



# Psychopharmacology

## Part 1

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UNIVERSITY OF  
**LOUISVILLE**<sup>®</sup>  
SCHOOL OF MEDICINE

# WHAT IS PSYCHOPHARMACOLOGY?

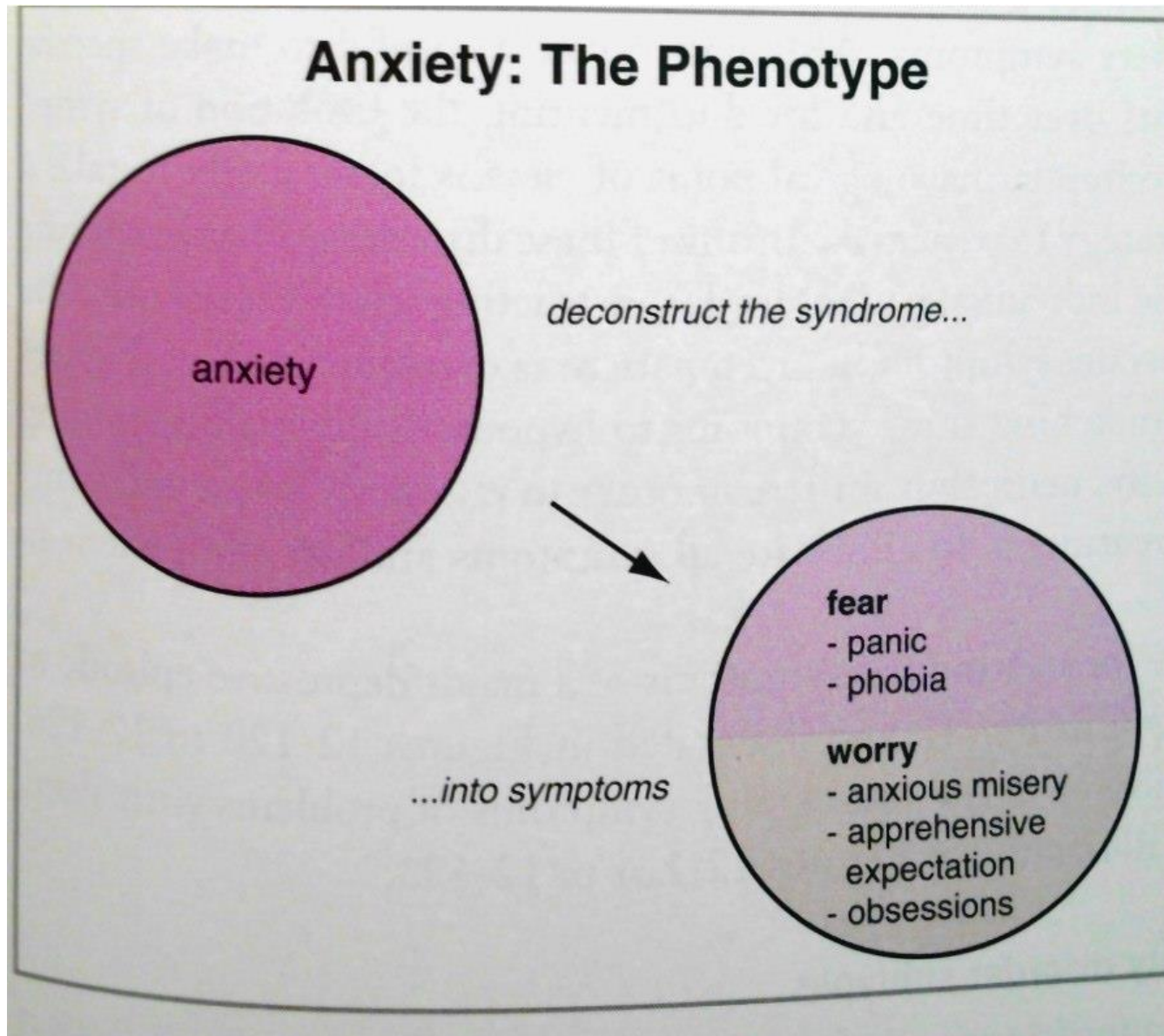
## Definition

1. The study of drugs that effect the brain.
  - Therapeutic Purposes
  - Non-Therapeutic Use
    - Short term abuse (intoxication)
    - Long term effects on neurotransmission
      - Particularly within rewards circuits

# TODAY

Time	Topics
10:30-12 noon	<ul style="list-style-type: none"><li>➤ Fear and Anxiety Circuits</li><li>➤ Connections between substance abuse and anxiety</li><li>➤ Self Medication</li></ul>
1:15-2:45 pm	<ul style="list-style-type: none"><li>➤ Mesolimbic Reward Circuits</li><li>➤ Substance Abuse Disorders</li><li>➤ Depressants</li><li>➤ Stimulants</li></ul>
3:00-4:45 pm	<ul style="list-style-type: none"><li>➤ Pain Medications</li><li>➤ Polypharmacy</li><li>➤ Cannabis</li><li>➤ Hallucinogens</li><li>➤ Steroids</li></ul>

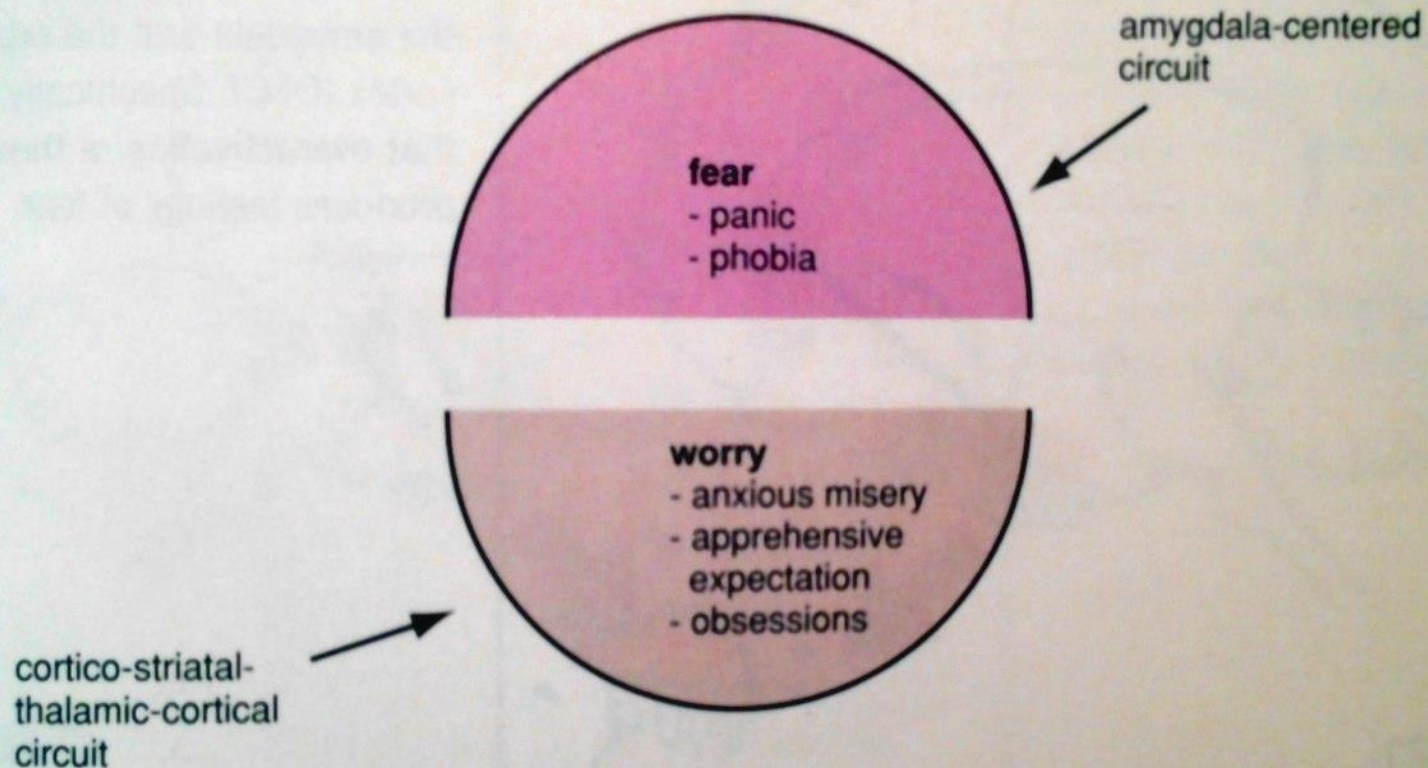
# FEAR AND ANXIETY CIRCUITS



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Essential  
Psychopharma  
cology 3<sup>rd</sup>  
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Stahl

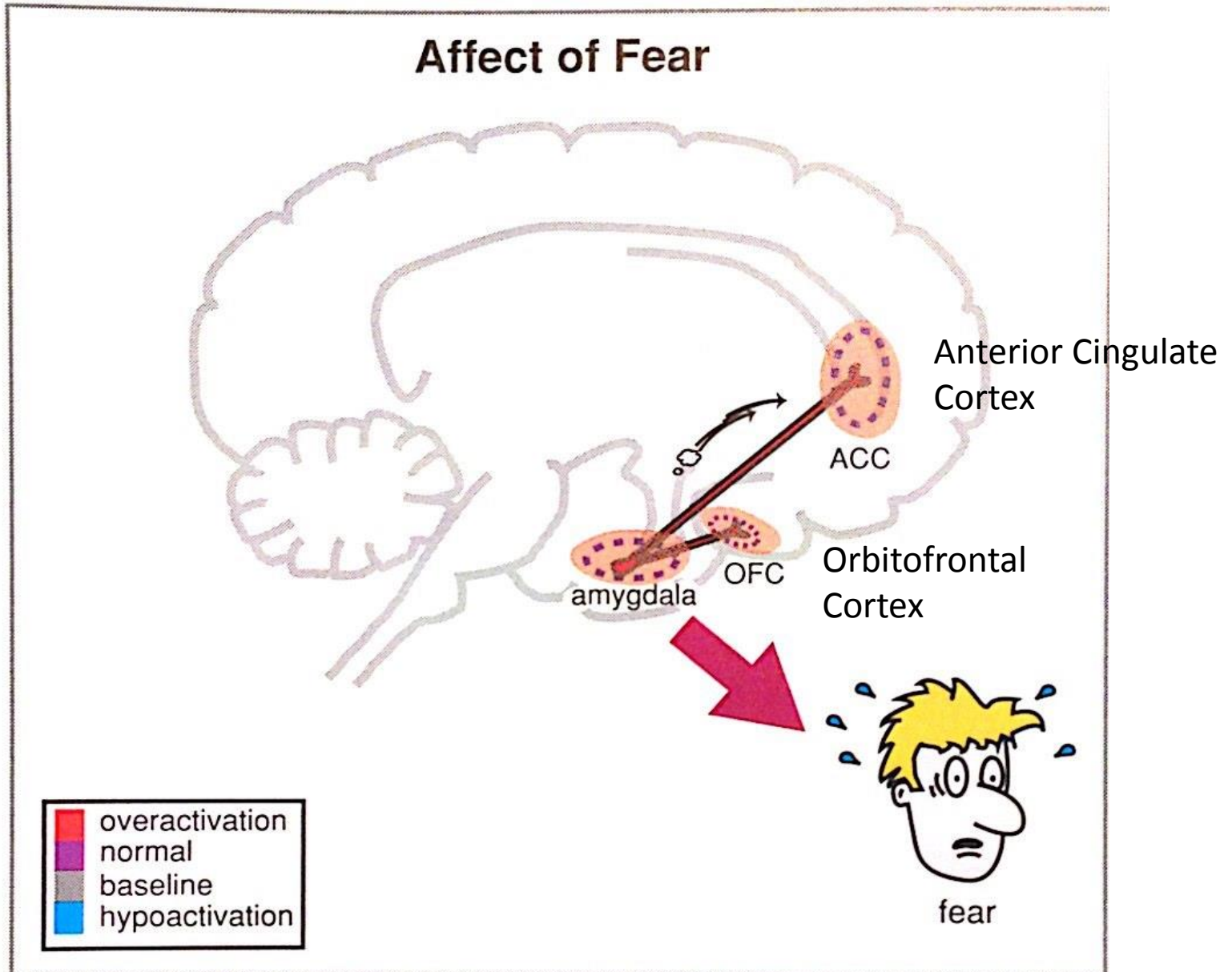
# ANXIETY AND FEAR

## Associate Symptoms of Anxiety With Brain Regions and Circuits That Regulate Them



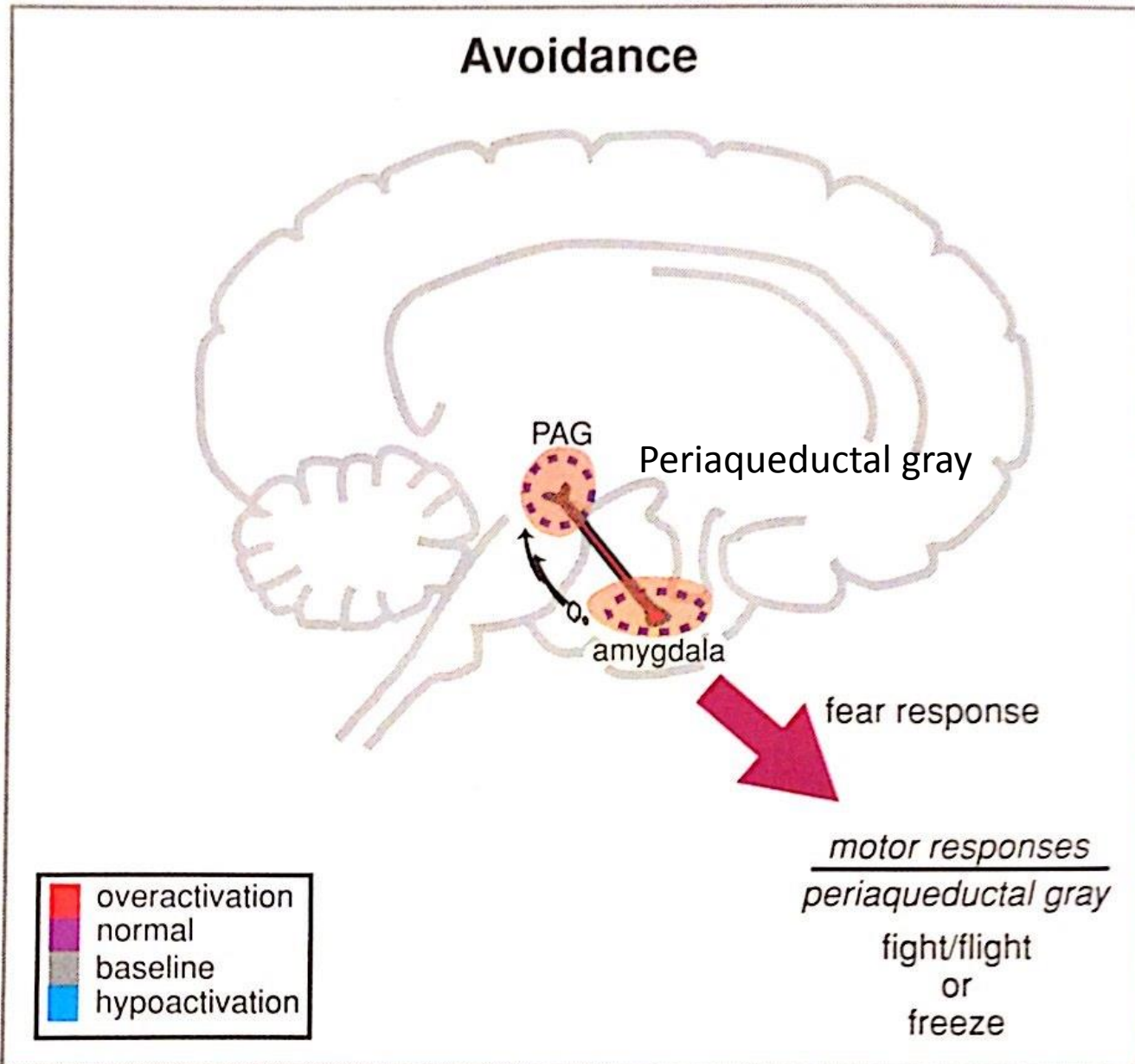
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# BRAIN REGULATION OF FEAR



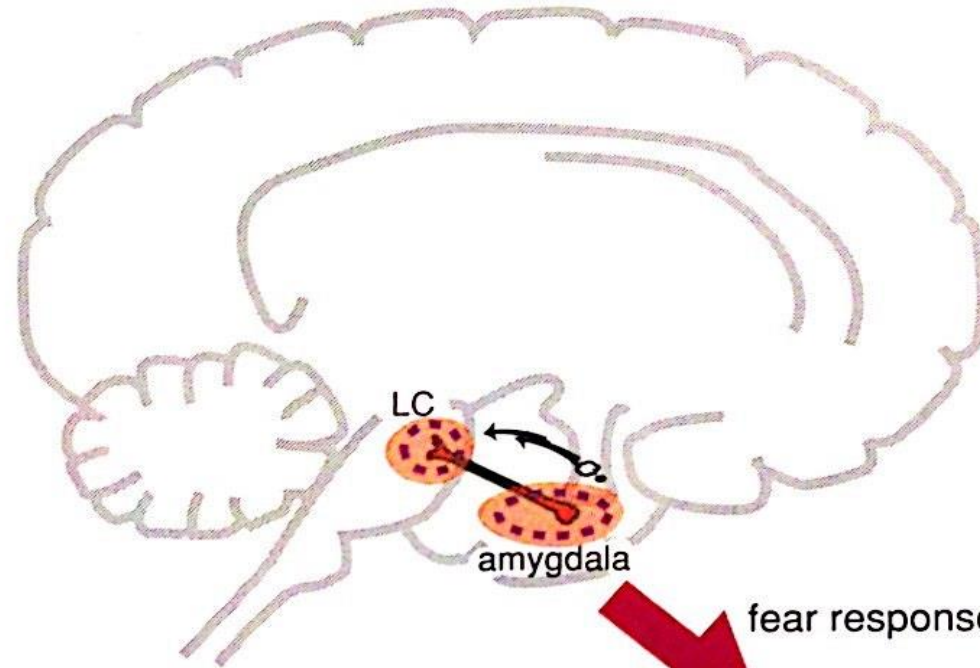
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# FEAR AND ANXIETY CIRCUITS



# BRAIN OUTPUT AND FEAR

## Autonomic Output of Fear

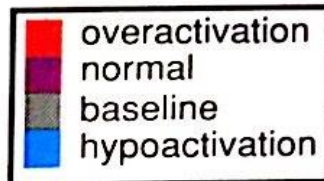


fear response

cardiovascular

*locus coeruleus*

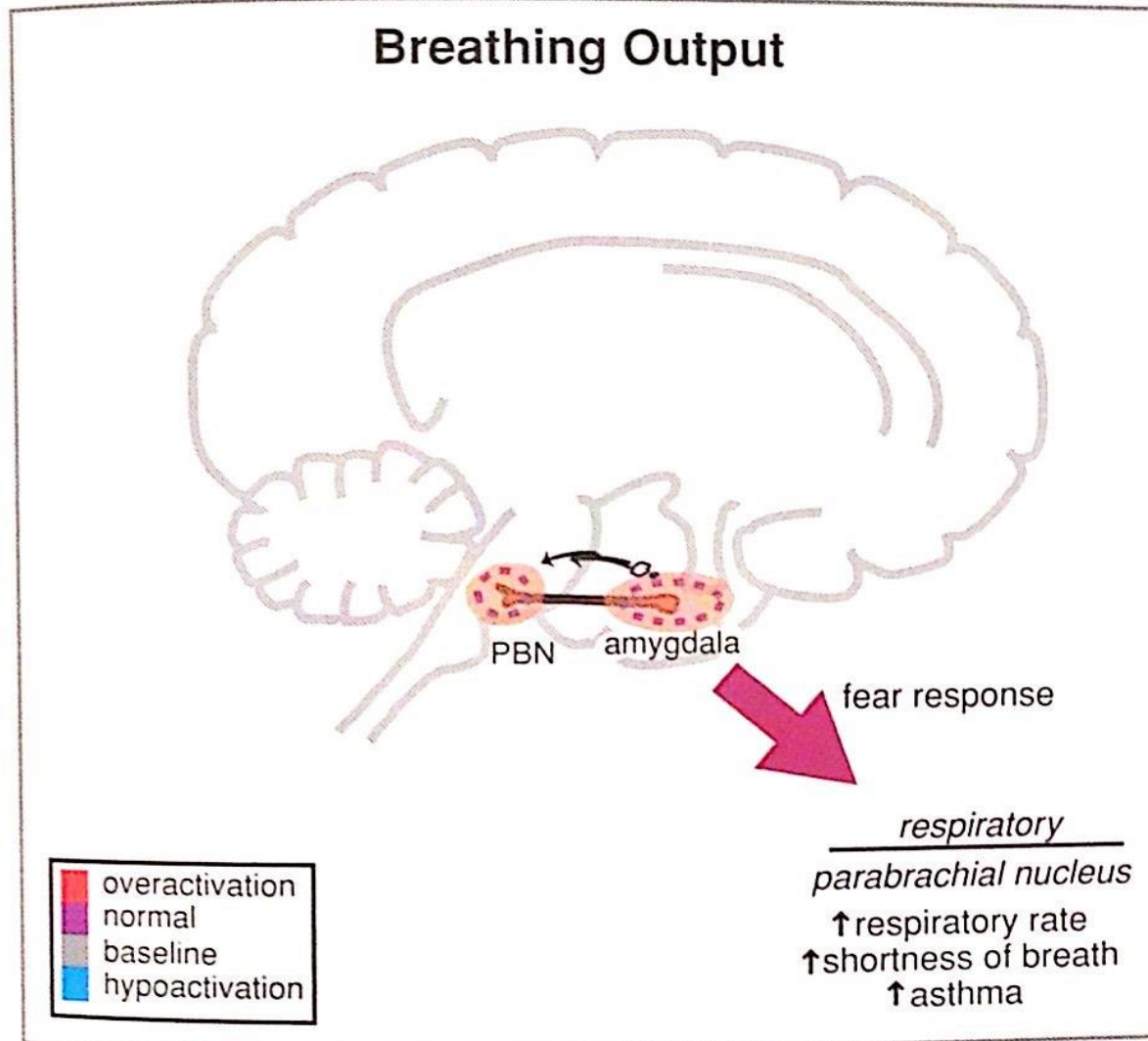
- ↑ atherosclerosis
- ↑ cardiac ischemia
- ↑ BP
- ↓ HR variability
- ↑ MI
- sudden death



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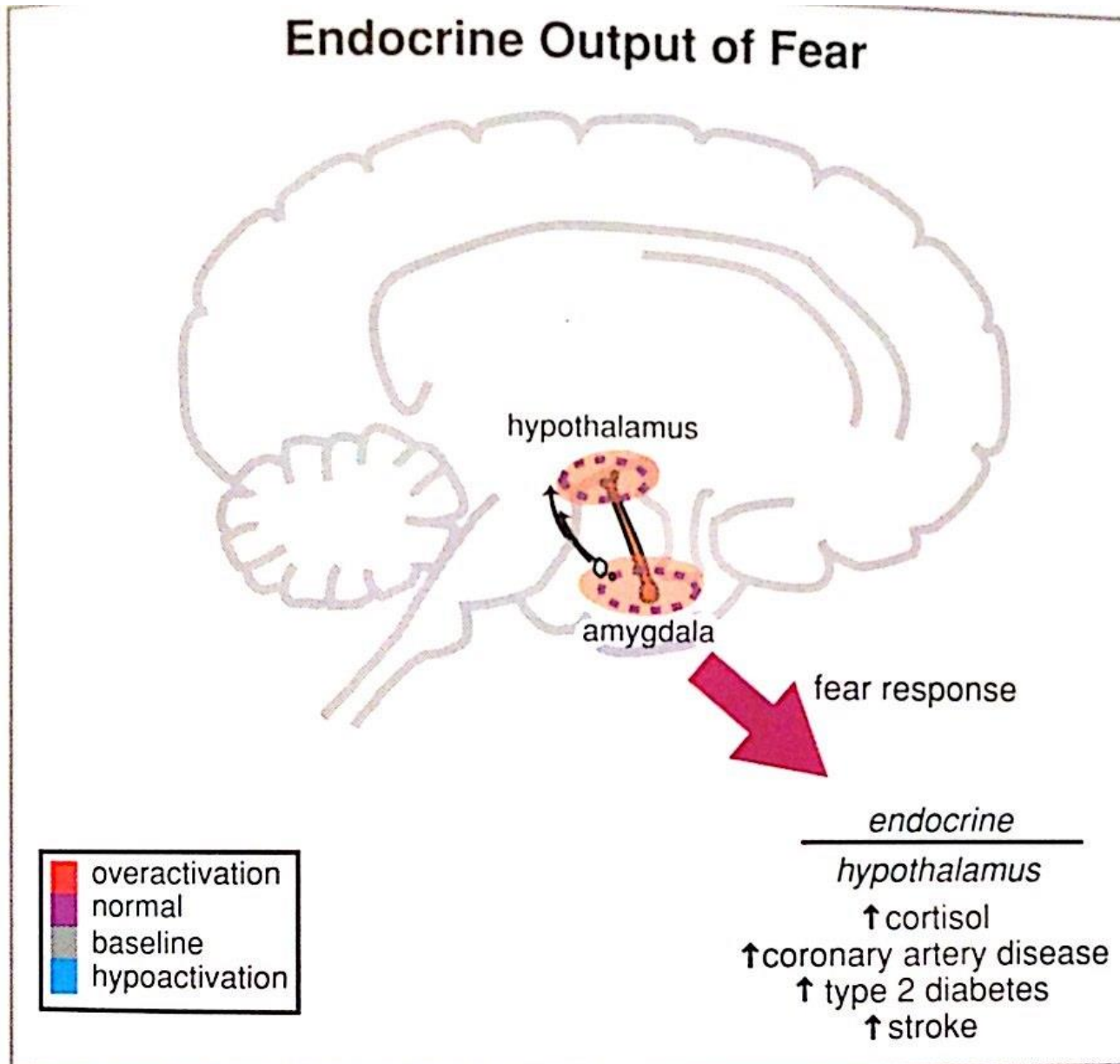


# BREATHING AND FEAR



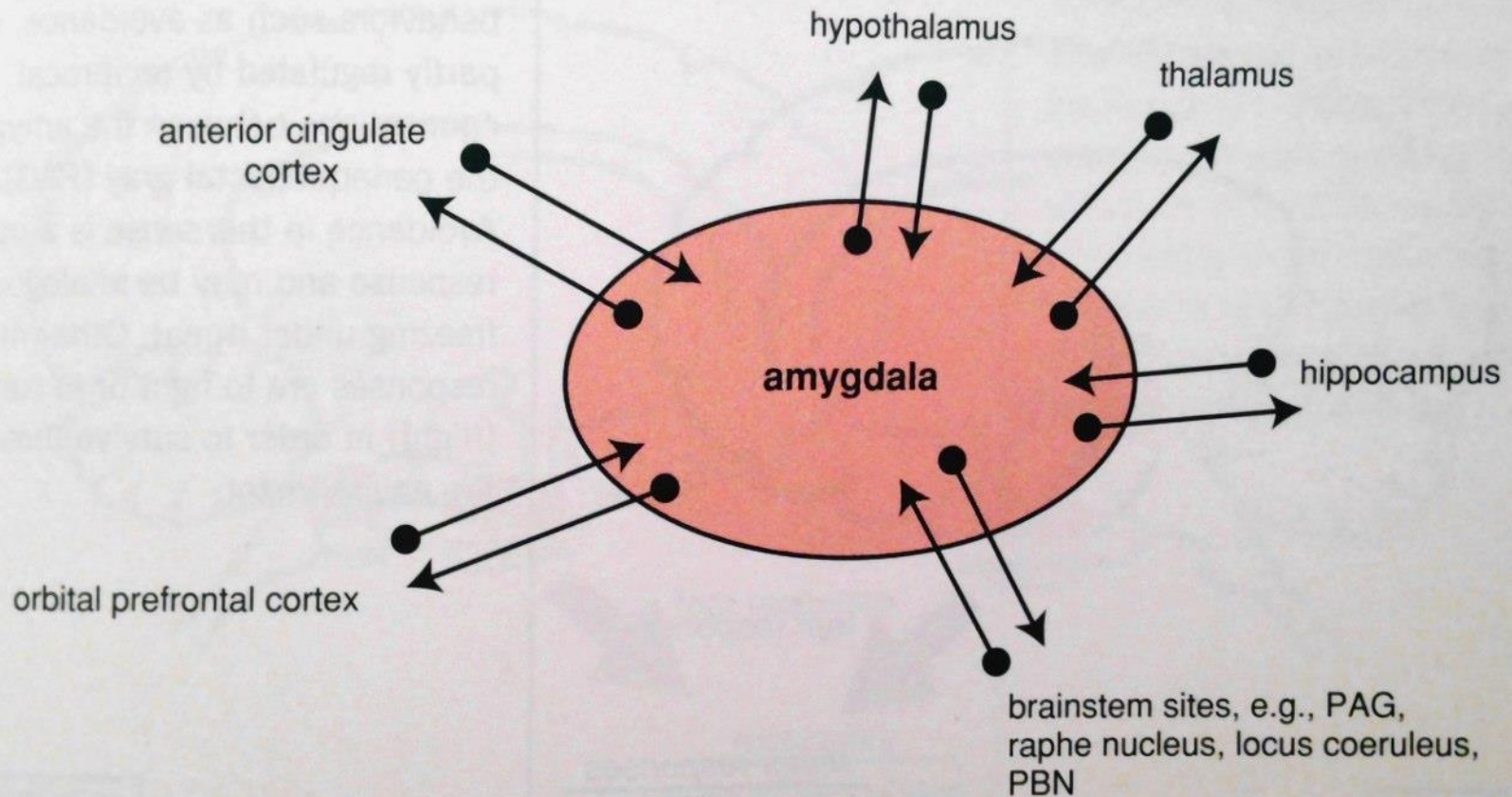
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# ENDOCRINE OUTPUT AND FEAR



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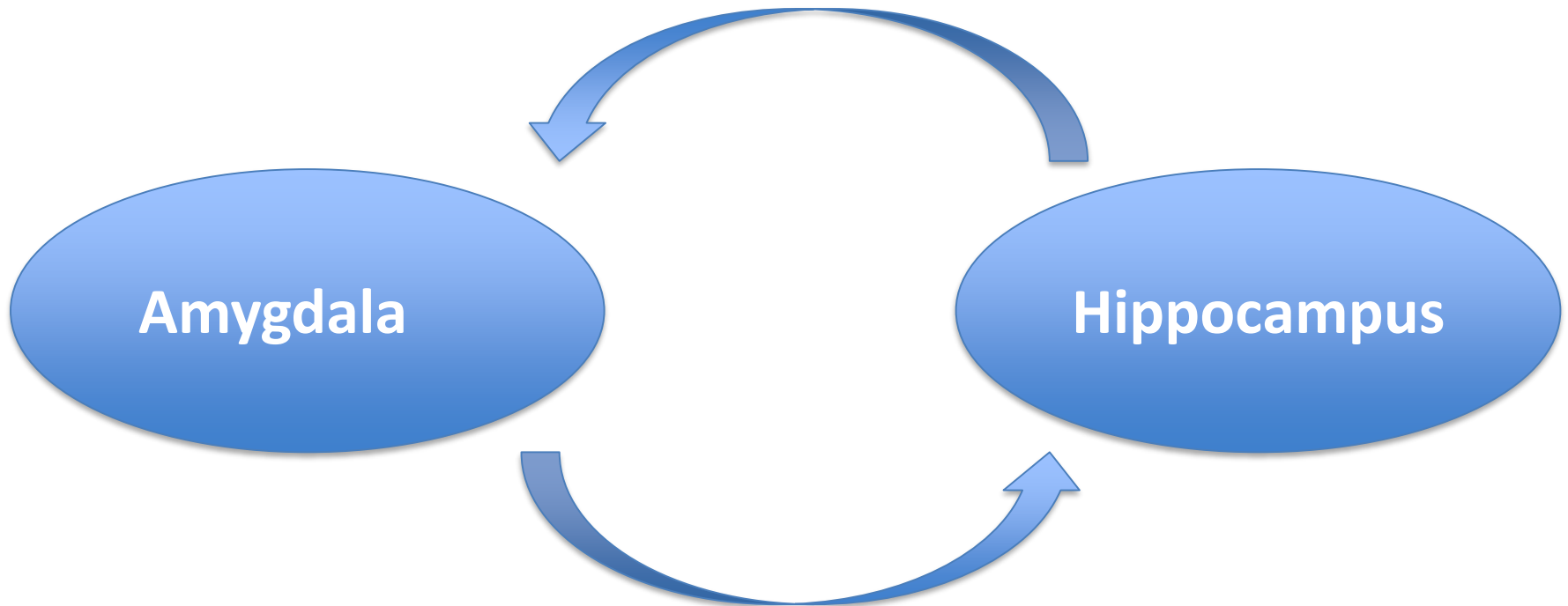
# AMYGDALA AND FEAR



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# RE EXPERIENCING FEAR

Anxiety can be triggered by memories (as well as outside stimuli): traumatic memories stored in the hippocampus can activate the amygdala which can in turn activate other brain regions causing fear response.

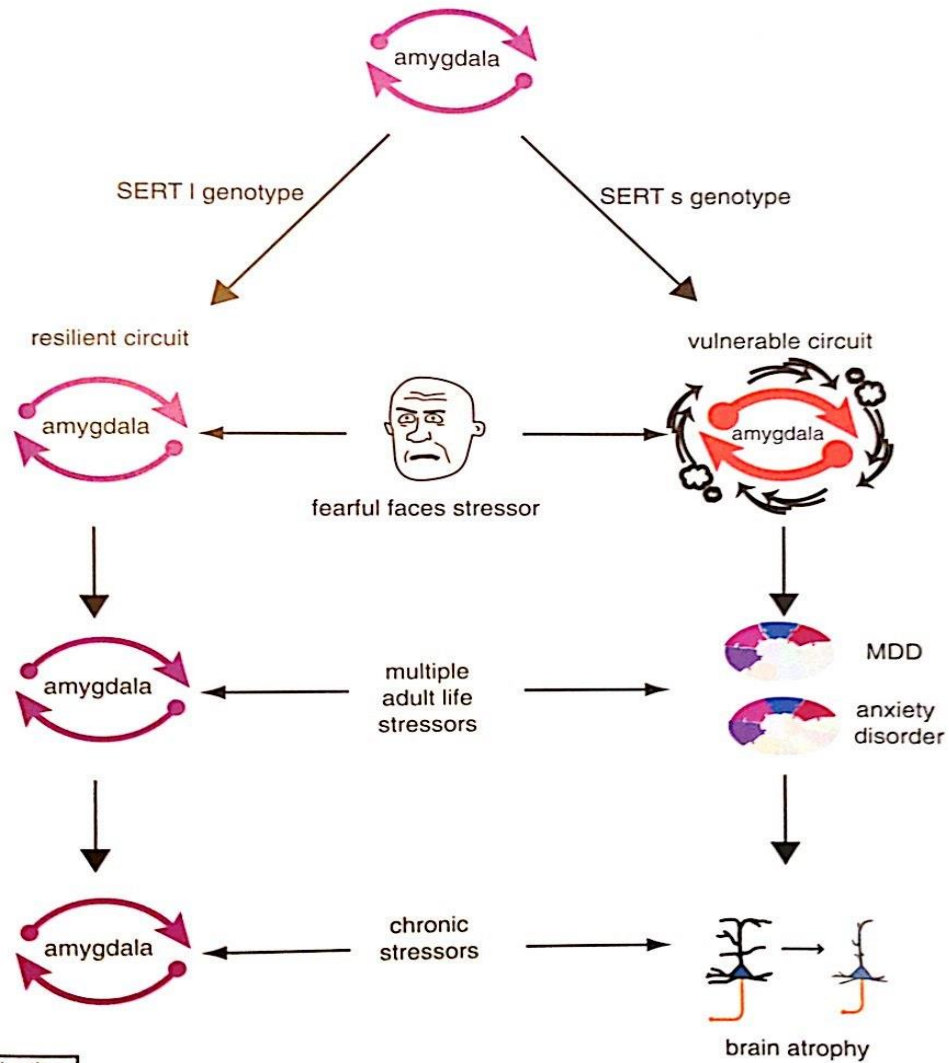


# IS FEARFULNESS GENETIC?

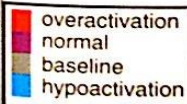
- SERT1 genotype
- SERT S genotype
  - Serotonin Transporter gene (s type)
  - Amygdala over reacts to fearful situations
  - Determines how well you respond to stress
  - Vulnerability or resilience of fear

# SEROTONIN GENETICS

## Born Fearful? Serotonin Genetics and Life Stressors



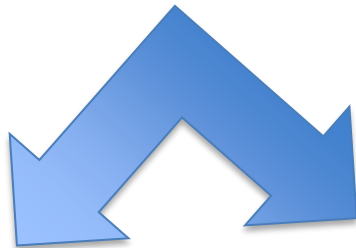
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# SENSITIZATION TO STRESS

## Stress Diathesis Hypothesis of Psychiatric Disorders

SERT  
Genotype



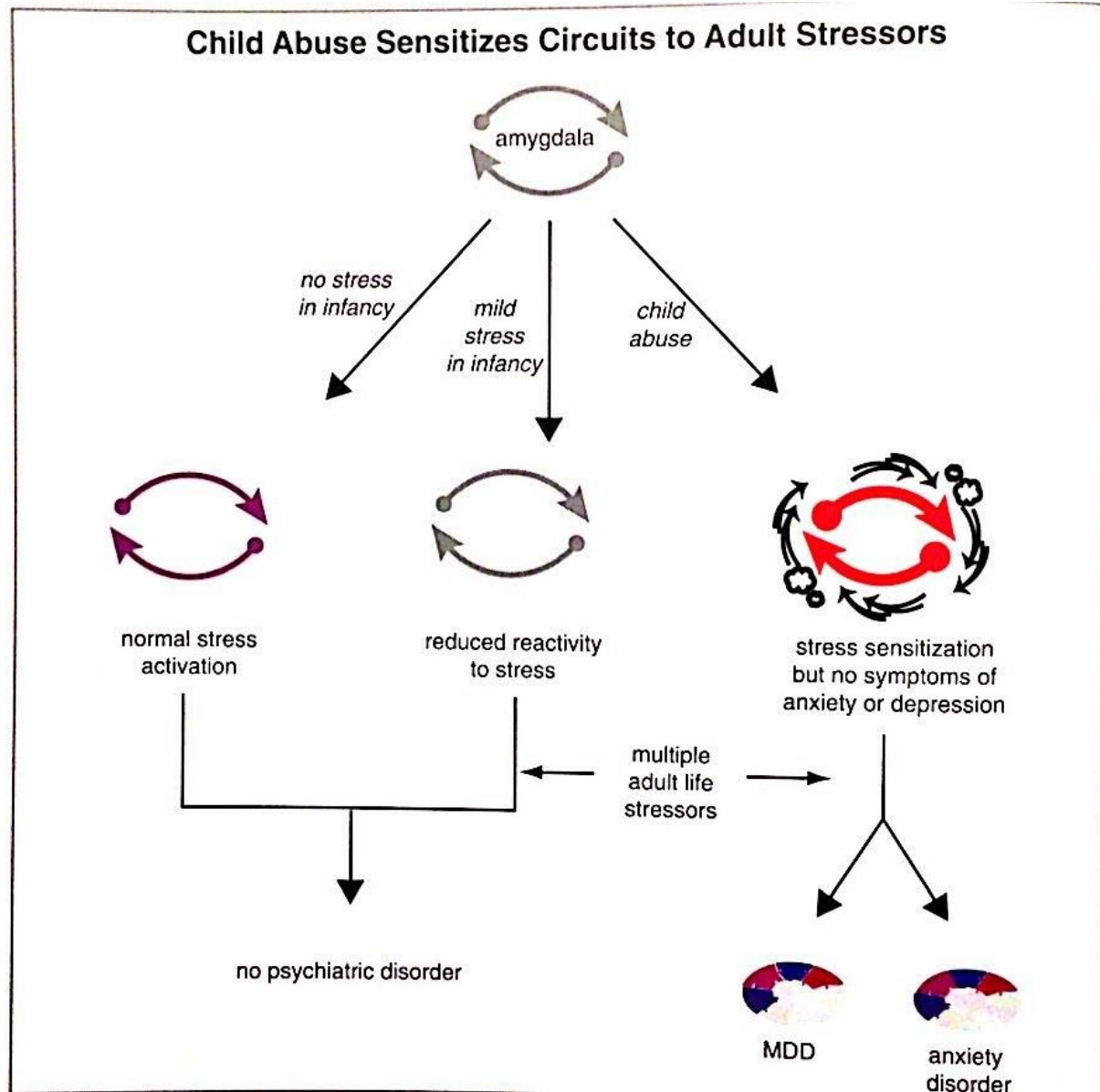
Environment

All stress in childhood may not be bad.

In animal models, exposure to mild stress in infancy can render an animal less reactive to stress later in life than animals not exposed to stress in infancy.

Mild stress may actually desensitize circuits to subsequent stress and produce a type of experience based resilience.

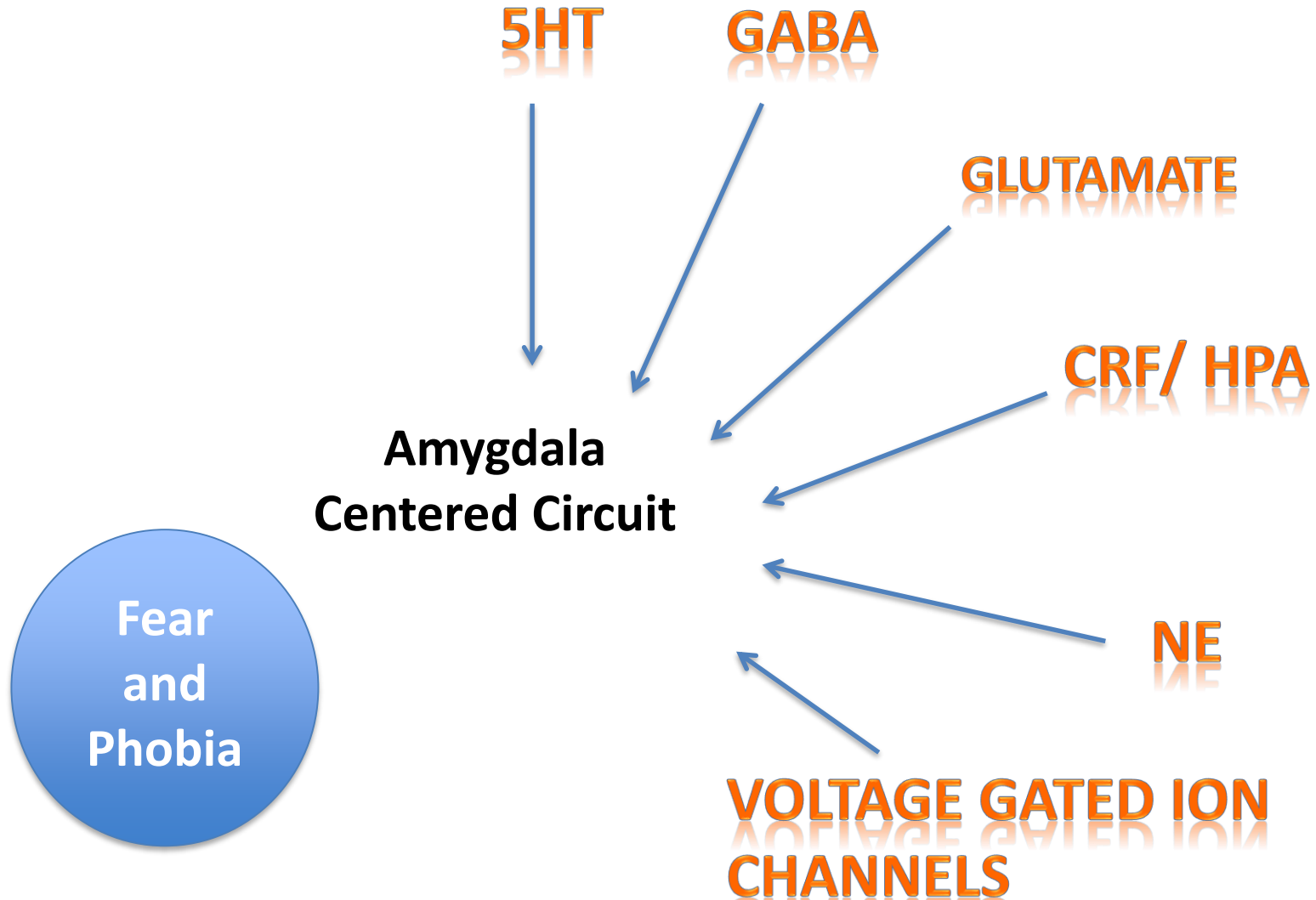
# STRESS IN EARLY YEARS



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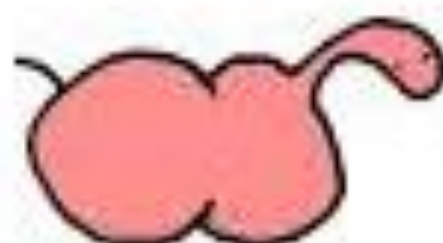
# AMYGDALA AND NEUROTRANSMITTERS



# WHAT ABOUT THOSE NEUROTRANSMITTERS?

DOPAMINE	→	Pleasure, Appetite Suppression
NOREPINEPHRINE	→	Arousal, Appetite Suppression
ACETYLCHOLINE	→	Arousal, Cognitive Enhancement
GLUTAMATE	→	Learning, Memory Enhancement
SEROTONIN	→	Mood Modulation, Appetite Suppression
BETA-ENDORPHIN	→	Reduction of Anxiety and Tension
GABA	→	Reduction of Anxiety and Tension

# SEROTONIN & DOPAMINE

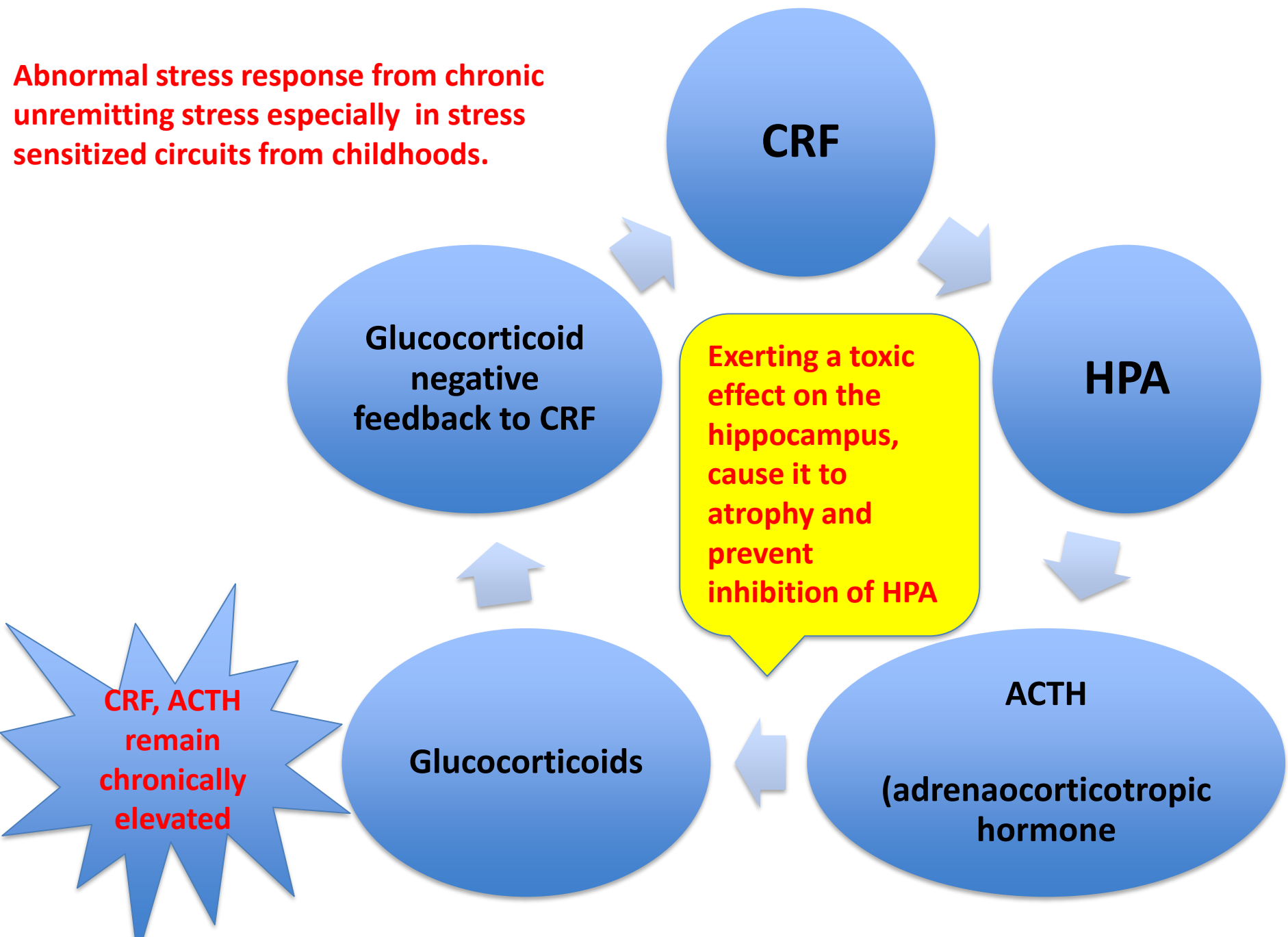


Technically, the only two things  
you enjoy

# WHAT ABOUT CRF/HPA?

- CRF is Corticotrophin releasing factor
- HPA stands for Hypothalamic-Pituitary-Adrenal Axis.
- Regulation of “steroids” or glucocorticoids to react to stress
  - Cortisol
  - Dopamine
  - Epinephrine
  - Norepinephrine

**Abnormal stress response from chronic unremitting stress especially in stress sensitized circuits from childhoods.**



# ANXIETY AND SUBSTANCE ABUSE

- Substance Abuse
  - Self medicating
    - Initially, a way to alleviate unpleasant symptoms of unmanageable stress.
    - Reward circuitry can overpower the use of substances and turn it into the abuse of substances.
      - Potent behavior reinforcing properties of some psychoactive drugs sustain the need and ability of drug to ameliorate underlying psychosocial symptoms.
      - \*we will discuss this topic next
  - Comorbid psychiatric disorders
    - 78 % of men and 86% of women also have at least one other psychiatric disorder.

*Piazza PV, Le Moal M. "The Role of Stress in Drug Self-Administration" Trends in Pharmacological Sciences 19 (1998): 67-74.*

# END PART 1

- Questions?
- Comments?
- Connect the Dots?
  - How do substances of abuse act on circuits of fear and stress?

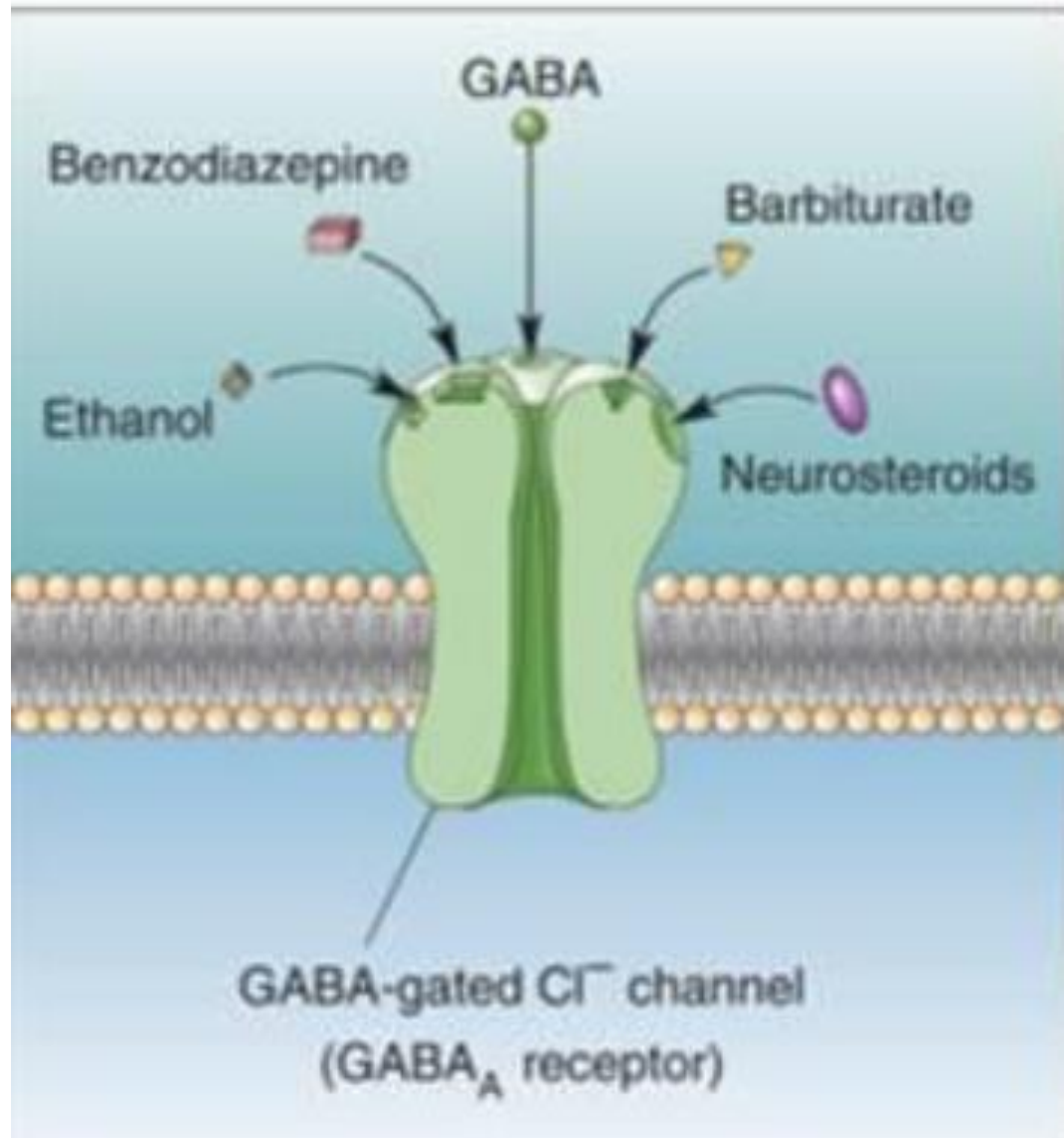
# CHALLENGE QUESTION:

- Ethanol, the second most widely used psychoactive drug in the world, is used as a sedative and intoxicant.
  - **Name a neurotransmitter that EtOH effects to alleviate the effects of stress and anxiety?**



# Ethanol and GABA-ergic system

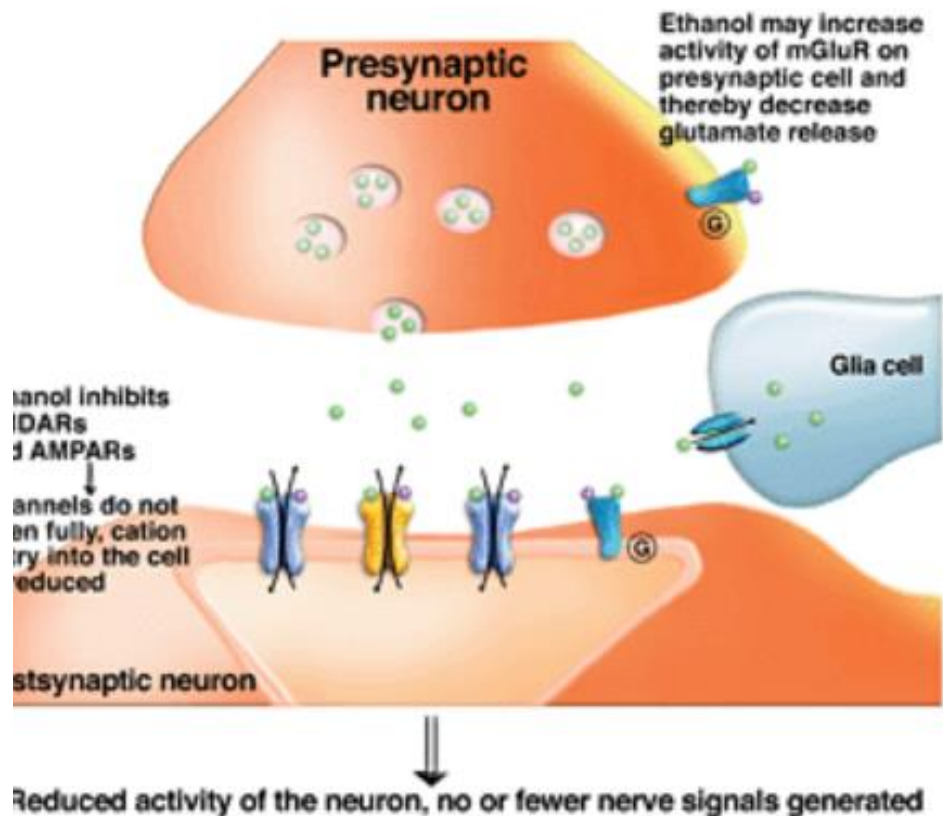
- EtOH enhances GABA system which is inhibitory to CNS overall.



# Ethanol and Glutaminergic System

A potent inhibitor of glutamate receptors (NMDA subtype receptor inhibitor) which disrupts glutamatergic neurotransmission.

- Glutamate system is excitatory.



# Alcohol effects disinhibition of DA effects

