



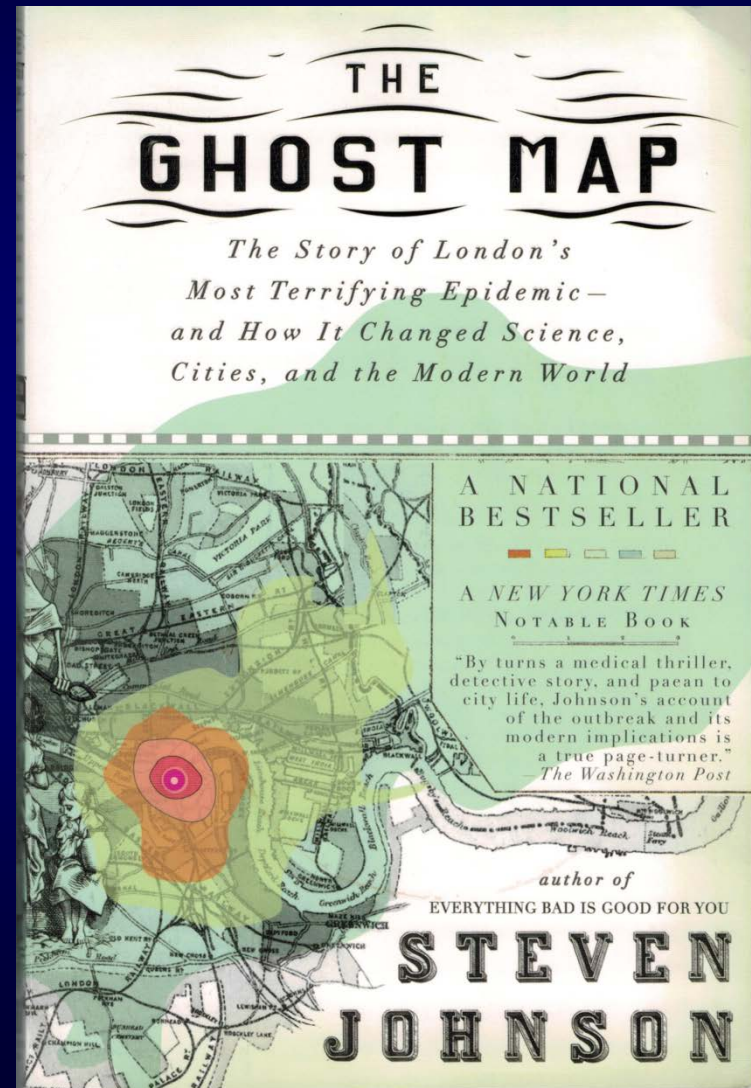


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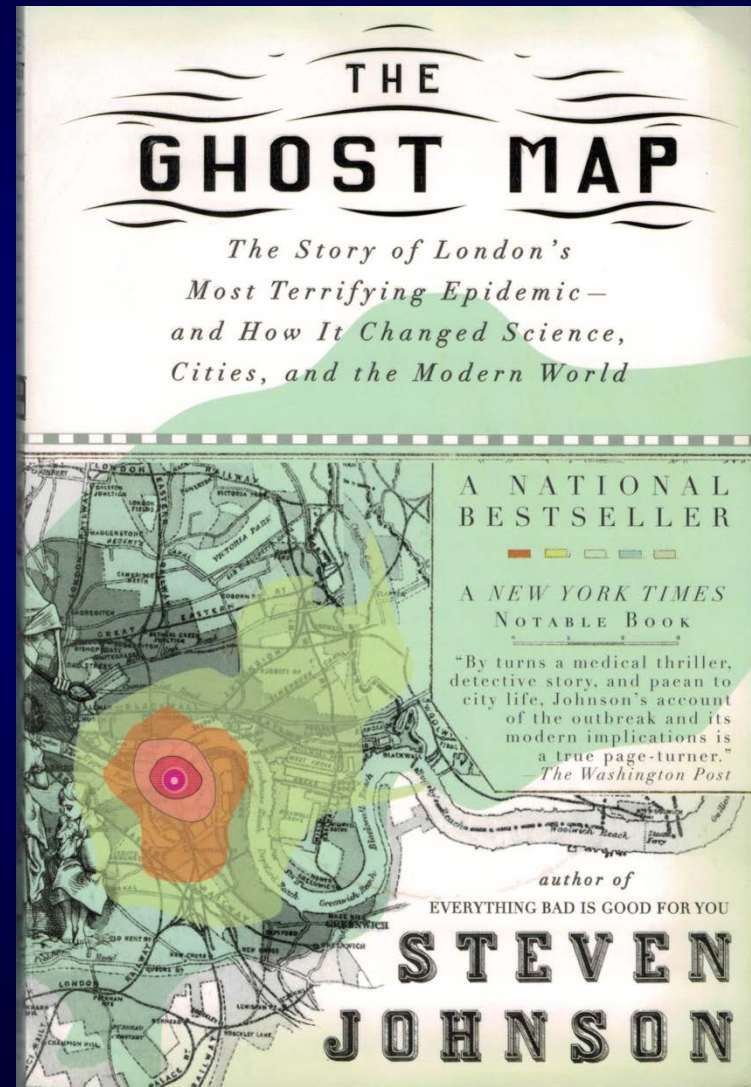
Water in cities was inevitably tainted with sewage, resulting in epidemics of cholera and dysentery

Those who preferred alcohol to water (and could handle its toxicity) survived more often and had children that survived



# Culture/Ancestry

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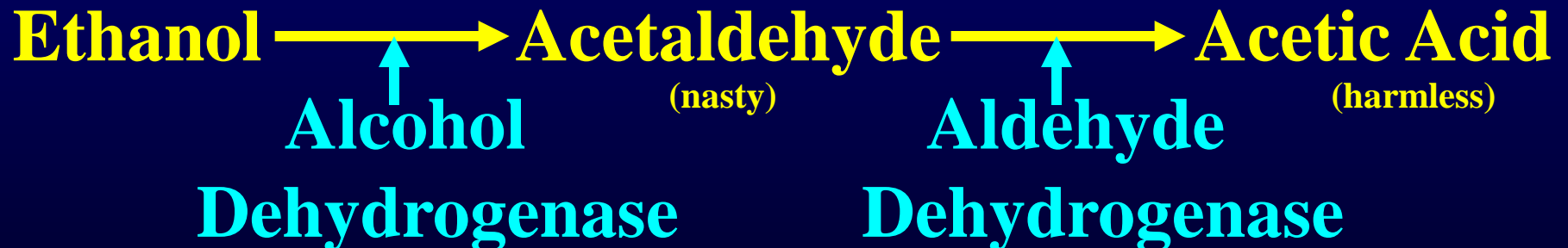
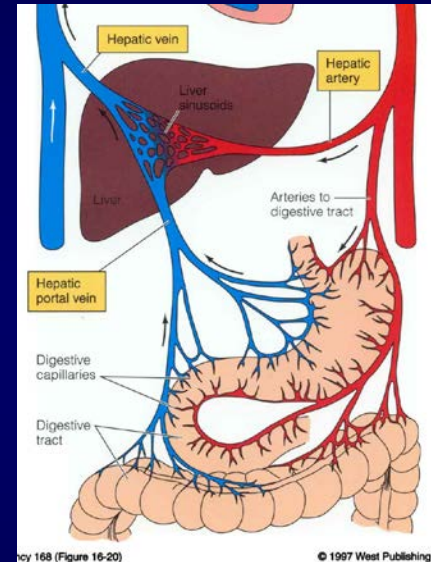
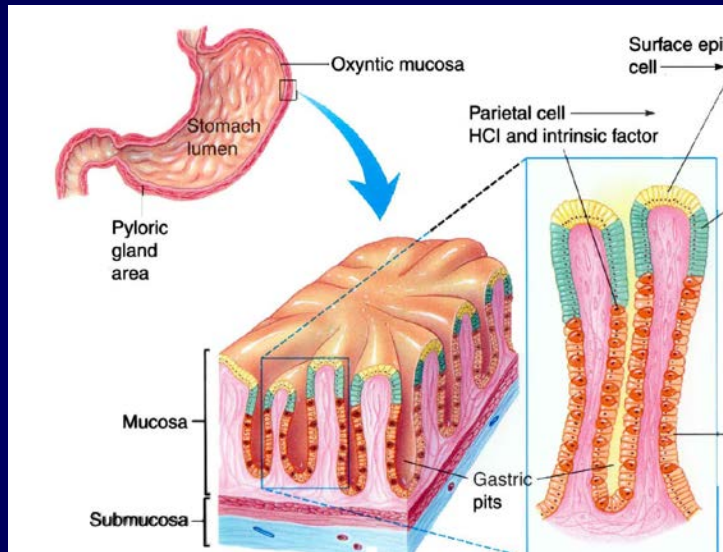


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**Native Americans and Australian Aborigines were not exposed to alcohol until modern times**

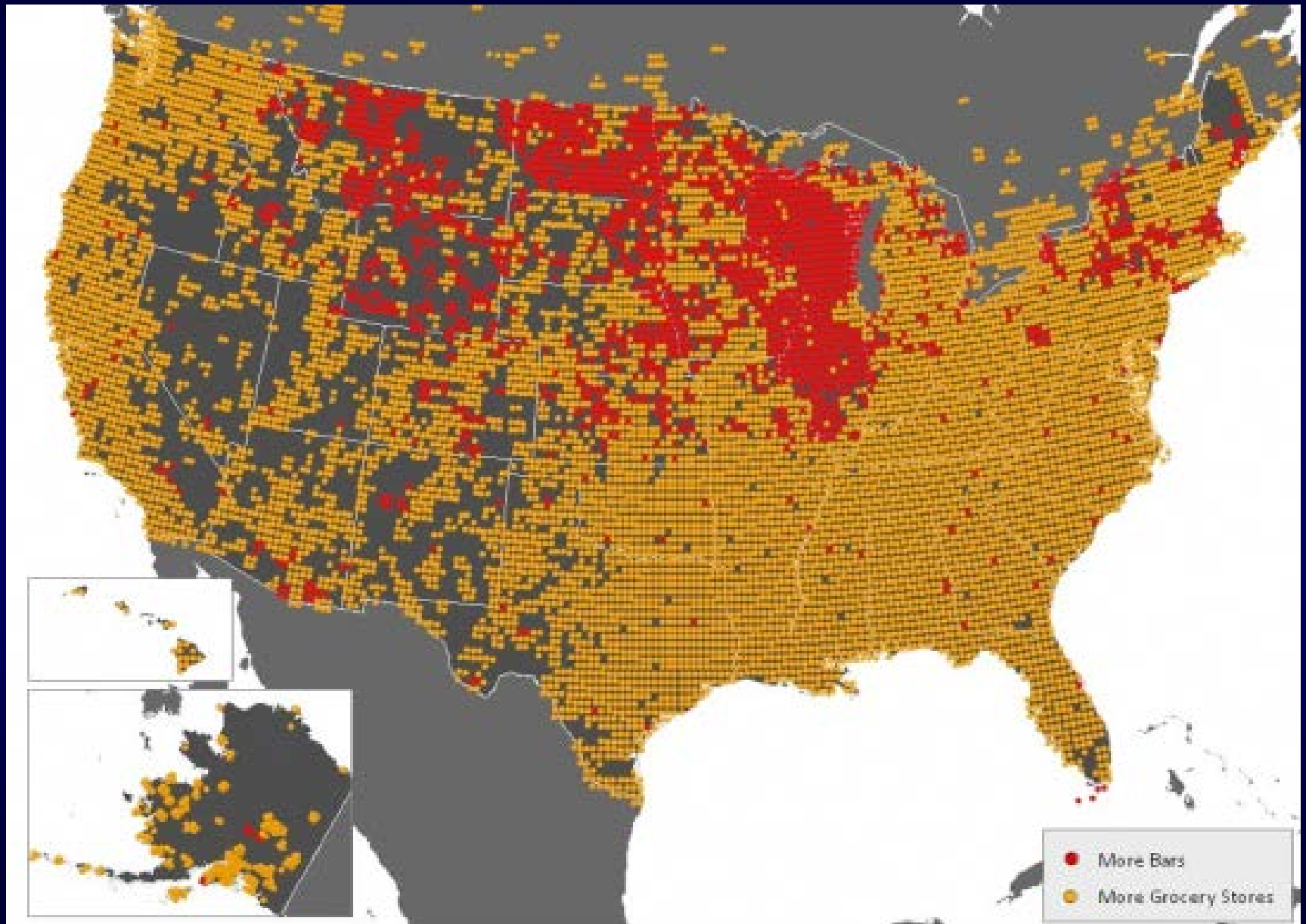
People vary not only in synapse proteins that determine neural effects of alcohol, but also in detox enzyme expression





**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**

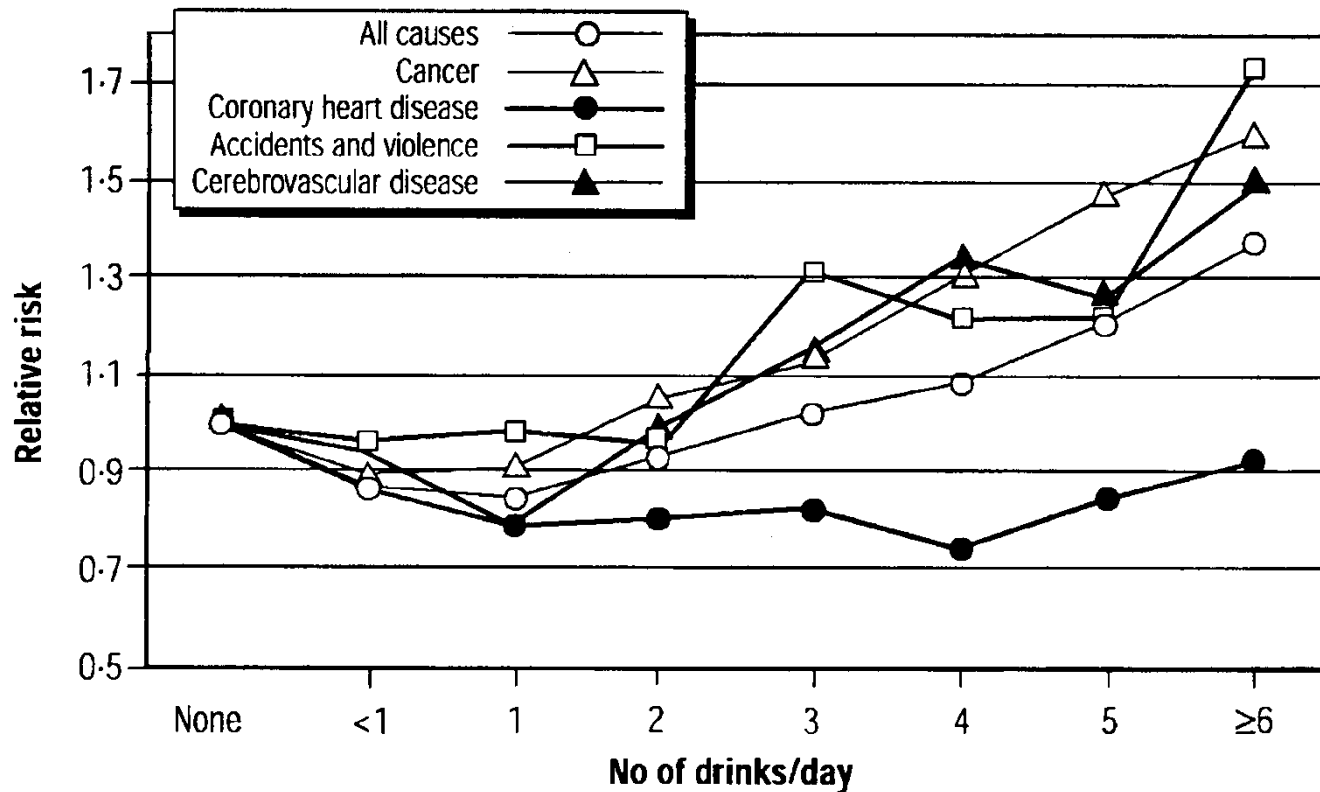
(#50!)  
~~We're #1!~~



**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....**