

Physiology of the World's Second-Most Popular Drug

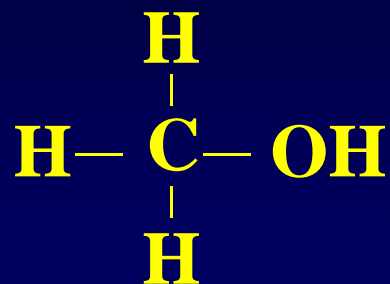
Kevin T. Strang, PhD
Department of Physiology



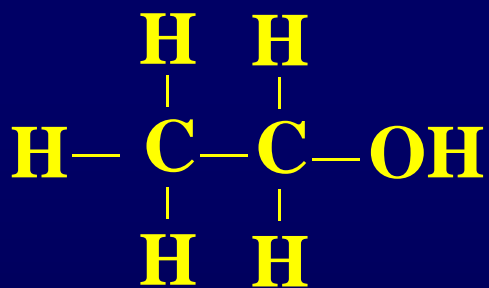
University of Wisconsin
**SCHOOL OF MEDICINE
AND PUBLIC HEALTH**

- 1. Cellular mechanism of ethanol effects**
- 2. Effects of ethanol on the nervous system**

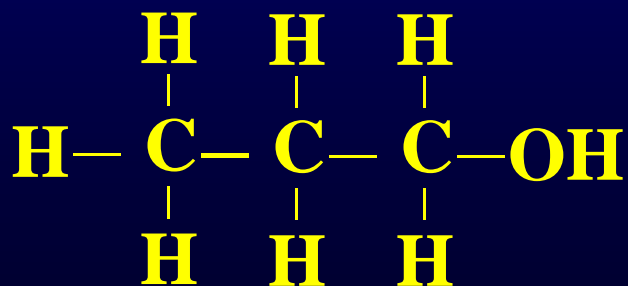
Alcohol Structure



Methanol

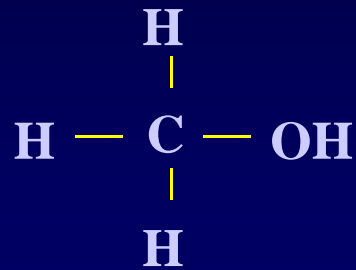


Ethanol

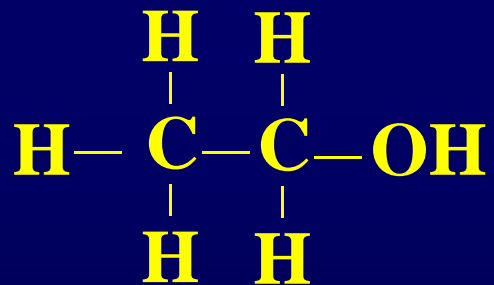


Propanol

Alcohol Structure

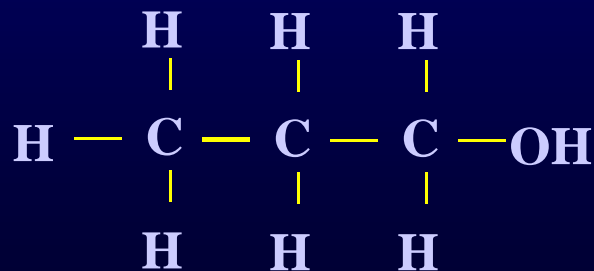


Methanol **Ingestion → blindness**



Ethanol

← **THE alcohol**



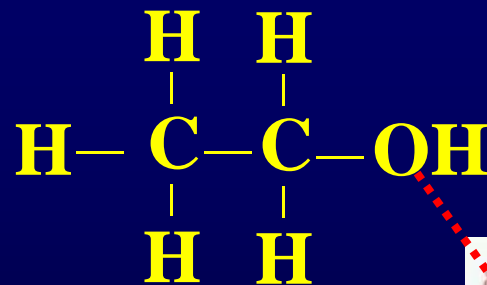
Propanol

Most “other” alcohols are highly toxic to the body

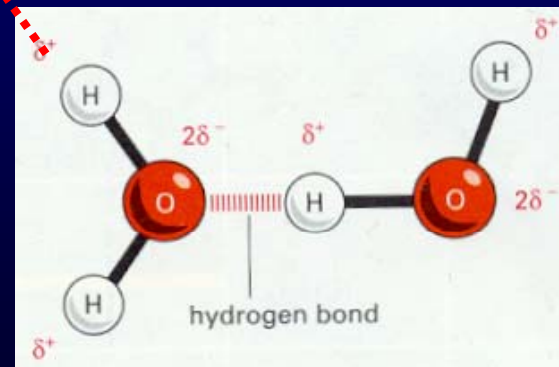
Ethanol Structure

- Clear, colorless liquid, miscible with H₂O and Organics

Carbon-Hydrogen chains
dissolve in lipids
(hydrophobic)

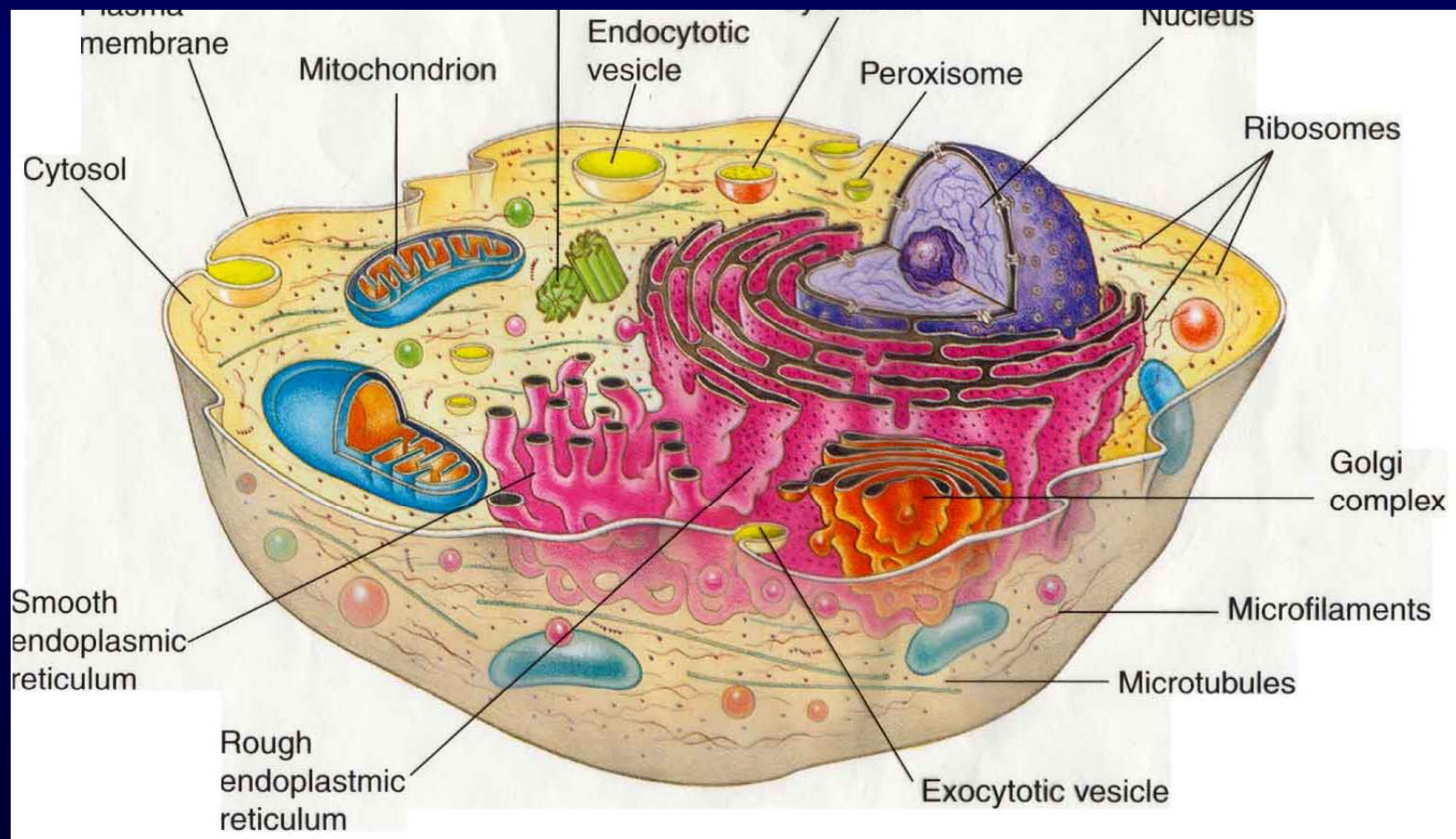


This end interacts and
dissolves in water
(hydrophilic)



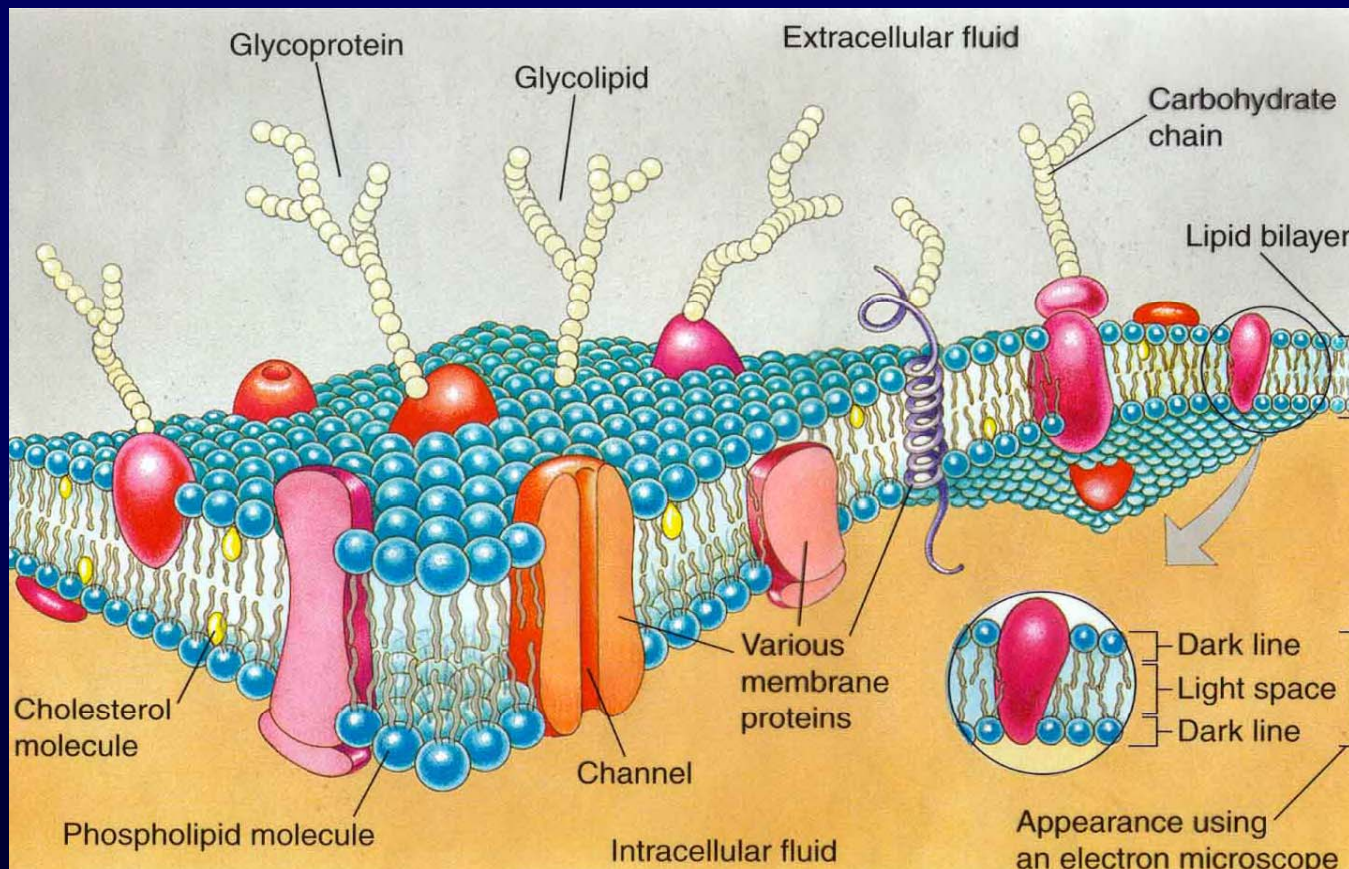
Basic Structure of Body Cells

Our bodies are made of 75 trillion specialized cells with phospholipid membranes, and aqueous environments inside and out.



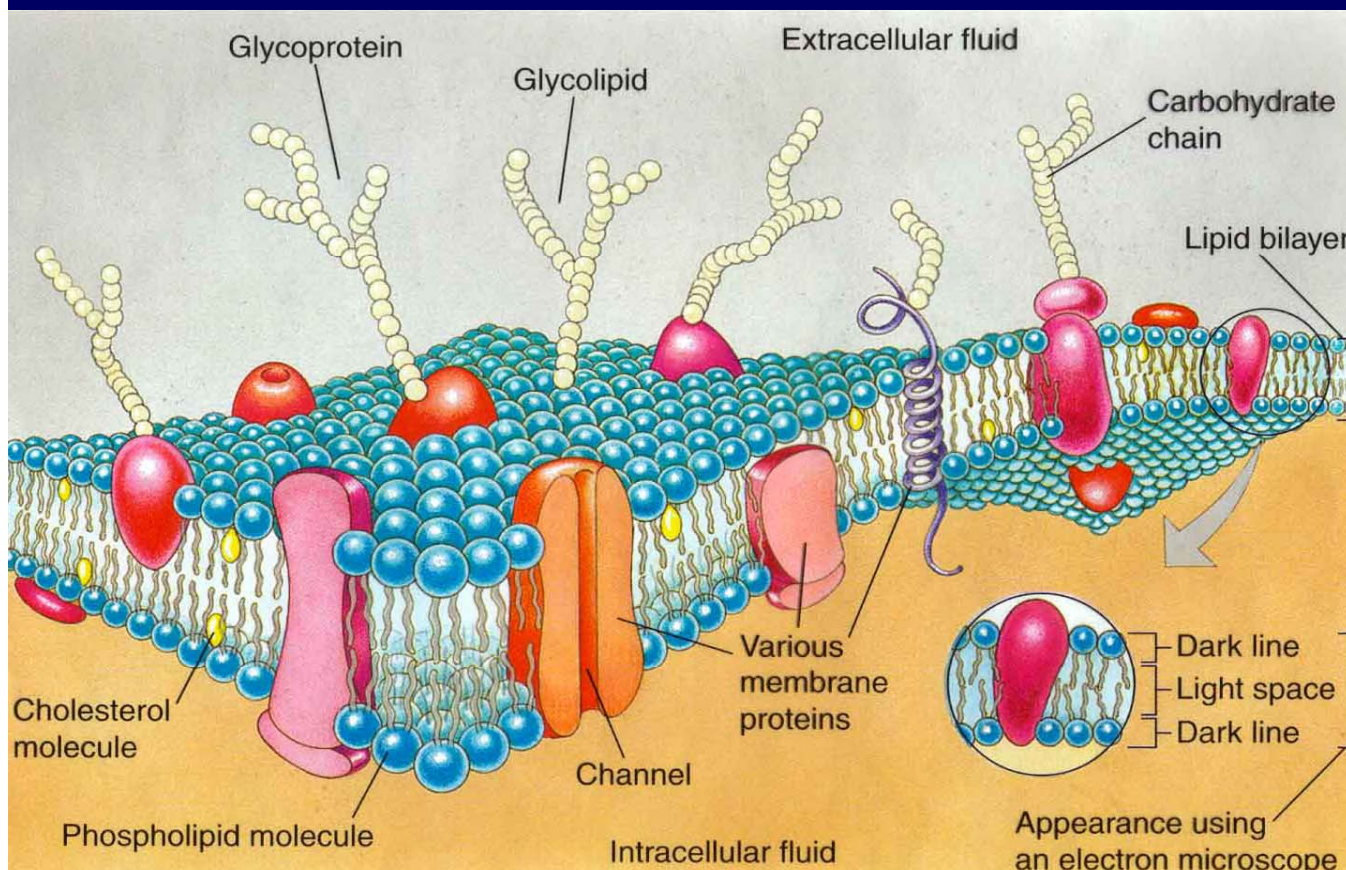
Basic Structure of Body Cells

Cell membranes are essentially oily bubbles formed from a bilayer of phospholipid molecules



Basic Structure of Body Cells

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})**

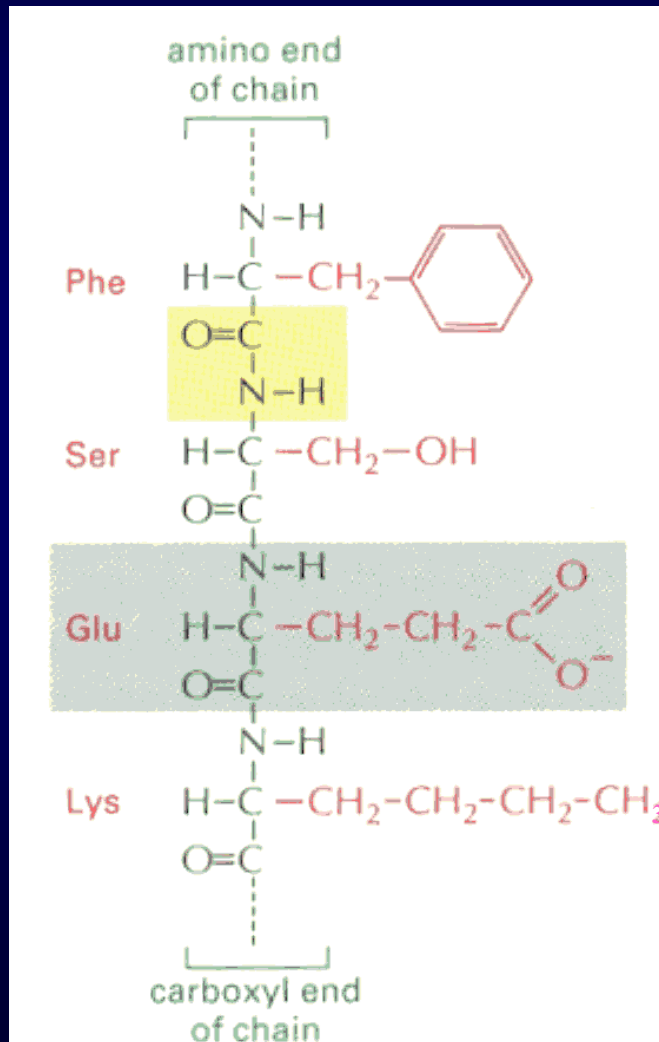
Enzymes

Receptors

Signals

Basic Structure of Body Cells

Proteins are made of amino acid chains:

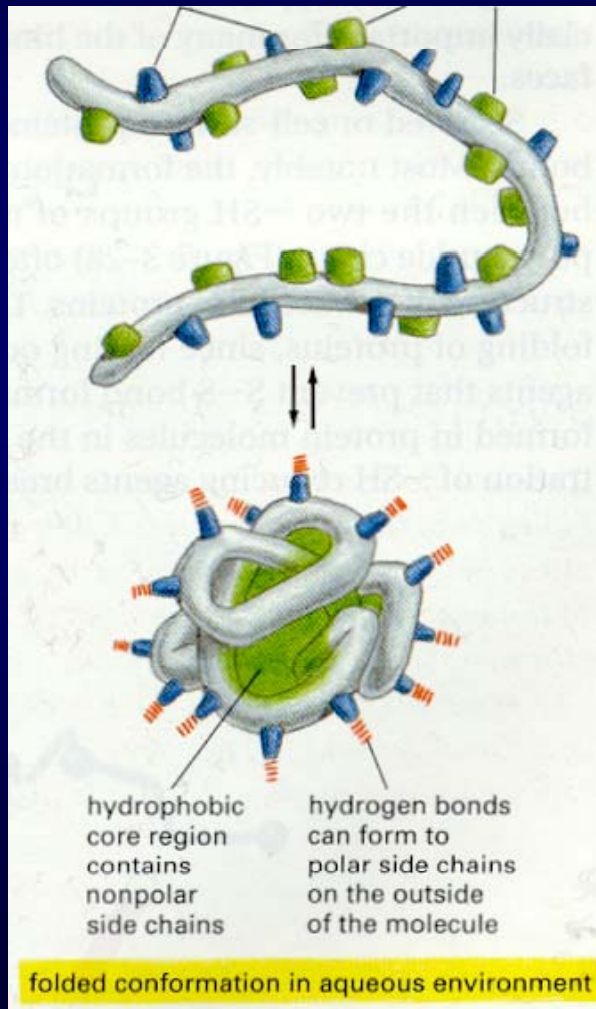


20 different amino acids have unique "R" groups:

- **Some are hydrophilic**
- **Some are hydrophobic**

Basic Structure of Body Cells

Proteins are made of amino acid chains:

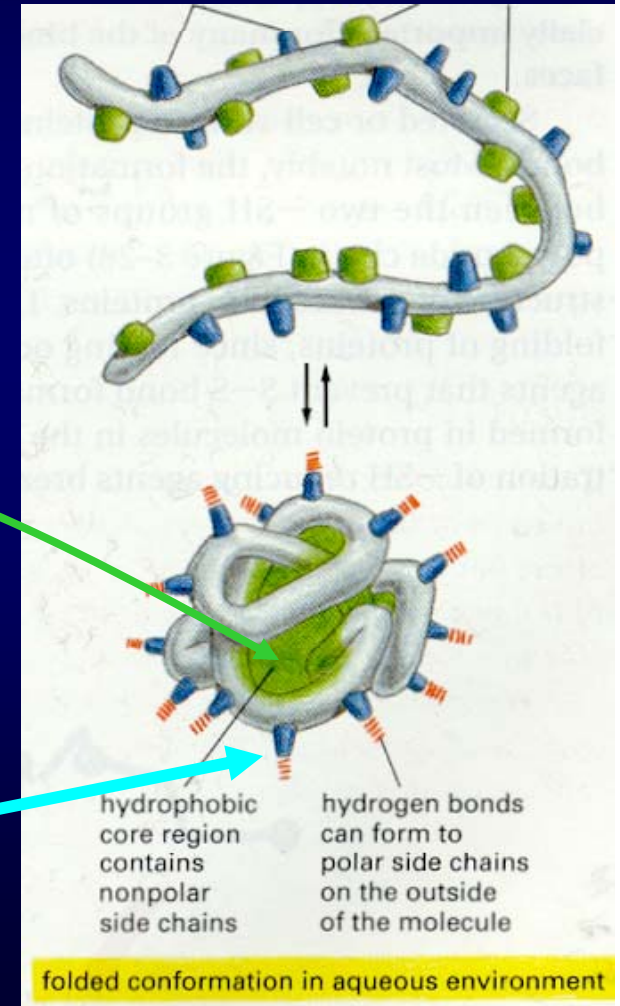
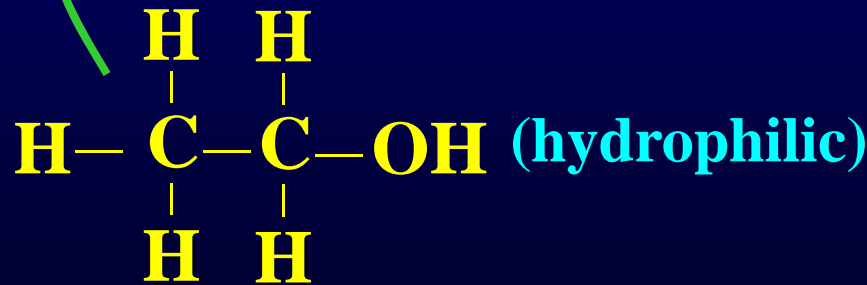


The “R”-group sequence determines the complex folding and final shape of a protein.

Ethanol Interacts with Cell Proteins

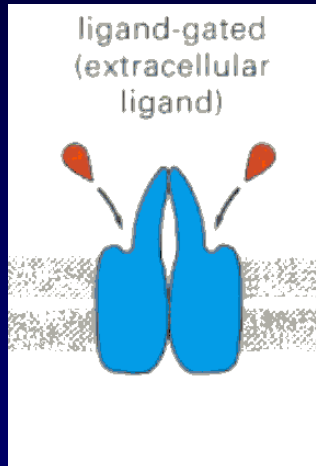
Ethanol's unique chemistry makes it a universal key that can interact with protein machinery of cells throughout the body.

(hydrophobic)



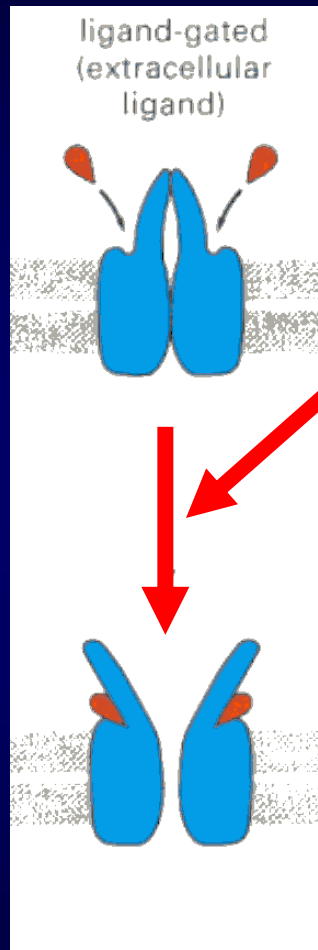
Why Does Whiskey ‘Burn’?

Why Does Whiskey “Burn”?



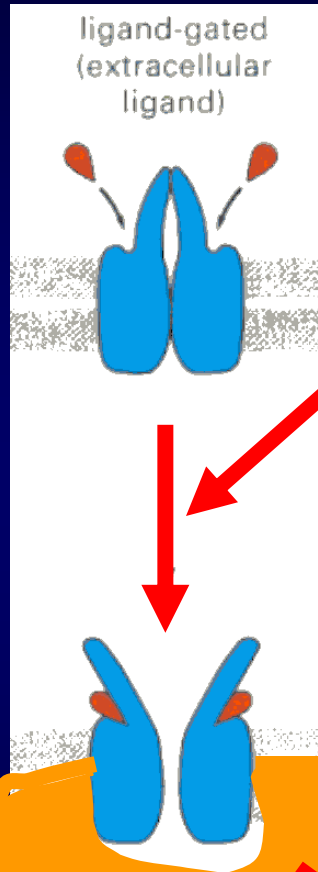
← **“TRPv1 (Vanillin1) receptor” (mouth, throat)**

Why Does Whiskey “Burn”?

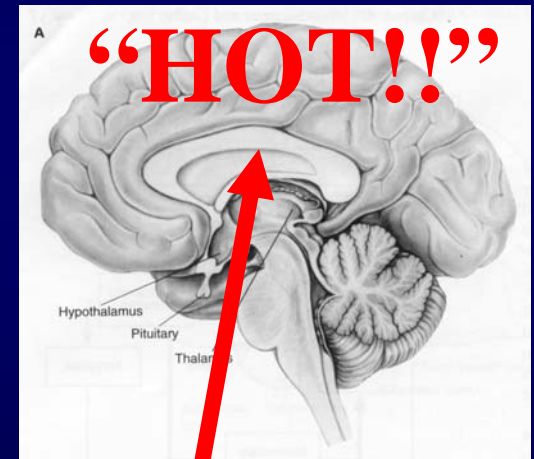


Heat, capsaicin...

Why Does Whiskey “Burn”?



Heat, capsaicin...and Ethanol!



**Nerve signal
to brain**

Why Do People Drink Alcohol?

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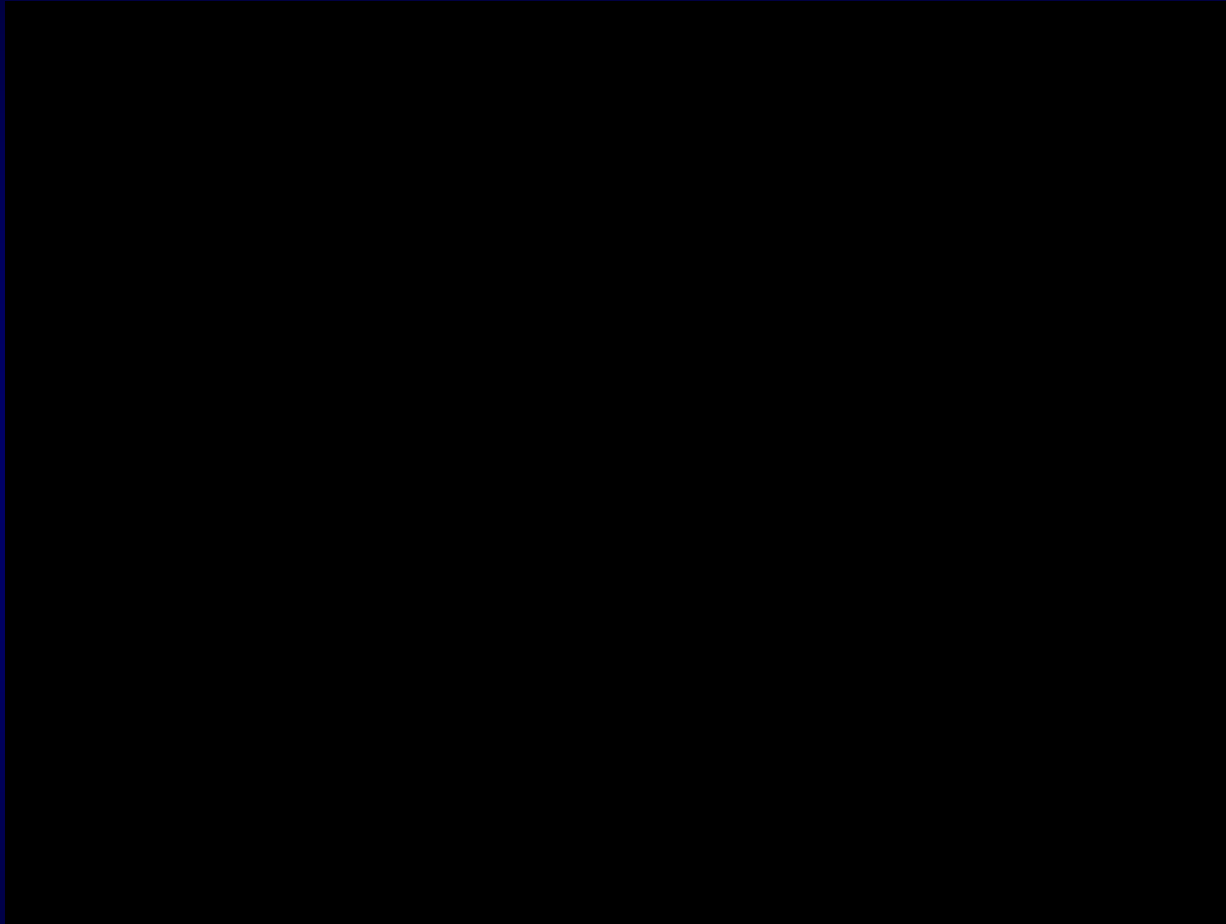
Euphoria/Mood elevation
Increase social confidence
Anti-anxiety (“to relax”)
Aphrodesiac
Escape from problems
To fit in with friends/family

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Because of great advertising?

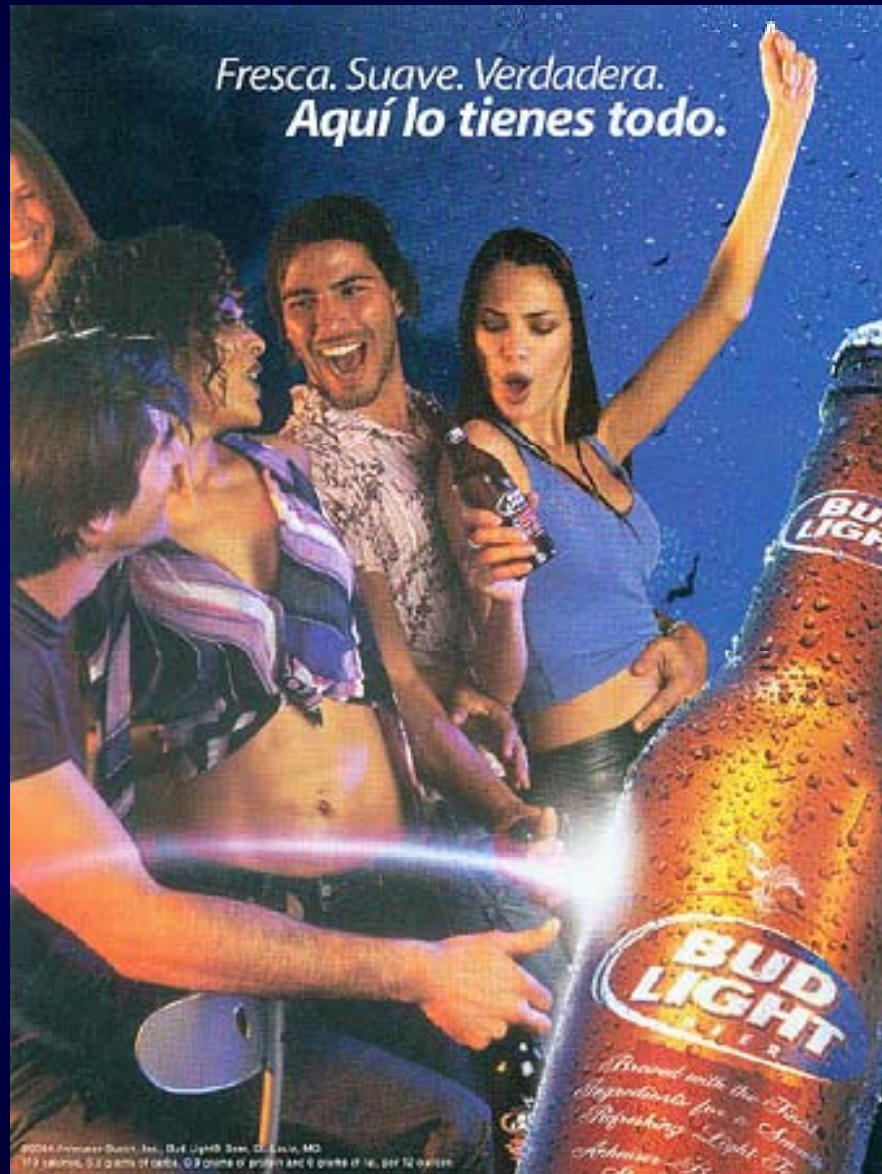
Why Do People Drink Alcohol?



Because of great advertising?

Why Do People Drink Too Much?

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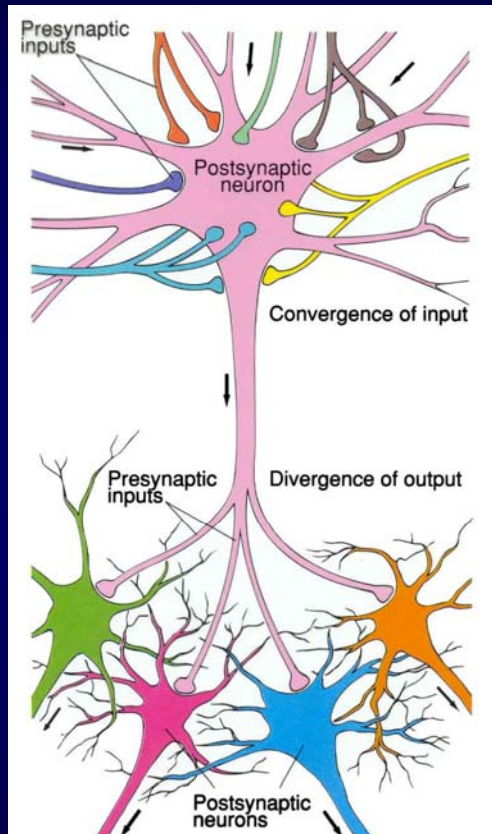




This happens a LOT.....but why?

Why Do People Drink Too Much?

Ethanol affects synapses

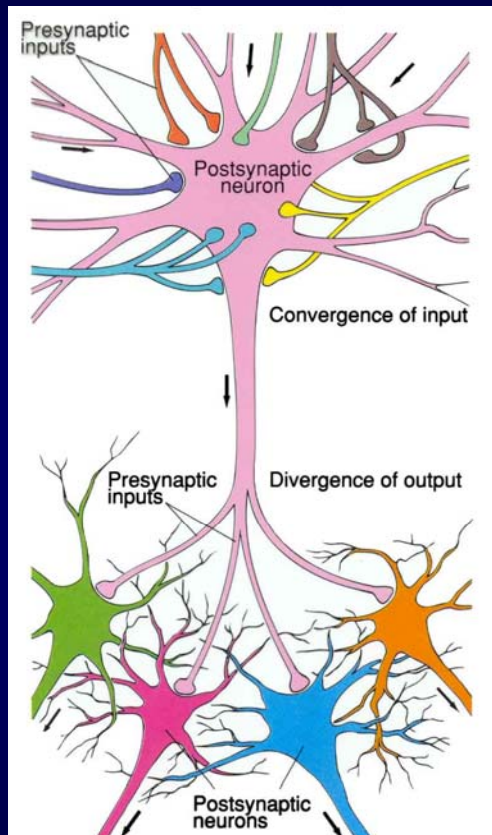


Neuron signals and networks

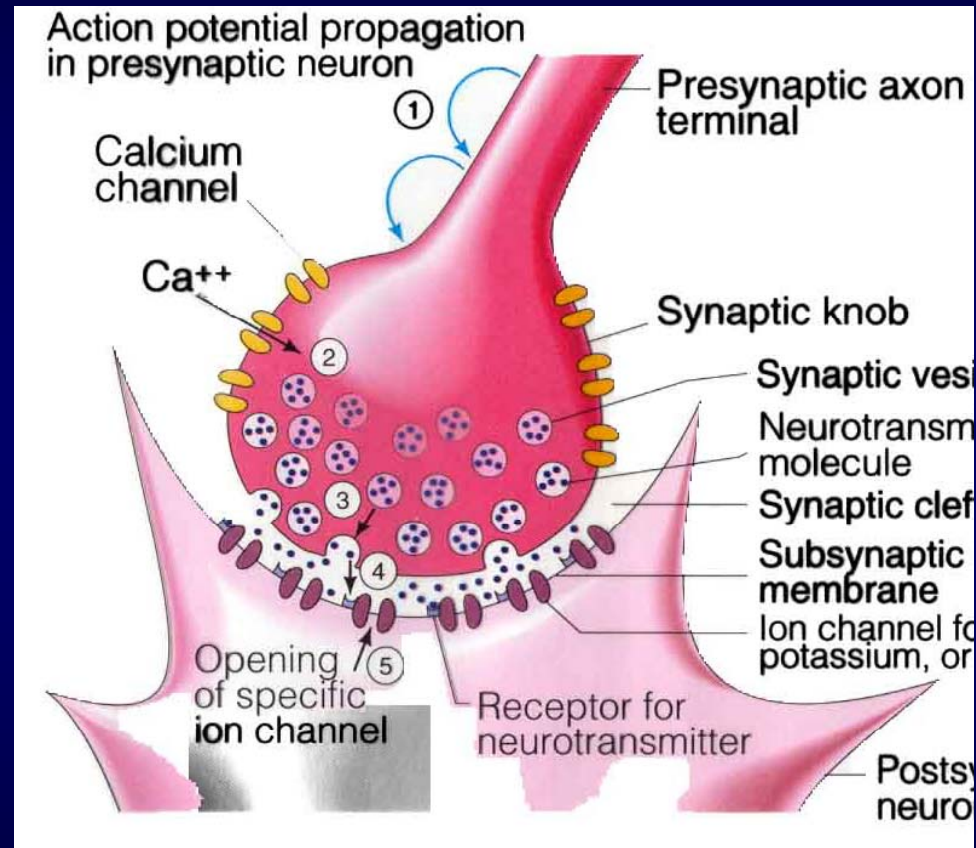
(x 100 billion!)

Why Do People Drink Too Much?

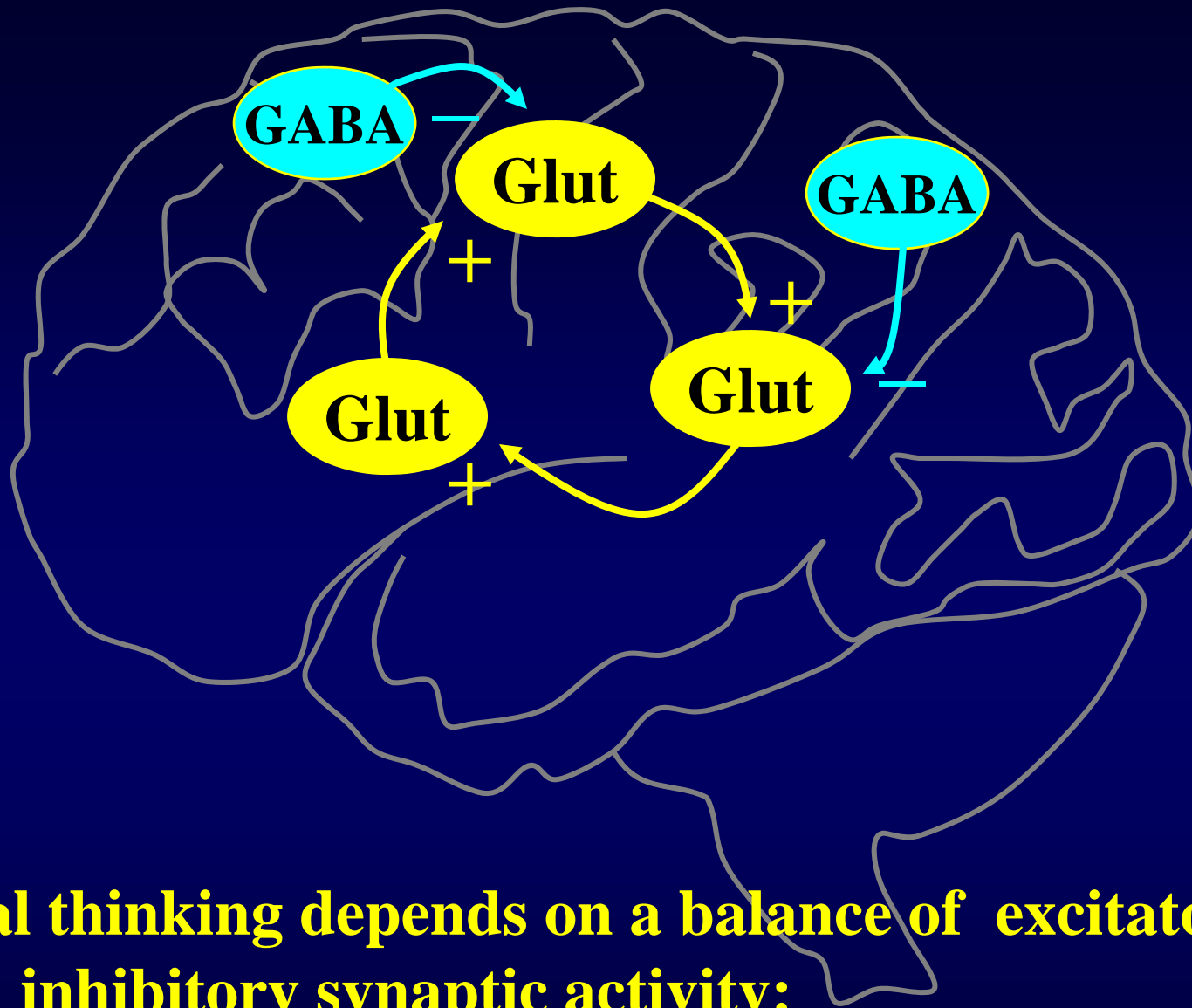
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**Neuron signals
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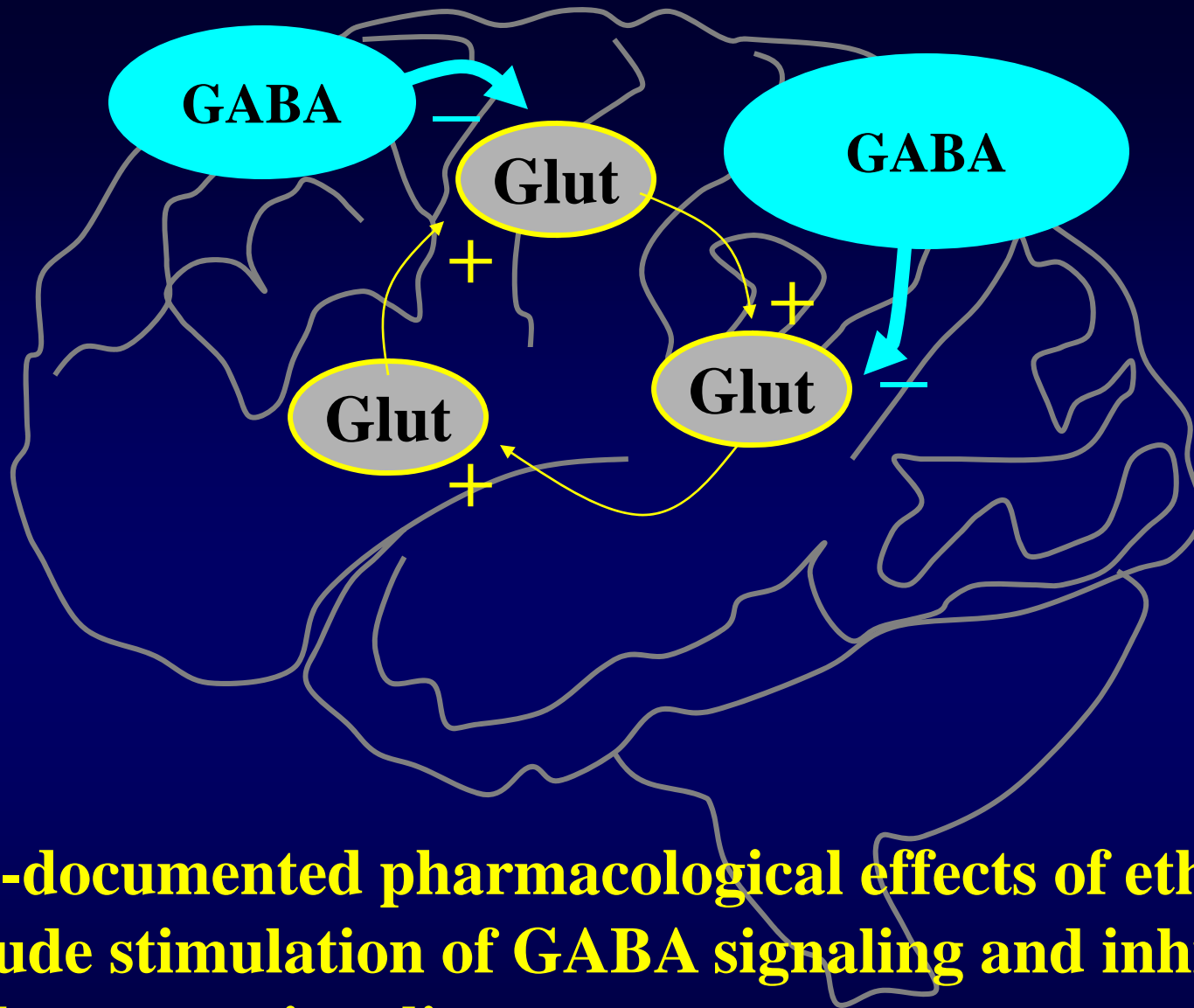
**Synapses, Neurotransmitters
and Receptors**



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

→50% of the brain's synapses use Glutamate

→40% use GABA (gamma-amino-butyric 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

STETTLE — 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.

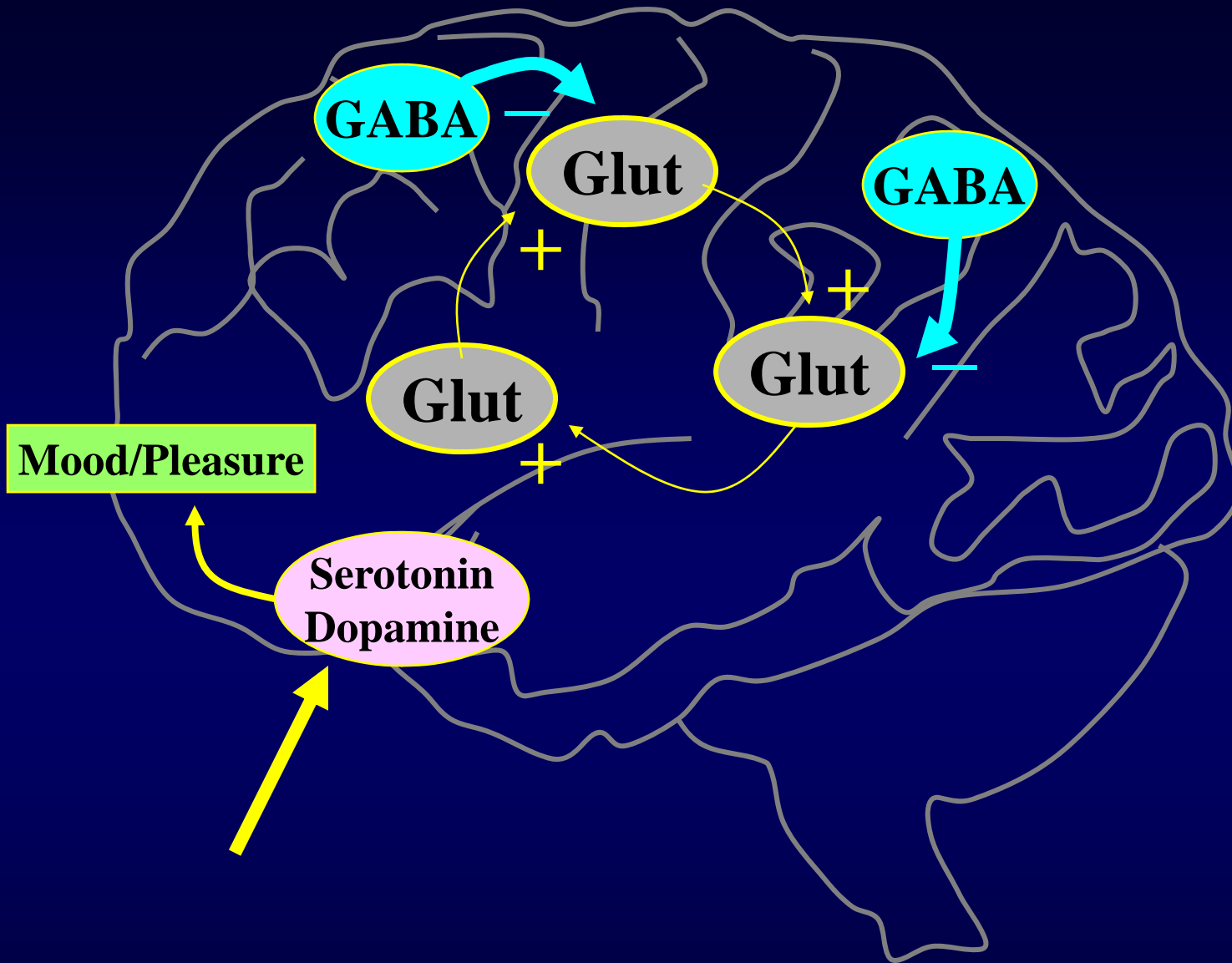
A class of law students from William E. Hay Composite High, in court as observers,

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

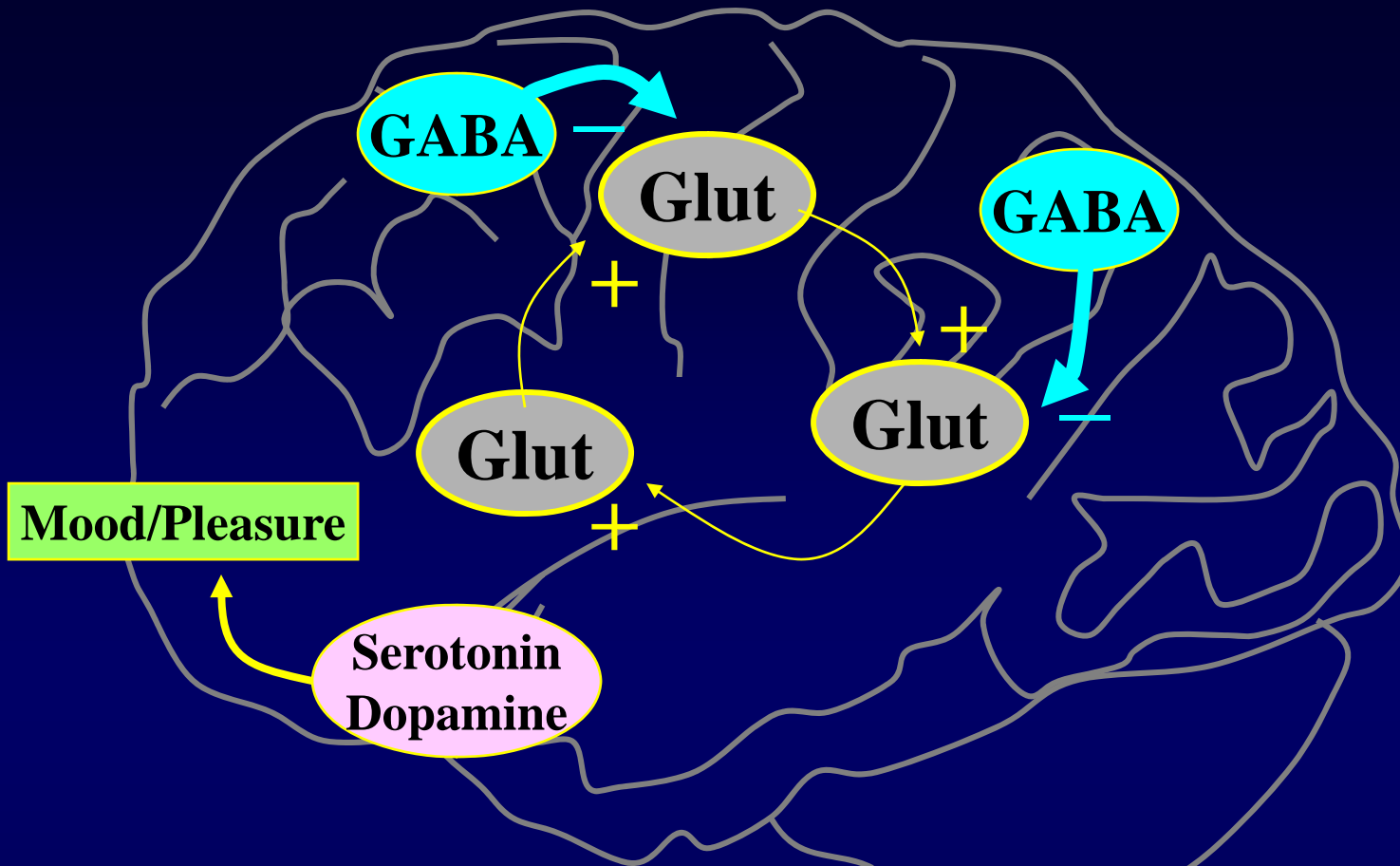
"People were leaving the courtroom with tears in their eyes, trying not to laugh," said RCMP Const. Peter McFarlane.







Other Neurotransmitters: Ethanol stimulates brain “reward” centers in a specific way....

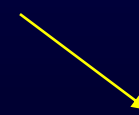


...which can explain why:

Short-term: Drinking leads to more drinking

Chronically: Addiction

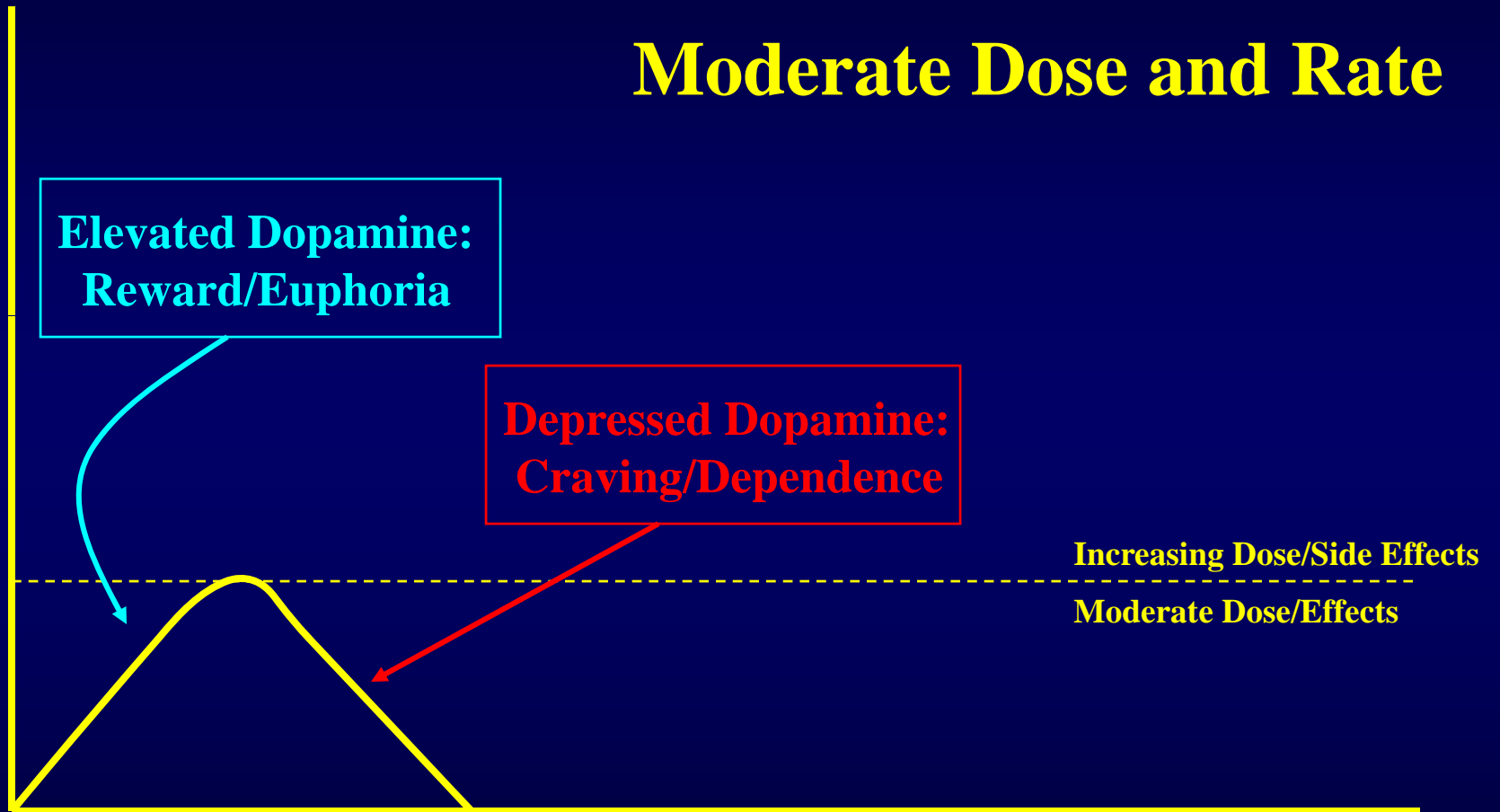
Both related to “Rising Phase Effect”



Rising Phase Effect

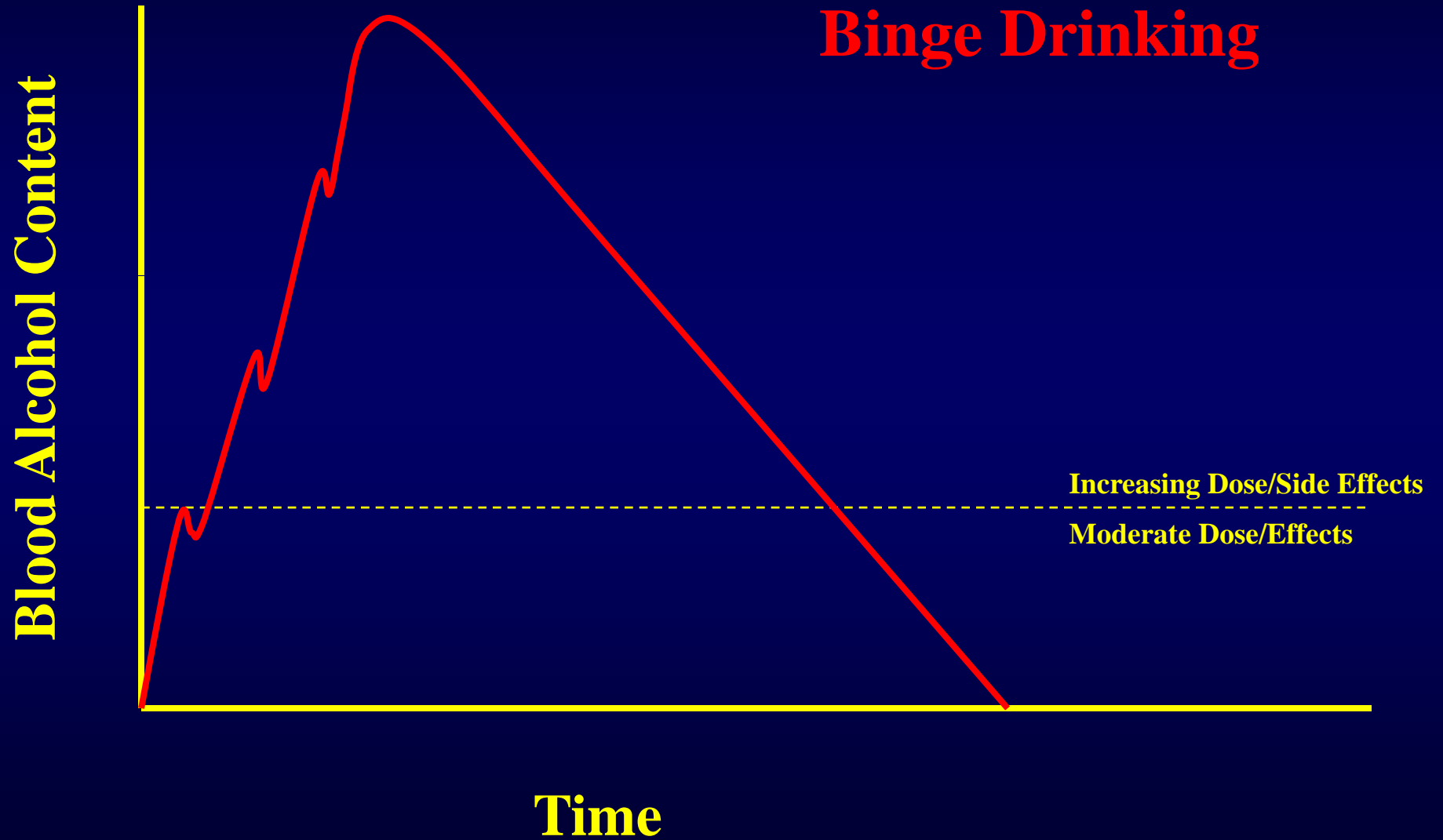
Moderate Dose and Rate

Blood Alcohol Content



Time

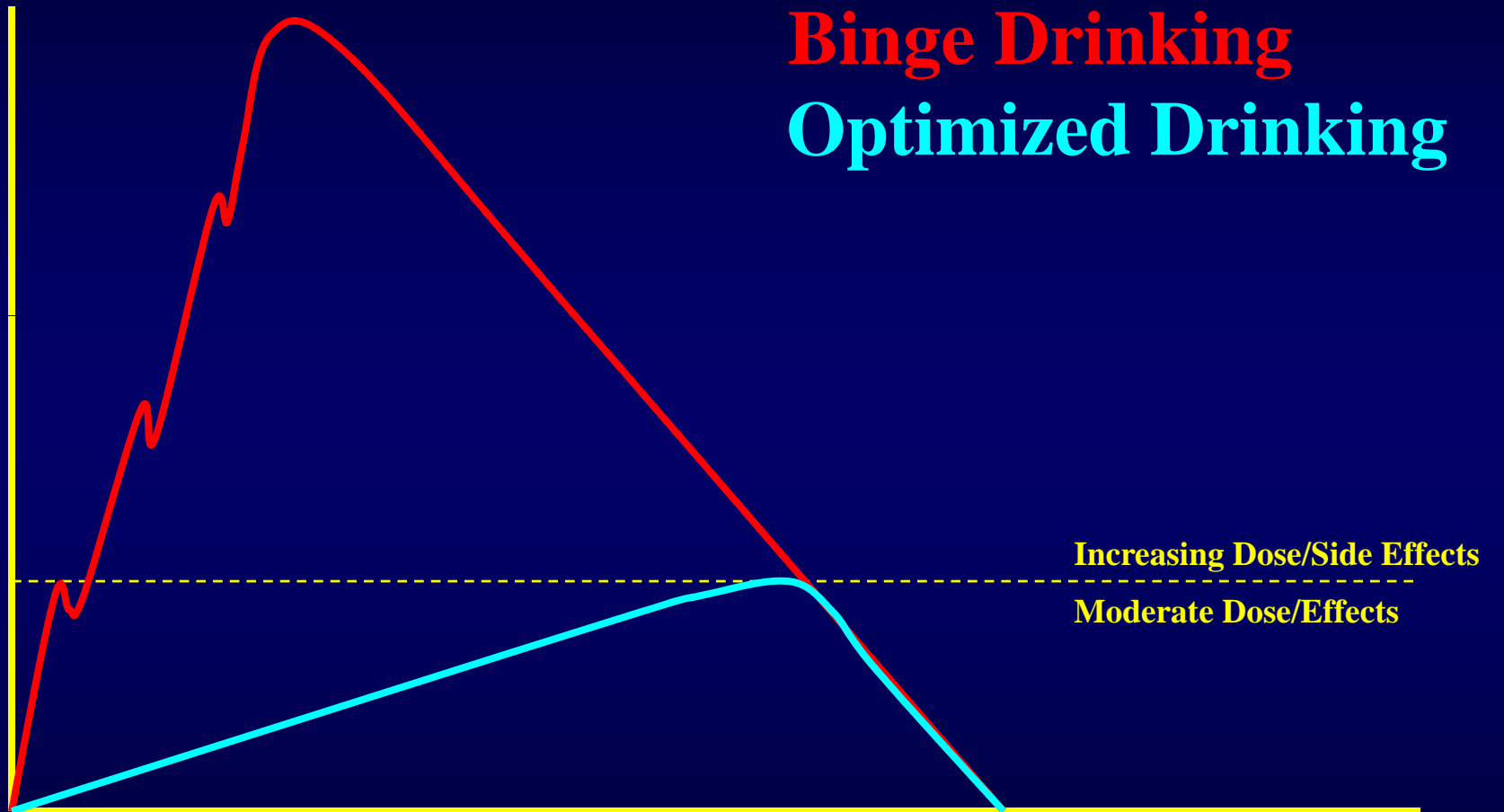
Rising Phase Effect



Rising Phase Effect

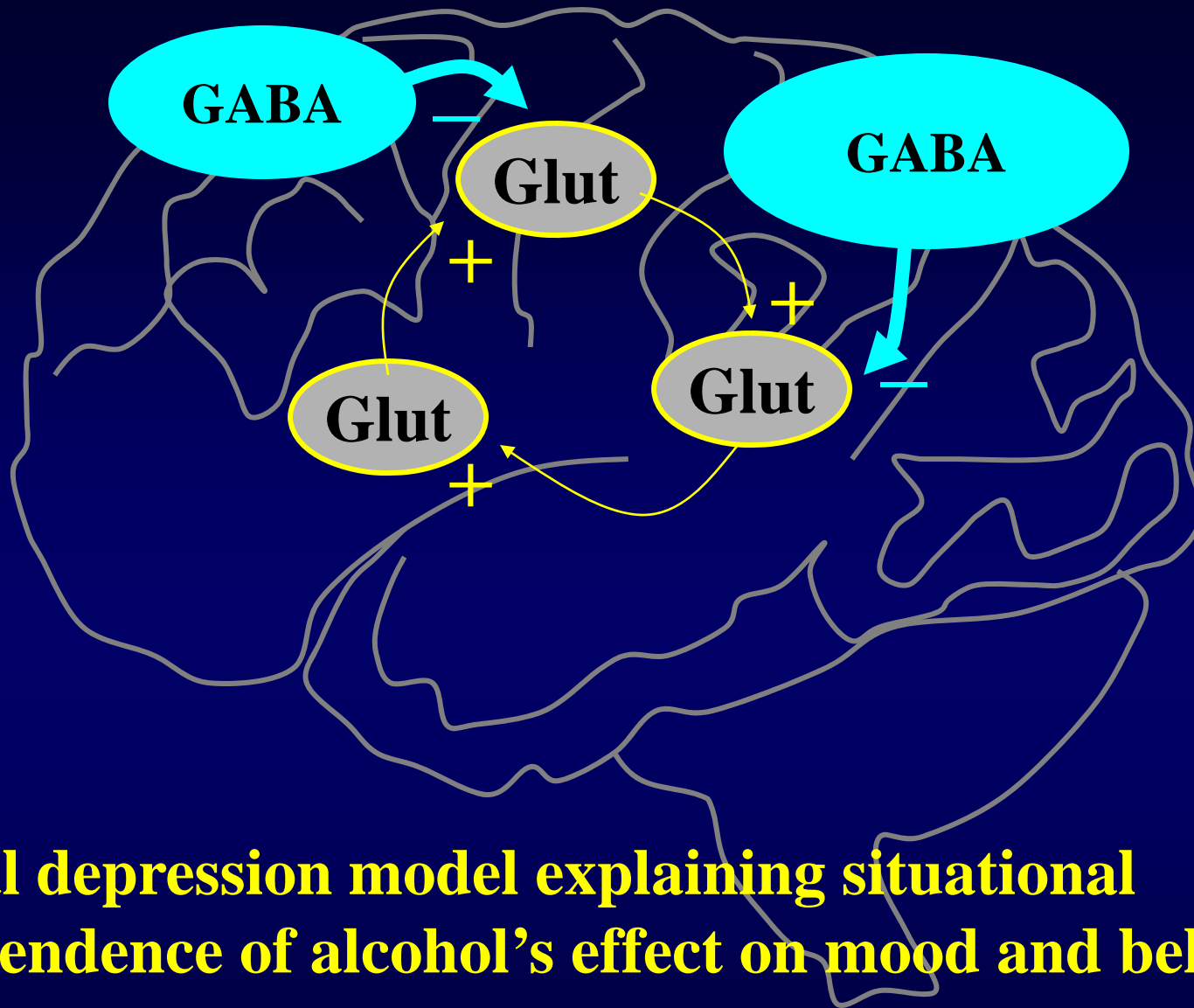
Blood Alcohol Content

Binge Drinking
Optimized Drinking



Time

**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.

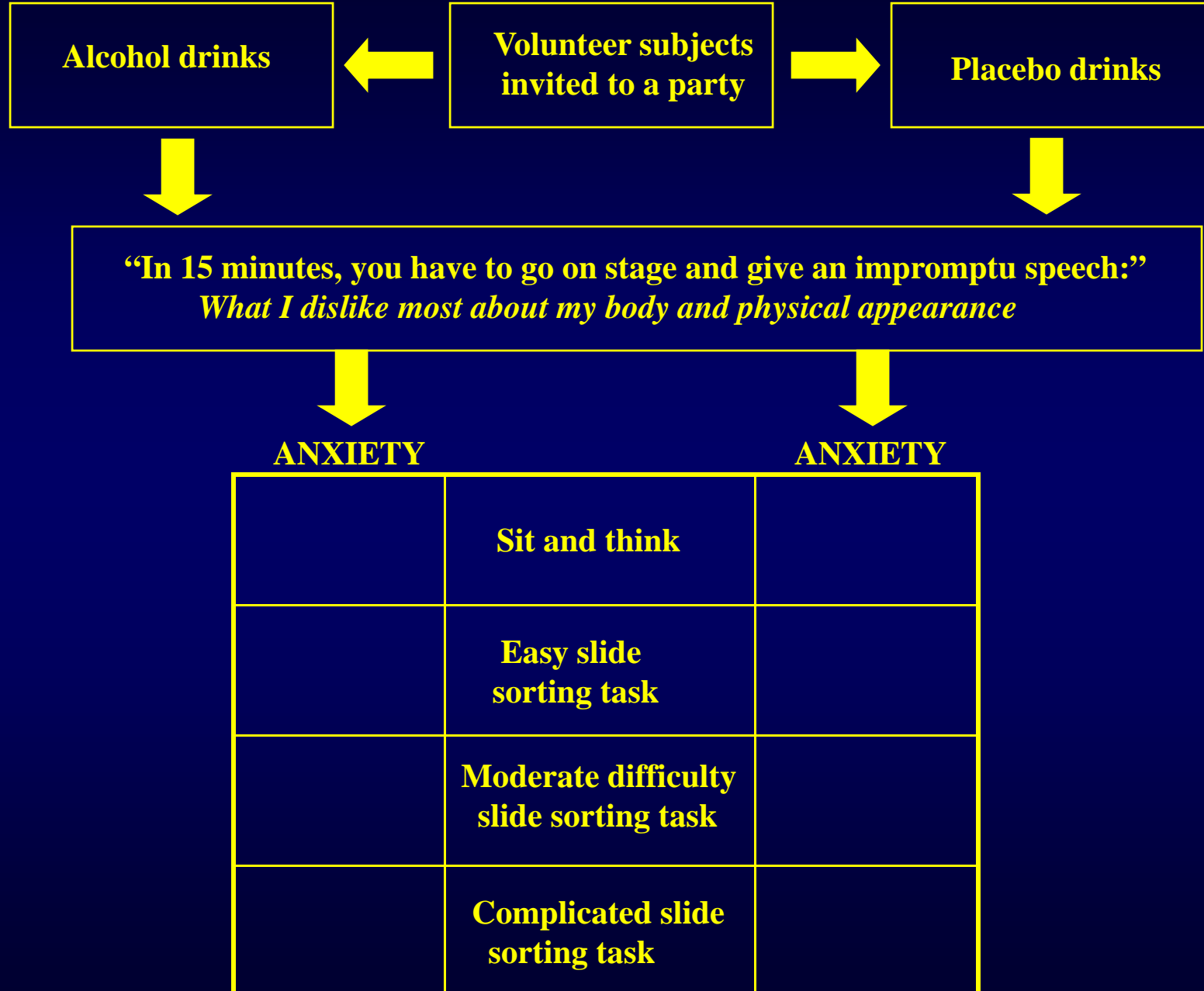
“Alcohol Myopia” Can Explain Variable Neural Effects

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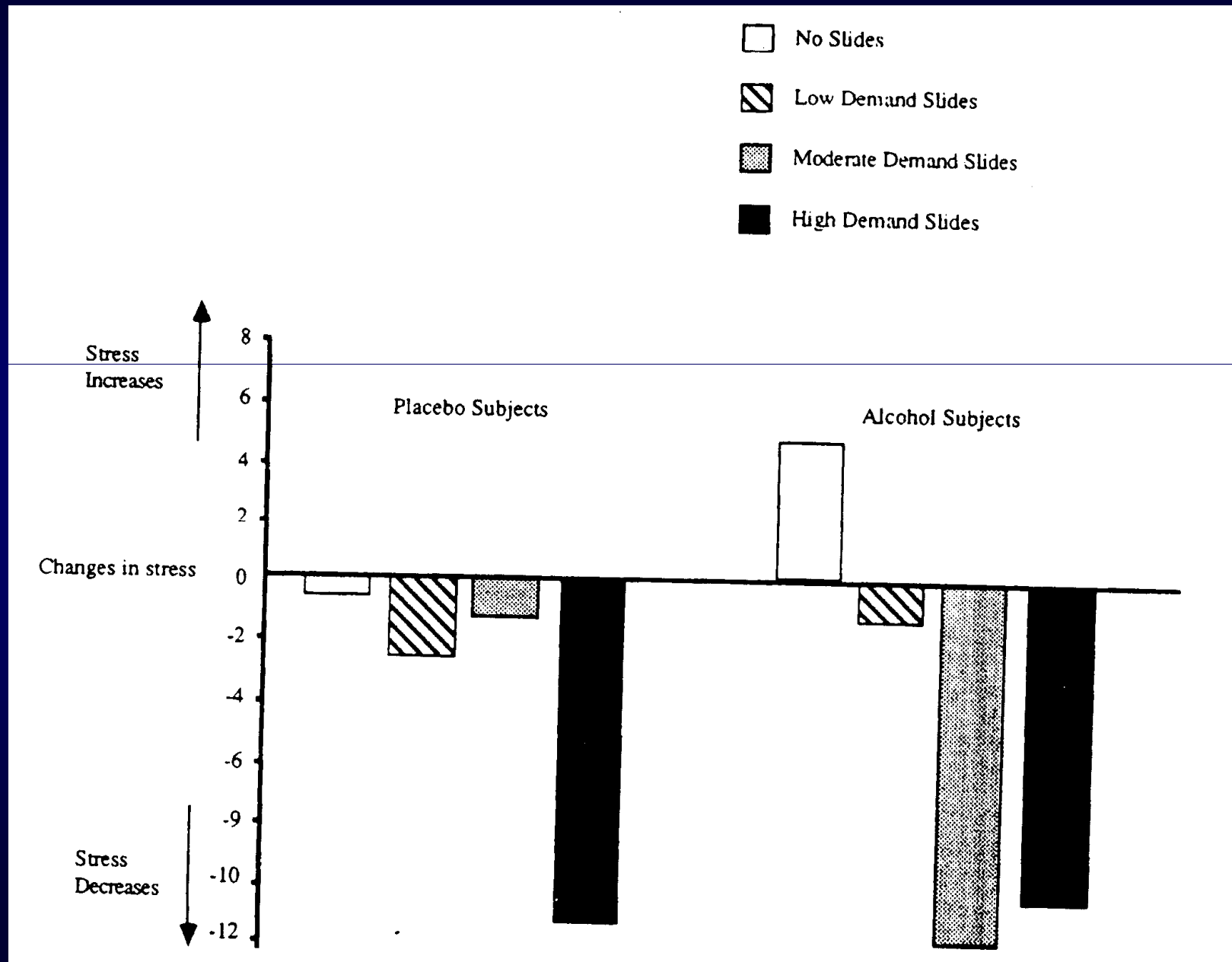
Ethanol globally suppresses cognition, reducing the mental focus of an individual to immediate internal thoughts or external stimuli.

Example: Study demonstrating that ethanol is NOT a good anti-anxiety drug....

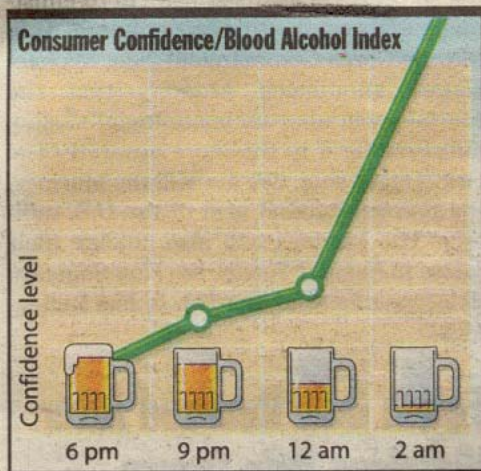
Alcohol, Anxiety, and Public Speaking



Alcohol, Anxiety, and Public Speaking



Myopia can boost your self-esteem!

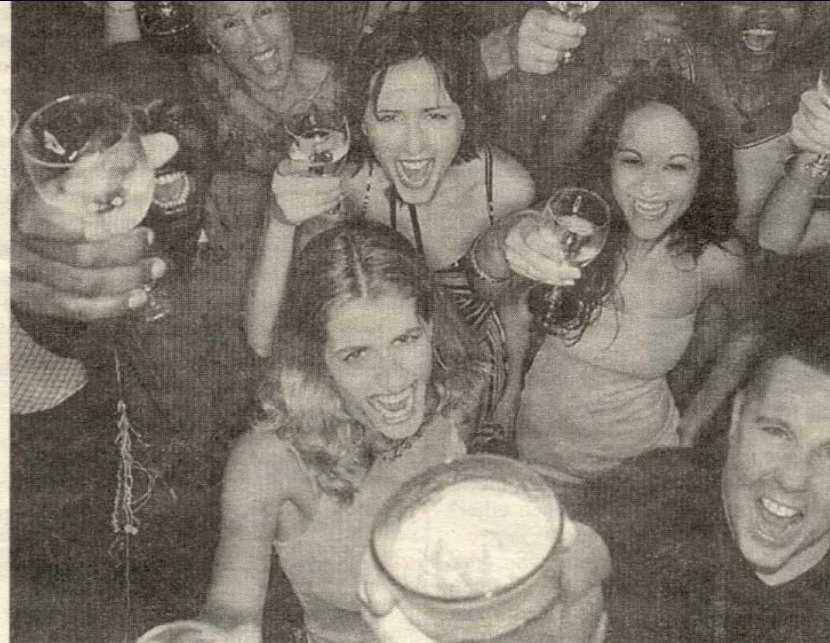


Alcoholic-Beverage-Consumer Confidence Skyrockets

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.

“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

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

showed a 47 percent increase in dancing on the bar and a 21 percent increase in the

maudlin conversations about relationship troubles. In severe cases, however, the 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 was up next to me, real close

**from:
The Onion**

Britmer, who lost three teeth in a fight

How Does Alcohol Affect Memory?

**Short-Term
Memory**
(“Working
memory”)
(RAM)

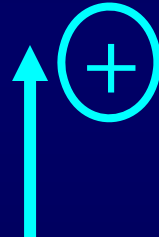


**Long-Term
Memory**
(“Learning”)
(Hard-drive)

**Short-Term
Memory**

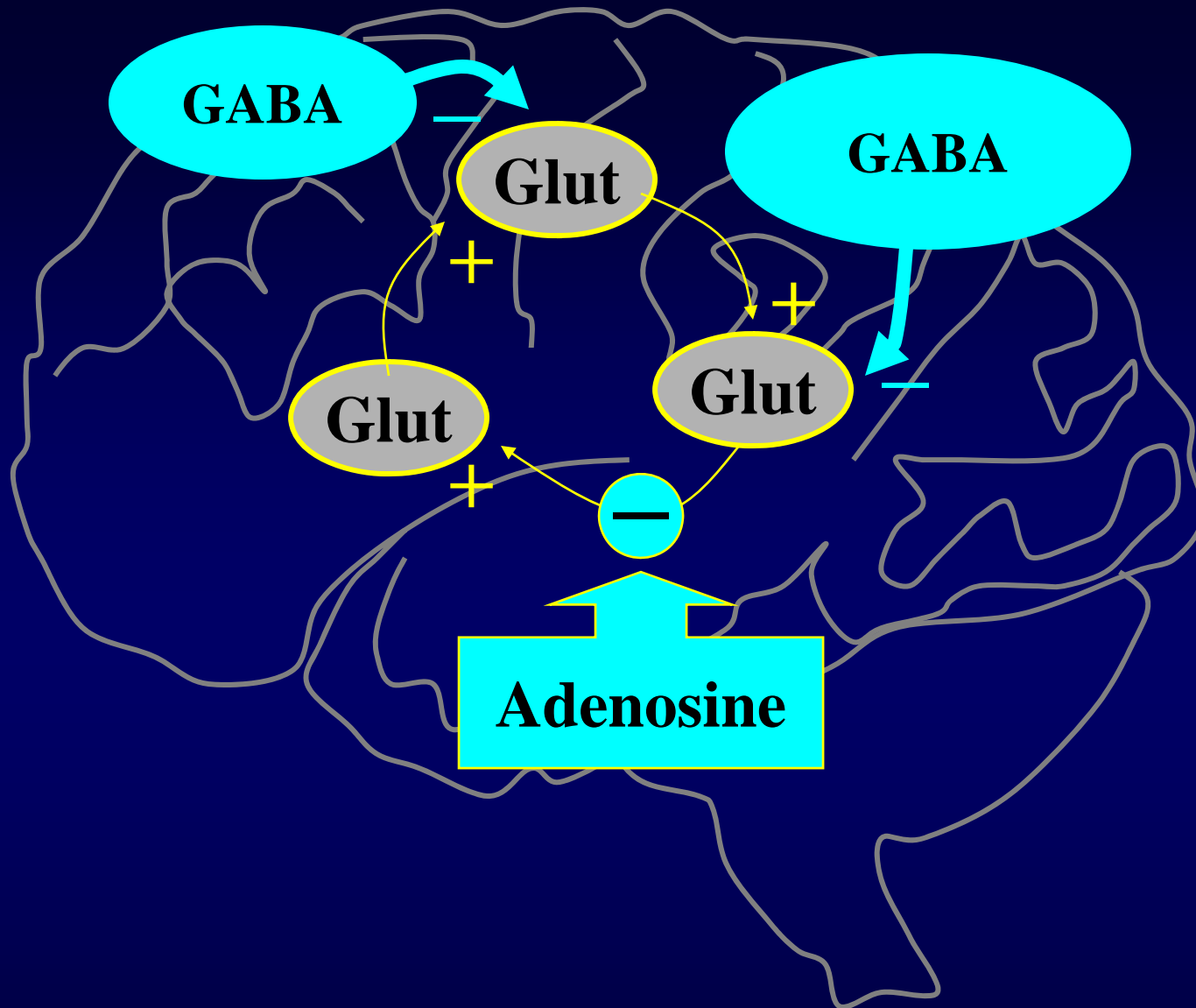


**Long-Term
Memory**

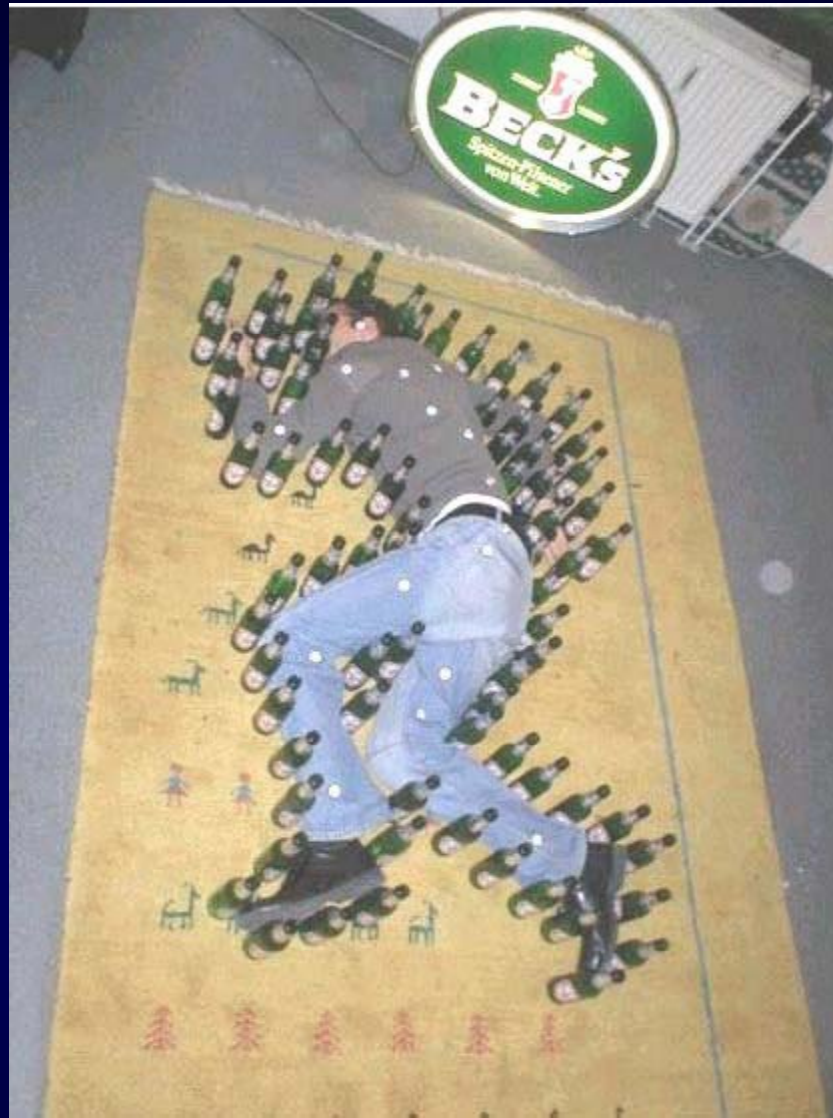


REM SLEEP

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”...

vu sur YATAHONGA.com



.....but.....

**Short-Term
Memory**



**Long-Term
Memory**



REM SLEEP

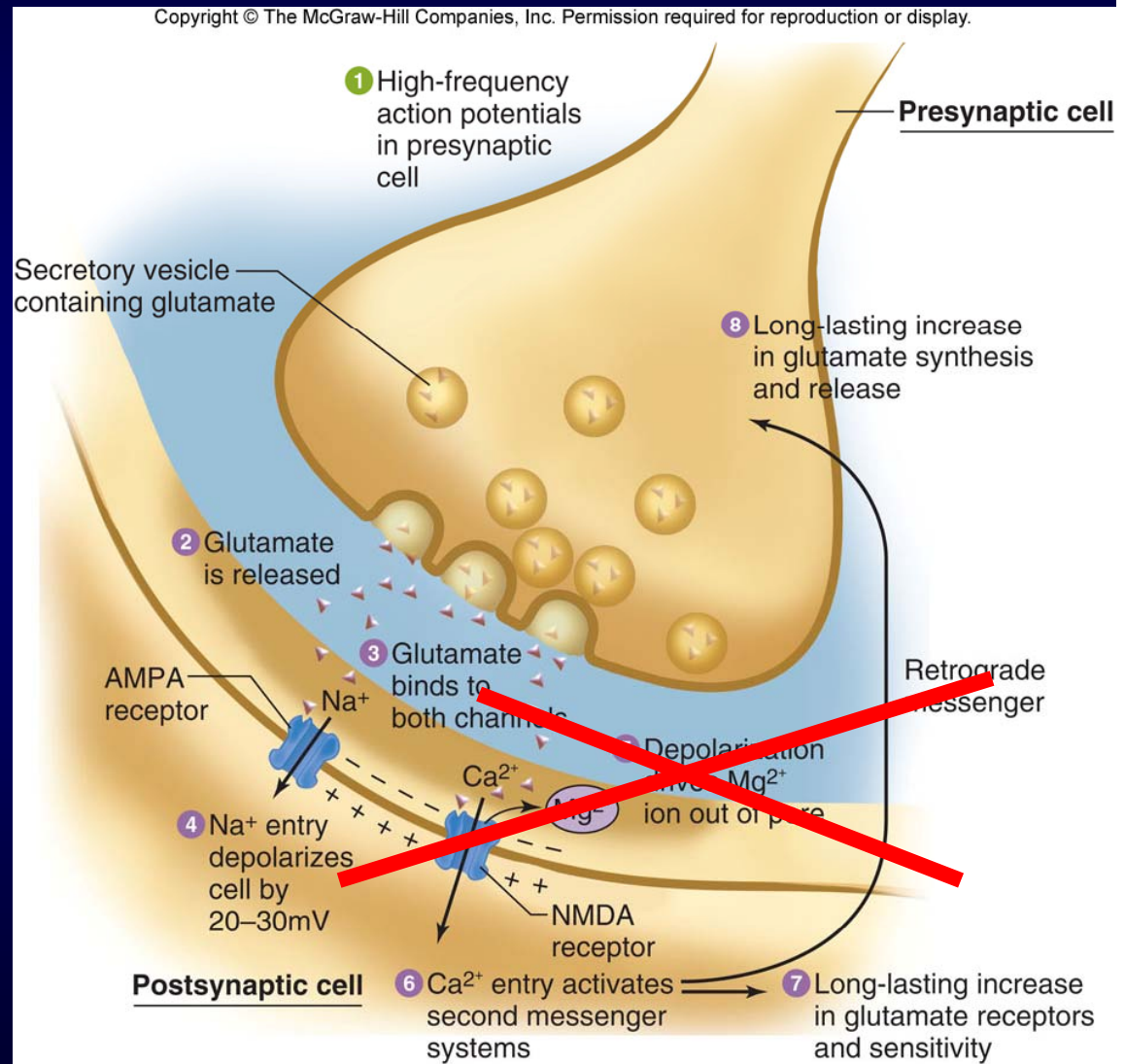


1. ETHANOL BLOCKS REM SLEEP

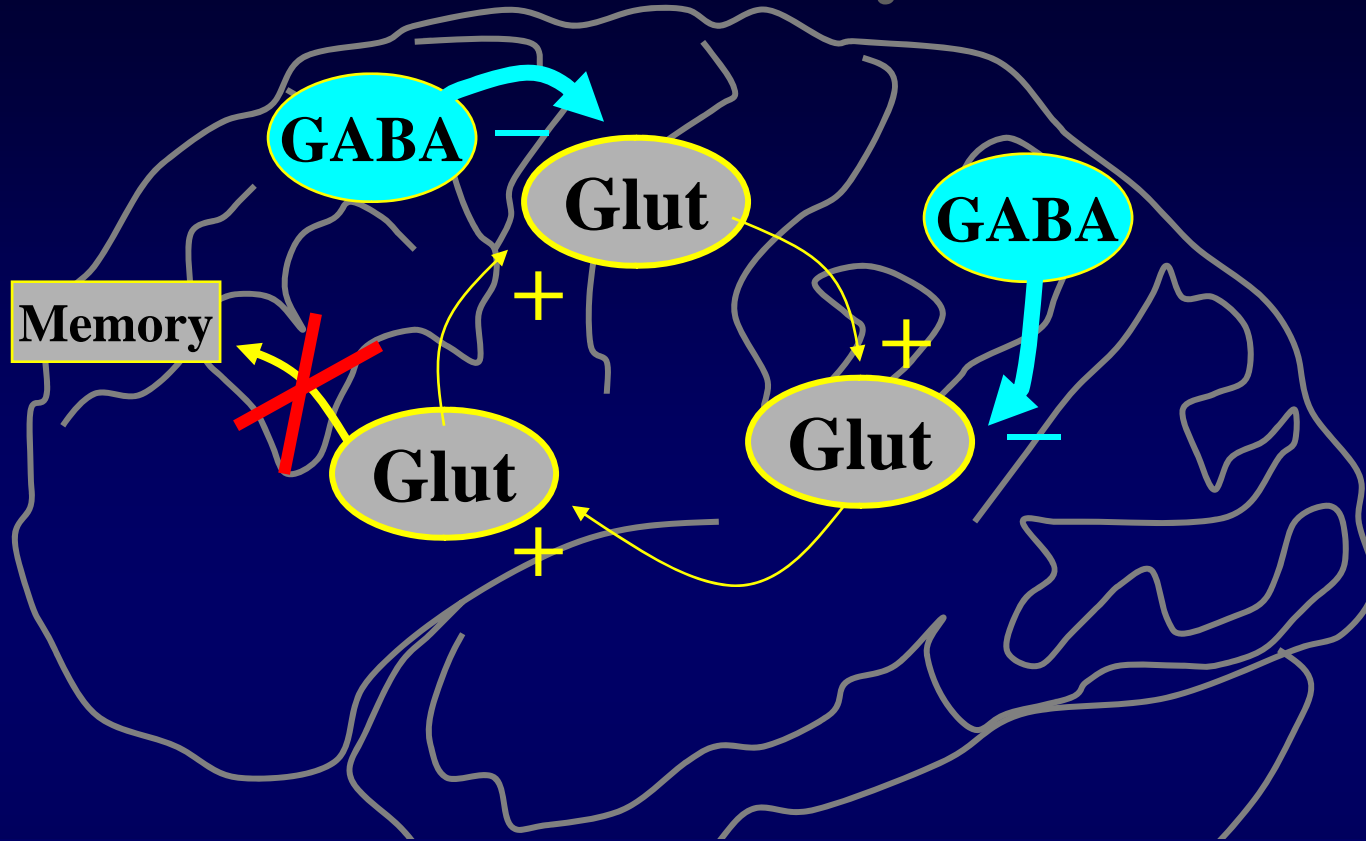
2. ETHANOL INHIBITS LTP

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...

GABA

Glut

GABA

Bar Skanks Announce Plans To Kiss

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.

After downing their third cosmo-



The skanks pose for one of the hundreds of pictures taken over the course of the night.

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."

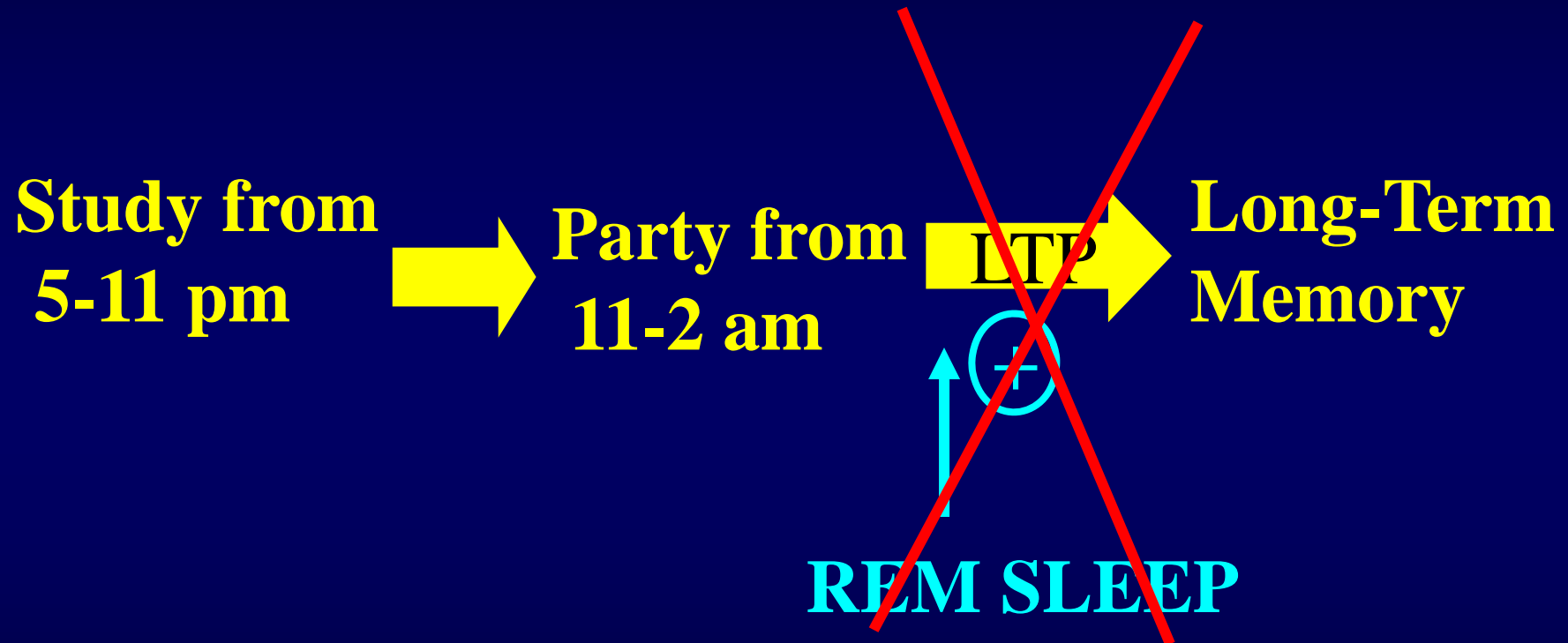
"Who knows what will go down," Fletcher said as she reached into Keneally's tight top and tweaked her left breast with her thumb and middle finger in front of seven rapt onlookers. "Possibly us."

In previous months, Keneally and Fletcher have, either separately or

see **SKANKS**, page 8

The Onion, June 21, 2007

THE COLLEGE STUDENT'S GRAND DELUSION...



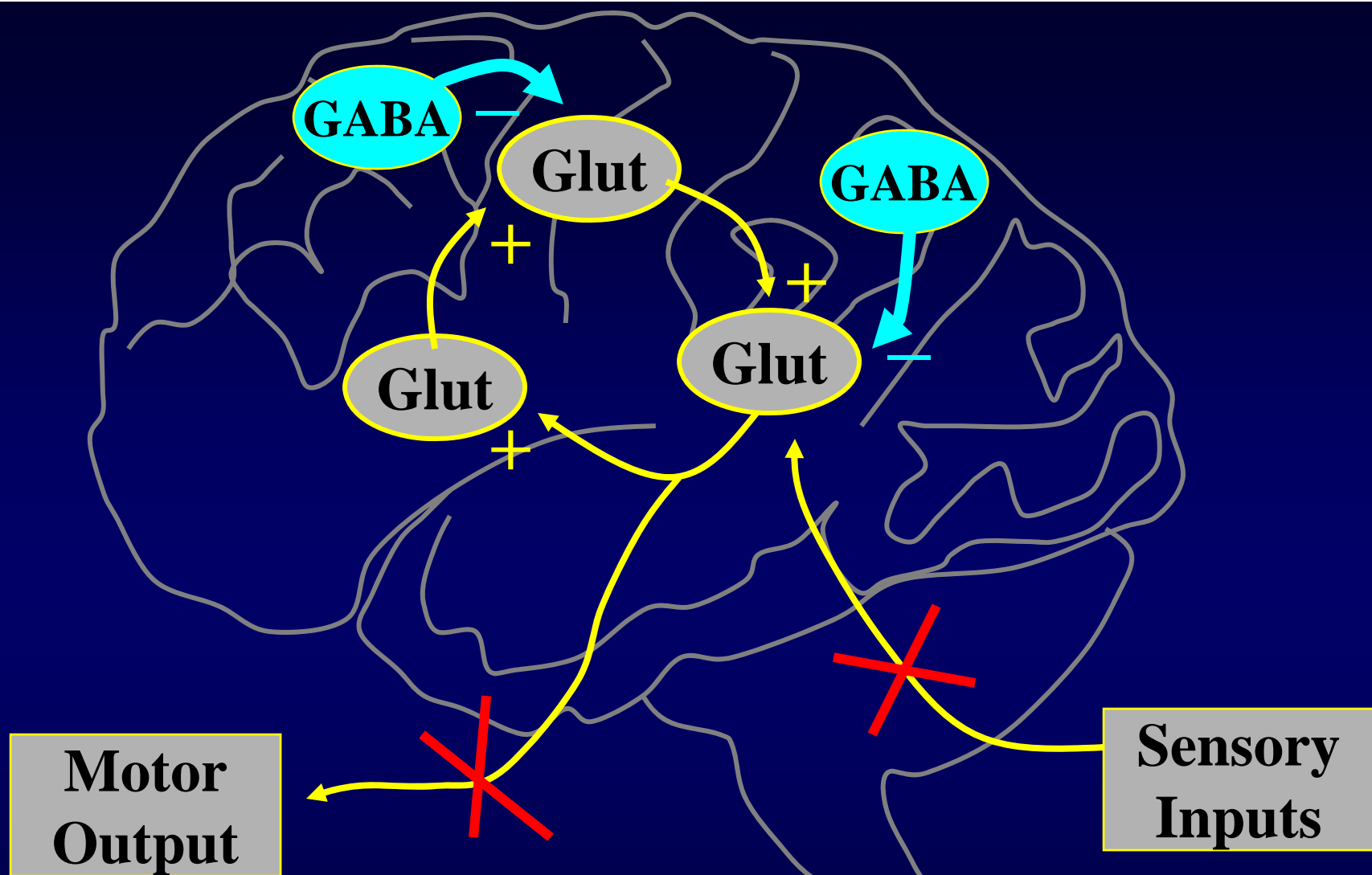
**Why Do Drunks Talk Loud, Fall Down,
and Get the Bed Spins?**



**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....

Prescription

Oxycontin

Prozac

Valium

Penicillin

Illegal

Cocaine

Ecstasy

THC

Heroin

OTC

Tylenol

Nyquil

Ipecac

Aspirin

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