

# Happy Forever

## The Importance of Neurotransmitter Balancing

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**LifeExtension**  
Foundation for Longer Life®

# SEROTONIN & DOPAMINE



Technically, the only two things  
you enjoy

<https://nootriment.com/serotonin-dopamine/>

# Who I am?



## Position:

- Full time staff at Life Extension
- Senior Wellness Specialist
- Review lab results including neurotransmitter & steroid hormone balancing.

## Education:

- Naturopathic Physician
- Doctorate from Bastyr University  
Kenmore, WA



# The Plan...

## Focus on Longevity, Wellness & Balance



- Introduction to the major Neurotransmitters
- Achieving Balance
  - How they are made
  - How they are broken down
- Neuroendocrine connection
- What YOU can do to be proactive

# Really, Happy Forever?

**That is a lot of  
pressure on  
neurotransmitters...**

However, neurotransmitter  
balancing is an important part  
of feeling good



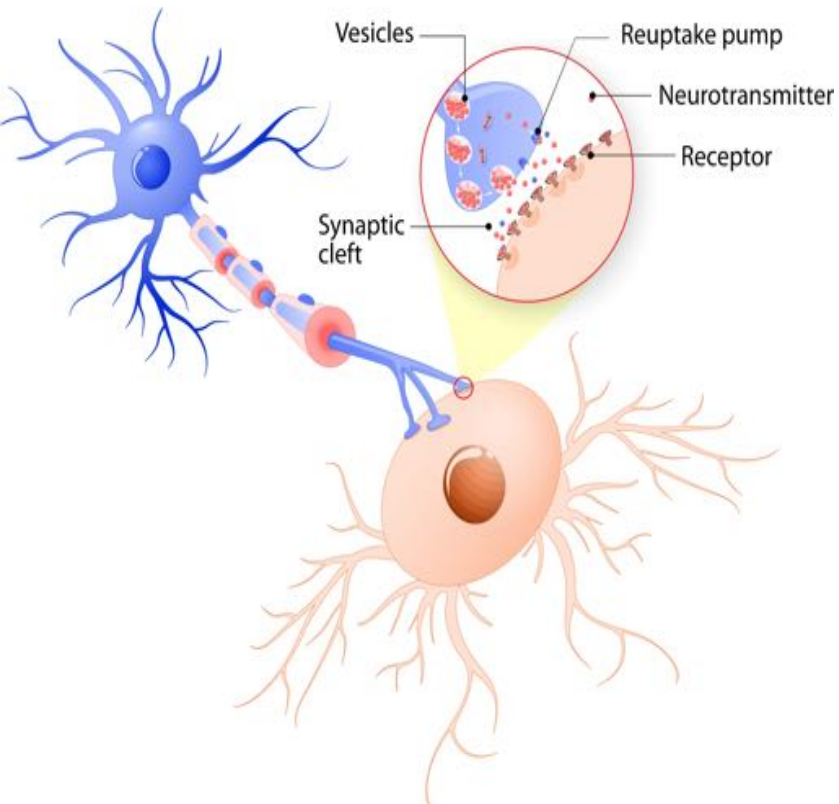
# Lets meet the Major Players...



- Serotonin
- Catecholamine's
  - Dopamine
  - Norepinephrine
  - Epinephrine
- Glutamate
- Gamma-Aminobutyric Acid (GABA)
- Phenylethylamine (PEA)
- Histamine
- Glycine
- Acetylcholine

# What are they?

## CHEMICAL SYNAPSE



## Neurotransmitters are chemical MESSENGERS

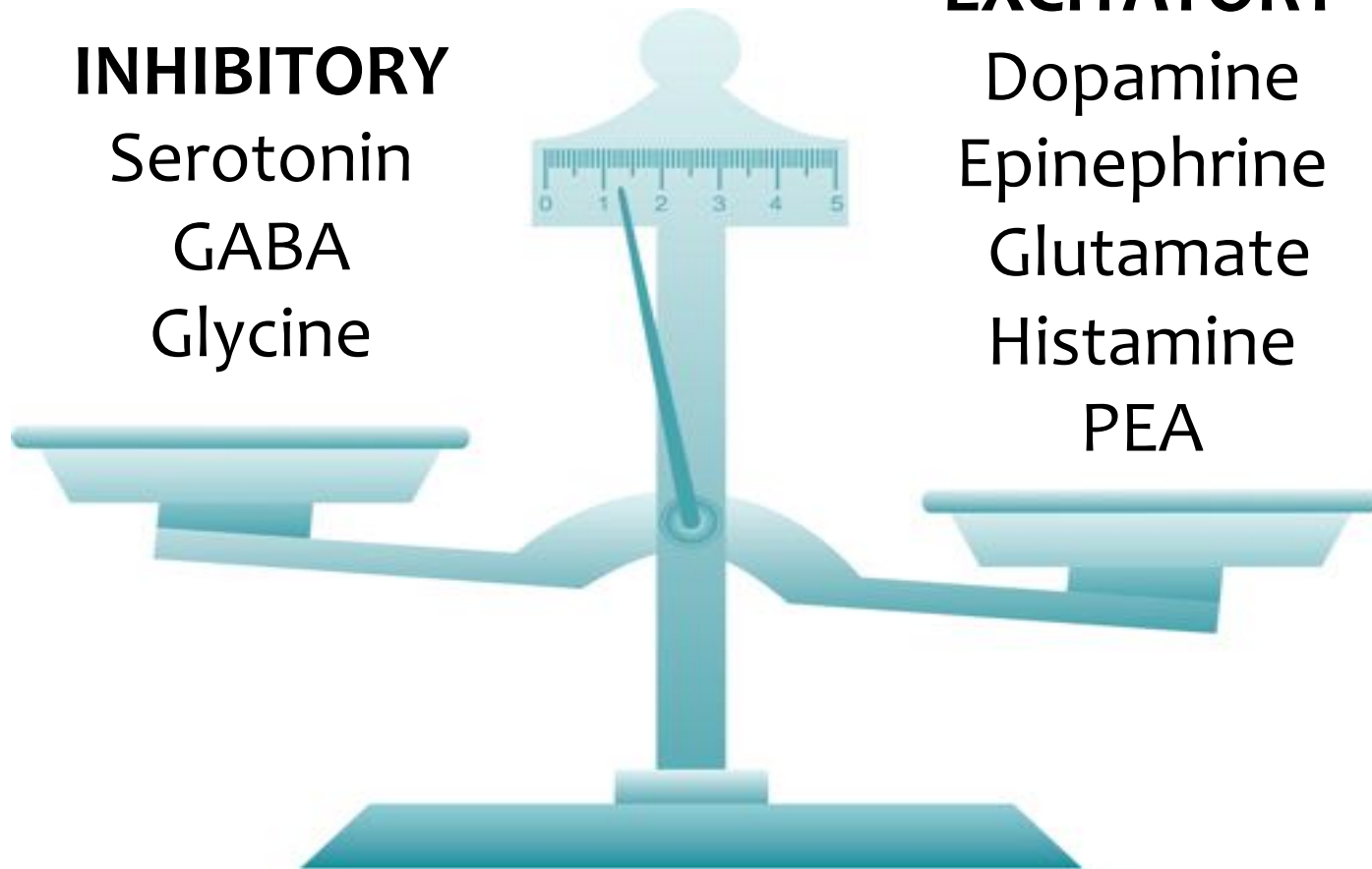
- Regulate: EMOTIONAL, COGNITIVE & PHYSICAL responses
- EX: memory, attention, movement appetite, energy

## **INHIBITORY**

Serotonin

GABA

Glycine



## **EXCITATORY**

Dopamine

Epinephrine

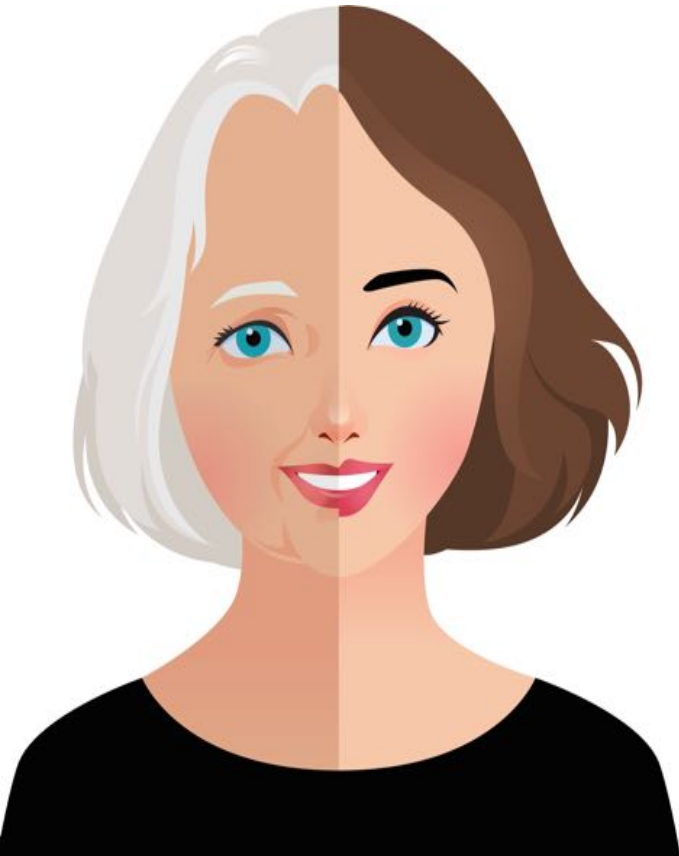
Glutamate

Histamine

PEA



# Why do we Care?



## From an Anti-Aging Perspective

- Live long enough to see a CURE for AGING
- ENJOY our time the longer we live
  - Feel vitality
  - Continue to feel motivated
  - Continue to learn & achieve
- Mood – optimistic people live longer
- Appetite – calorie restriction
- Pleasure – sexual satisfaction
- Focus & Attention – learning & expanding knowledge

Curr Biol. 2012 Aug 21; 22(16): 1477–1481.  
doi: [10.1016/j.cub.2012.05.053](https://doi.org/10.1016/j.cub.2012.05.053)

PMCID: PMC3424419  
PMID: [22795698](https://pubmed.ncbi.nlm.nih.gov/22795698/)

## How Dopamine Enhances an Optimism Bias in Humans

Tali Sharot,<sup>1,\*</sup> Marc Guitart-Masip,<sup>2,3</sup> Christoph W. Korn,<sup>4,5</sup> Rumana Chowdhury,<sup>2,3</sup> and Raymond J. Dolan<sup>2</sup>

This effect is due to L-DOPA impairing the ability to update belief in response to undesirable information about the future. These findings provide the first evidence that the neuromodulator dopamine impacts on belief formation by reducing negative expectations regarding the future.

... or professional success [4], people habitually underestimate the likelihood of future negative events (for review see [5]). This well-known bias, termed unrealistic optimism [6], is observed across age [7], culture [8], and species [9] and has a significant societal impact on domains ranging from financial markets to health and well being. However, it is unknown how neuromodulatory systems impact on the generation of optimistically biased beliefs. This question assumes great importance in light of evidence that common neuropsychiatric disorders, such as depression, are characterized by pessimism [10, 11]. Here, we show that administration of a drug that enhances dopaminergic function (dihydroxy-L-phenylalanine; L-DOPA) increases an optimism bias. This effect is due to L-DOPA impairing the ability to update belief in response to undesirable information about the future. These findings provide the first evidence that the neuromodulator dopamine impacts on belief formation by reducing negative expectations regarding the future.



# HHS Public Access

Author manuscript

Health Behav Policy Rev. Author manuscript; available in PMC 2016 January 01.

Published in final edited form as:

Health Behav Policy Rev. 2015 January ; 2(1): 62–73. doi:10.14485/HBPR.2.1.6.

## Optimism and Cardiovascular Health: Multi-Ethnic Study of Atherosclerosis (MESA)

Rosalba Hernandez, PhD<sup>1</sup>, Kiarri N. Kershaw, PhD<sup>2</sup>, Juned Siddique, DrPH<sup>2</sup>, Julia K. Boehm, PhD<sup>3</sup>, Laura D. Kubzansky, PhD, MPH<sup>4</sup>, Ana Diez-Roux, MD, PhD, MPH<sup>5</sup>, Hongyan Ning, MD<sup>2</sup>, and Donald M. Lloyd-Jones, MD, ScM<sup>2</sup>

<sup>1</sup>School of Social Work, University of Illinois at Urbana-Champaign, Urbana, IL

<sup>2</sup>Dept of Preventive Medicine,

<sup>3</sup>Dept of Psychology, Chapman

<sup>4</sup>Dept of Social and Behavioral

<sup>5</sup>School of Public Health, Drexel

Participants in the highest quartile of optimism were more likely to have intermediate [OR=1.51:95%CI=1.25,1.82] and ideal [OR=1.92:95%CI=1.30,2.85] CVH when compared to the least optimistic group.

### Abstract

**Objectives**— We examined the cross-sectional association between optimism and cardiovascular health (CVH).

**Methods**— We used data collected from adults aged 52–84 who participated in the Multi-Ethnic Study of Atherosclerosis (MESA) (n=5,134) during the first follow-up visit (2002–2004). Multinomial logistic regression was used to examine associations of optimism with ideal and intermediate CVH (with reference being poor CVH), after adjusting for socio-demographic factors and psychological ill-being.

**Results**— Participants in the highest quartile of optimism were more likely to have intermediate [OR=1.51:95%CI=1.25,1.82] and ideal [OR=1.92:95%CI=1.30,2.85] CVH when compared to the least optimistic group. Individual CVH metrics of diet, physical activity, BMI, smoking, blood sugar and total cholesterol contributed to the overall association.

**Conclusions**— We offer evidence for a cross-sectional association between optimism and CVH.

Am J Epidemiol. 2017 Jan 1; 185(1): 21–29.  
Published online 2016 Dec 27. doi: [10.1093/aje/kww182](https://doi.org/10.1093/aje/kww182)

PMCID: PMC5209589  
PMID: [27927621](https://pubmed.ncbi.nlm.nih.gov/27927621/)

## Optimism and Cause-Specific Mortality: A Prospective Cohort Study

Eric S. Kim,<sup>\*</sup> Kaitlin A. Hagan, Francine Grodstein, Dawn L. DeMeo, Immaculata De Vivo, and Laura D. Kubzansky

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This article has been [cited by](#) other articles in PMC.

### Abstract

Go to:

Growing evidence has linked positive psychological attributes like optimism to a lower risk of poor health outcomes, especially cardiovascular disease. It has been demonstrated in randomized trials that optimism can be learned. If associations between optimism and broader health outcomes are established, it may lead to novel interventions that improve public health and longevity. In the present study, we evaluated the association between optimism and cause-specific mortality in women after considering the role of potential confounding (sociodemographic characteristics, depression) and intermediary (health behaviors, health conditions) variables. We used prospective data from the Nurses' Health Study ( $n = 70,021$ ). Dispositional optimism was measured in 2004; all-cause and cause-specific mortality rates were assessed from 2006 to 2012. Using Cox proportional hazard models, we found that a higher degree of optimism was associated with a lower mortality risk, independent of sociodemographic characteristics. The association remained for the highest quartile of optimism. Adding health behaviors and health conditions to the models did not change the associations (hazard ratios were maintained for various causes of death, including cancer, heart disease, stroke, respiratory disease, and

Using Cox proportional hazard models, we found that a higher degree of optimism was associated with a lower mortality risk.

# OPTIMISM

## Optimism and Cause-Specific Mortality: A Prospective Cohort Study

After adjusting for sociodemographic & depression confounders, analysis of data from the Nurse's Health Study found the most optimistic women had:

- 16% lower risk of dying from cancer
- 38% lower risk of dying from heart disease
- 39% lower risk of dying from stroke



# Next, Appetite & Longevity



- Calorie Restriction has shown to prolong life span<sup>1,2,3</sup>
- Obesity increases risk of all cause mortality<sup>4</sup>
- Neurotransmitters like Serotonin & Histamine regulate appetite<sup>5, 6, 7,8</sup>

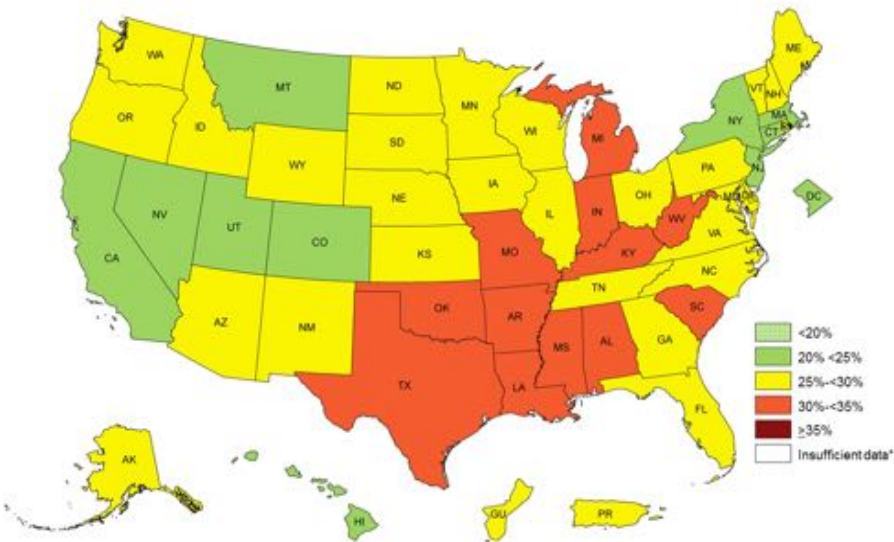
1. Nat Commun. 2014 Apr 1;5:3557
2. Comp Biochem Physiol A Mol Integr Physiol. 2018 Sep;223:1-9
3. Proc Nutr Soc. 2018 May;77(2):174-188
4. <https://www.cdc.gov/healthyweight/effects/index.html>. Accessed August 12, 2018
5. Pharmacol Res. 2016 Nov;113(Pt A):100-107
6. PLoS One. 2016 Feb 4;11(2):e0148484
7. Nature. 2012 Sep 13;489(7415):318-21
8. Ann N Y Acad Sci. 2007 Oct;1114:434-55

# Obesity on the Rise!

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS. **Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.**

## 2011

## 2016



Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.

<https://www.cdc.gov/obesity/data/prevalence-maps.html> Accessed August 12, 2018



# And, long life would not be complete without... Pleasure

- **Dopamine regulates PLEASURE!**
- In regions of the brain that regulate movement, emotion, cognition, & pleasure
  - We find **Dopamine**
- For repetition of activities required for life, dopamine is release
  - Activities include: Eating, Sex & Exercise
  - Can provide temporary relief of discomfort





Article

## Dopamine and sexual behavior

Maria Rosaria Mellis <sup>✉</sup>, Antonio Argiolas

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[https://doi.org/10.1016/0149-7634\(94\)00020-2](https://doi.org/10.1016/0149-7634(94)00020-2)

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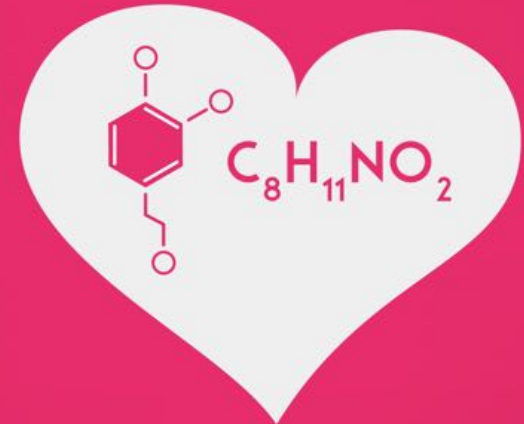
### Abstract

Among central neurotransmitters involved in the control of sexual behavior, dopamine is certainly one of the most extensively studied. Our attempt to review old and recent neuropharmacological, biochemical, electrophysiological, and psychobiological studies performed so far only in rats, monkeys, and humans, provides evidence that dopamine through its different neuronal systems and

Among central neurotransmitters involved in the control of sexual behavior, dopamine is certainly one of the most extensively studied.

emission and erectile performance, but evidence for its involvement in sexual motivation also exists. The dopaminergic receptors playing the major role in the control of male sexual behavior belong to the D<sub>2</sub> receptor subtype. However a D<sub>1</sub> D<sub>2</sub> receptor interaction is well established and an opposite role for D<sub>1</sub> and D<sub>2</sub> receptors in the preoptic area suggested. Despite some differences, most studies show that treatments that increase or decrease, respectively, brain dopaminergic activity improve or worsen, respectively, several parameters of copulatory activity, supporting a facilitatory role of dopamine in male sexual behavior. In contrast, no conclusion can be deduced from the available studies on the role of central dopaminergic systems in the control of proceptivity and receptivity, the two main components of female sexual behavior.

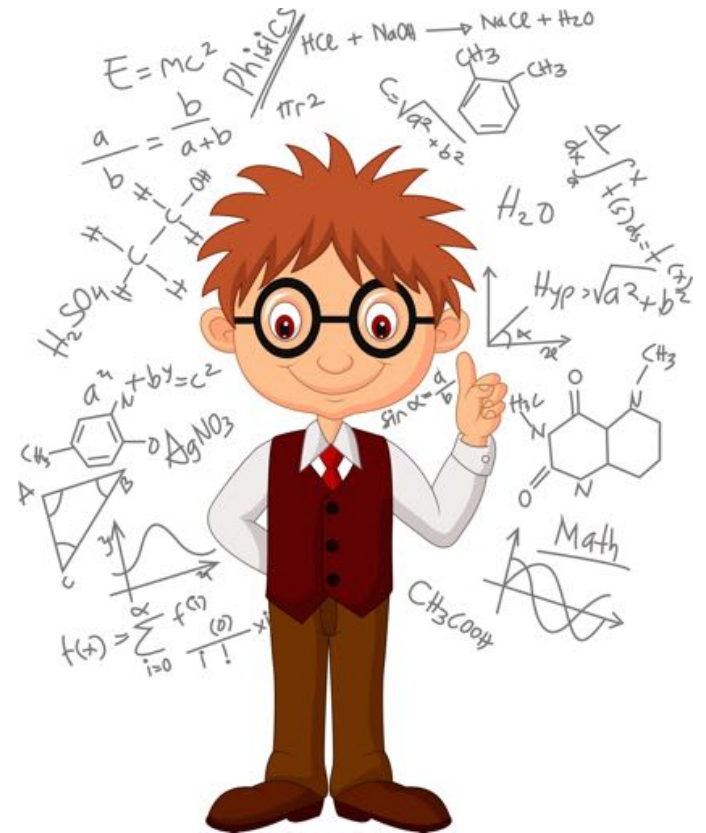
## DOPAMINE LOVE AND PASSION



# Now... Learning for Life

Neurotransmitters that regulate  
Memory, Focus, Attention:

**Dopamine**  
**Norepinephrine**  
**Histamine**  
**Phenylethylamine**



# ATTENTION/FOCUS/COGNITION



## ARTICLE

DOI: [10.1038/s41467-018-05214-4](https://doi.org/10.1038/s41467-018-05214-4)

OPEN

## Impaired recruitment of dopamine neurons during working memory in mice with striatal D2 receptor overexpression

Sevil Duvarci<sup>1</sup>, Eleanor H. Simpson<sup>2,3</sup>, Gaby Schneider<sup>4</sup>, Eric R. Kandel<sup>3,5,6,7,8</sup>, Jochen R. Torfi Sigurdsson<sup>1</sup>

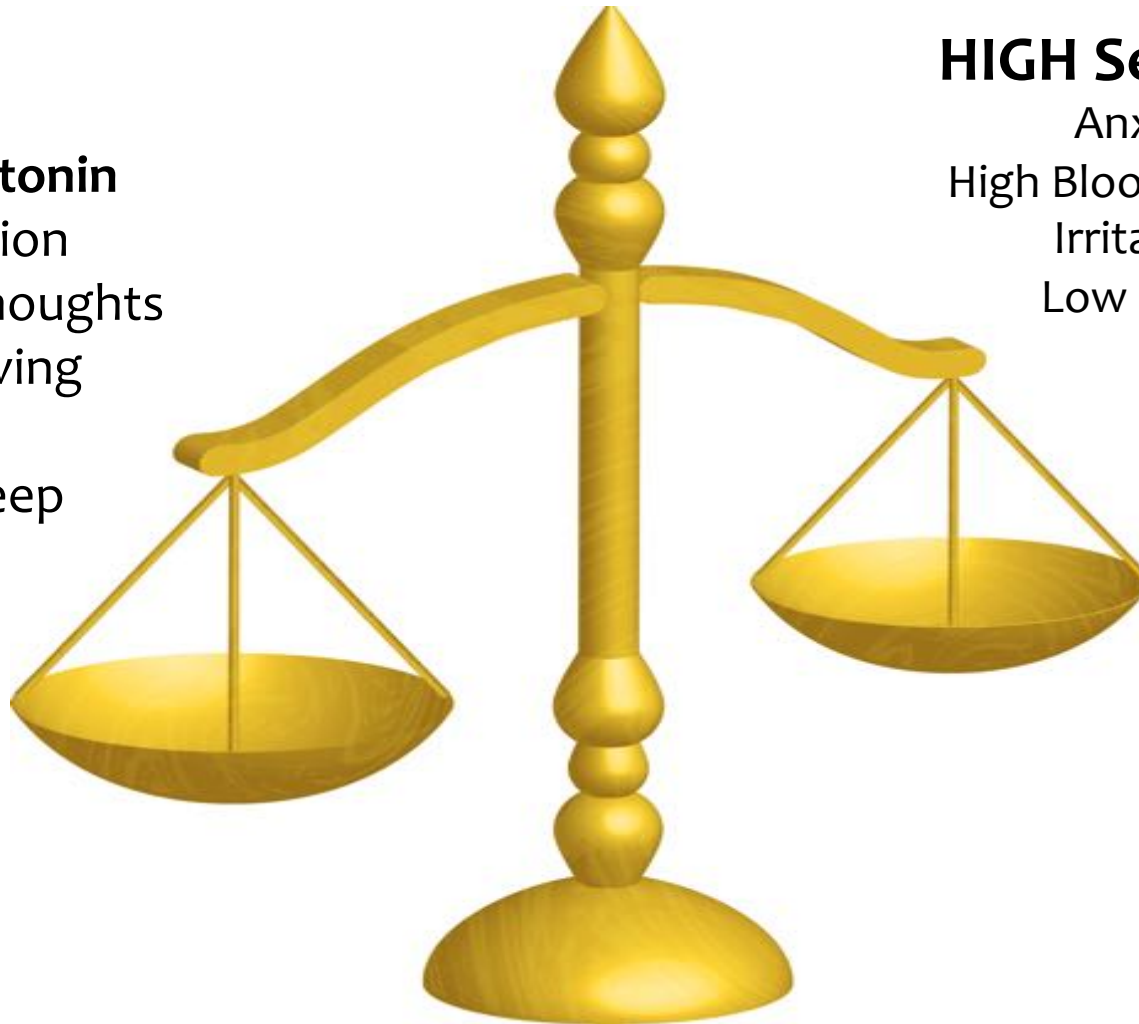
The dopamine (DA) system plays a major role in cognitive functions through its interactions with several brain regions including the prefrontal cortex (PFC). Conversely, disturbances in the DA system contribute to cognitive deficits in psychiatric diseases, yet exactly how they do so remains poorly understood. Here we show, using mice with disease-relevant alterations in DA signaling (D2R-OE mice), that deficits in working memory (WM) are associated with impairments in the WM-dependent firing patterns of DA neurons in the ventral tegmental area (VTA). The WM-dependent phase-locking of DA neurons to 4 Hz VTA-PFC oscillations is absent in D2R-OE mice and VTA-PFC synchrony deficits scale with their WM impairments. We also find reduced 4 Hz synchrony between VTA DA neurons and selective impairments in their representation of WM demand. These results identify how altered DA neuron activity—at the level of long-range network activity and task-related firing patterns—may underlie cognitive impairments.

The dopamine (DA) system plays a major role in cognitive functions through its interactions with several brain regions including the prefrontal cortex (PFC).

# Now... Lets Discuss How to Achieve Balance

## **LOW Serotonin**

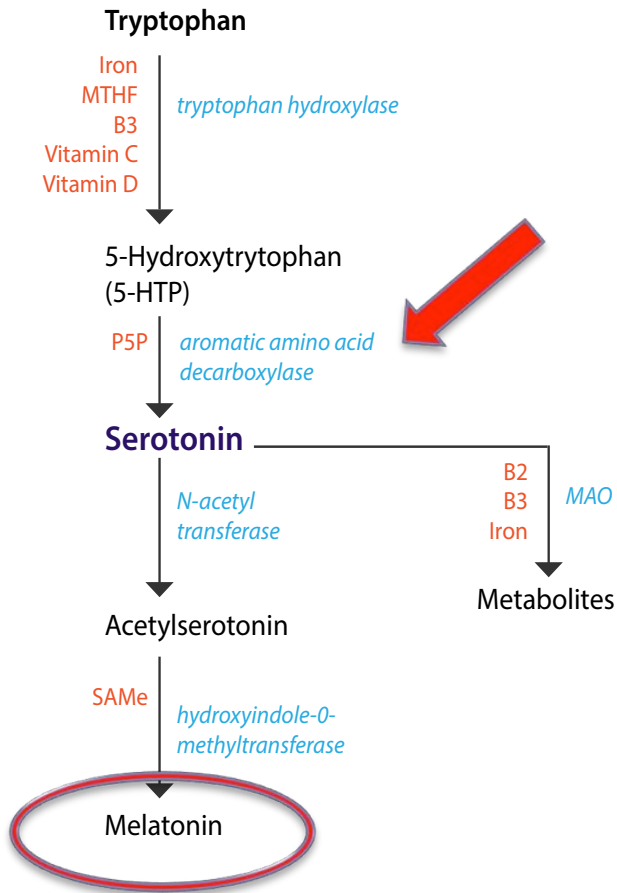
Depression  
Obsessive thoughts  
Carb craving  
PMS  
Poor Sleep  
IBS



## **HIGH Serotonin**

Anxiety  
High Blood Pressure  
Irritability  
Low Libido

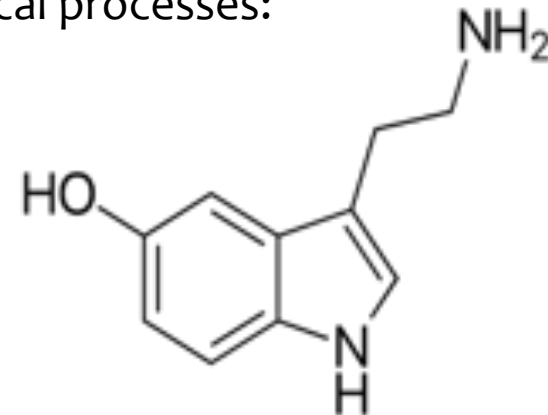
# Serotonin: The “Master” Neurotransmitter



## Happiness & Well-being

•Tied to many biological processes:

- MOOD
- Sleep**
- Digestion
- Appetite
- Pain



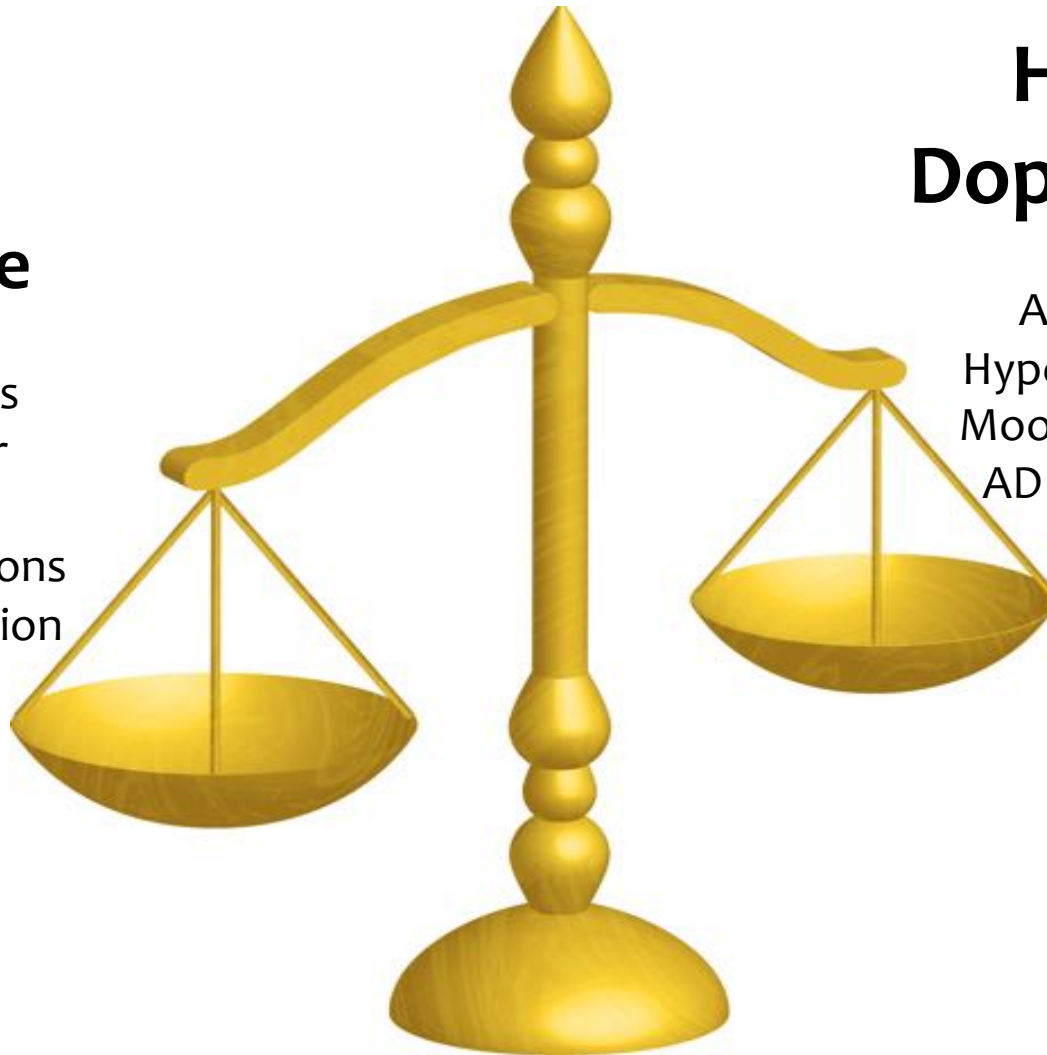
# Comedy Break



**"Every time he lectures about serotonin,  
he puts me to sleep."**

## Low Dopamine

Memory Issues  
Loss of motor  
control  
Cravings/Addictions  
Loss of Satisfaction

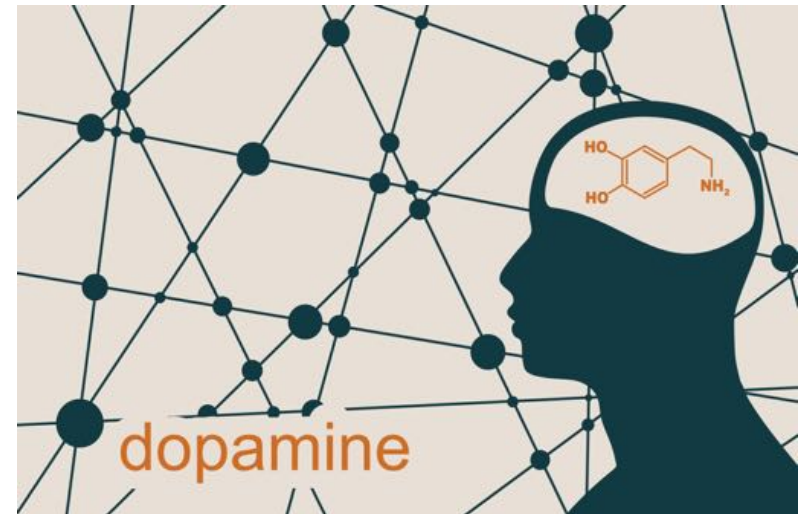
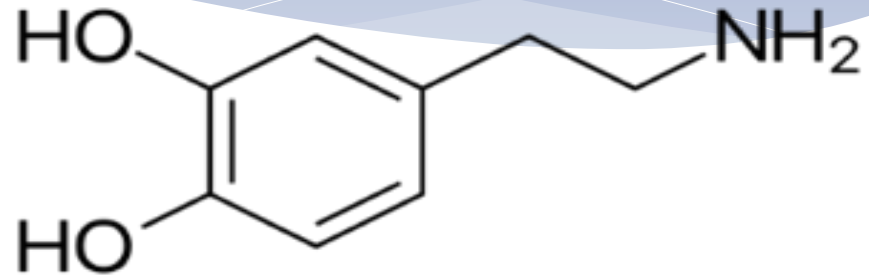
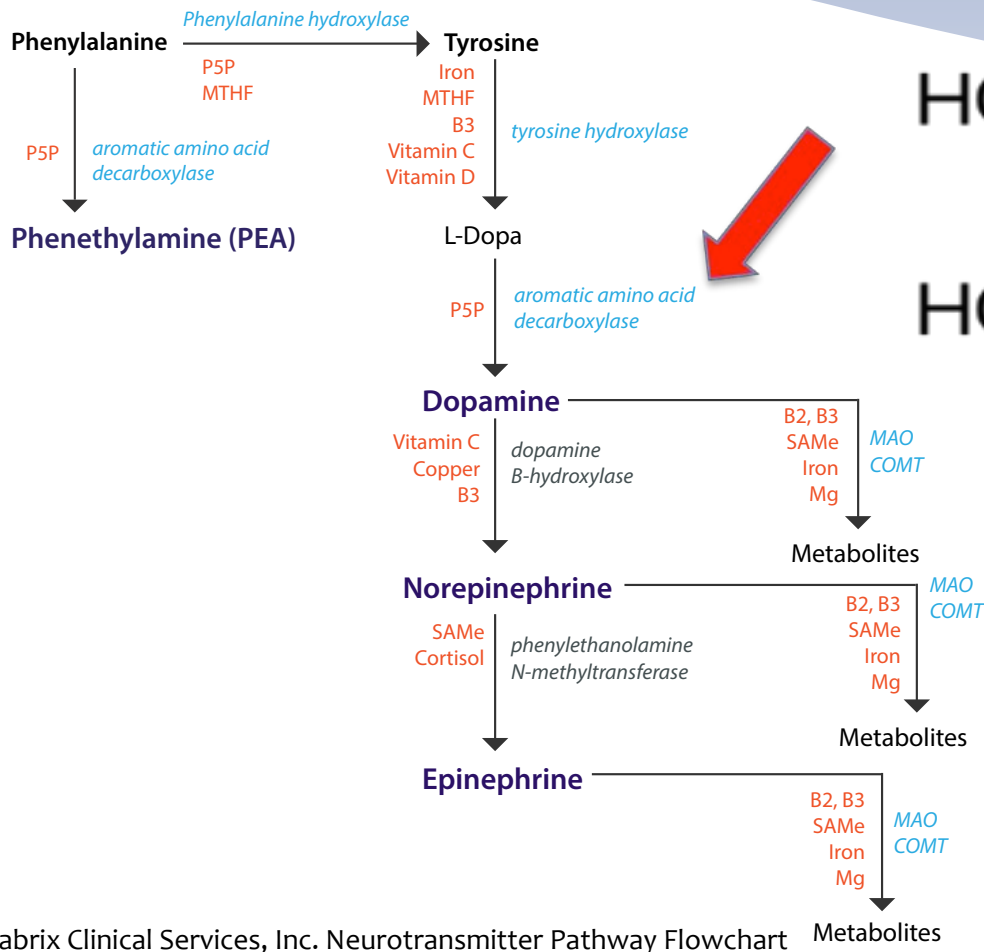


## High Dopamine

Anxiety  
Hyperactivity  
Mood Swings  
ADD/ADHD

# Dopamine: That Feeling We “Chase”

## The Catecholamines





# How To Balance Dopamine & Serotonin

## DOPAMINE PRODUCTION:

- Amino Acid Precursors: Phenylalanine, **Tyrosine**, L-DOPA
- Cofactors: Iron, MTHF, B3, Vitamin C, Vitamin D, P5P
- Other considerations: Wild Green Oat

## DOPAMINE BREAKDOWN:

- MOA: B2, B3, Iron / Support
- COMT: SAME, Mg
- Other considerations: Vinpocetine

## SEROTONIN PRODUCTION:

- Amino Acid Precursors: Tryptophan & 5HTP
- Cofactors: Iron, MTHF, B3, Vitamin C, P5P
- Other considerations: Saffron, St. John Wort, Rhodiola

## SEROTONIN BREAKDOWN:

- MAO: B2, B3, Iron
- Other considerations: SAME



**HINT: need to support Serotonin & Dopamine TOGETHER**

# Also...



**Tyrosine** is a precursor to making Thyroid hormones:

**ASSESS FOR:**

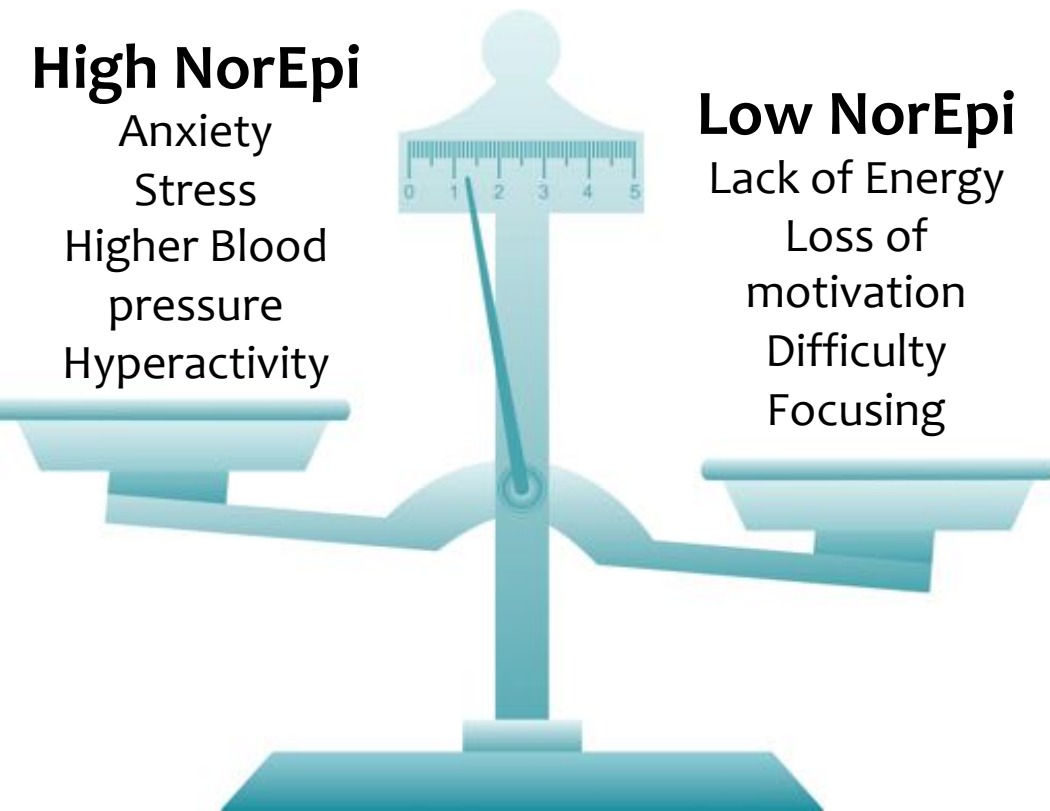
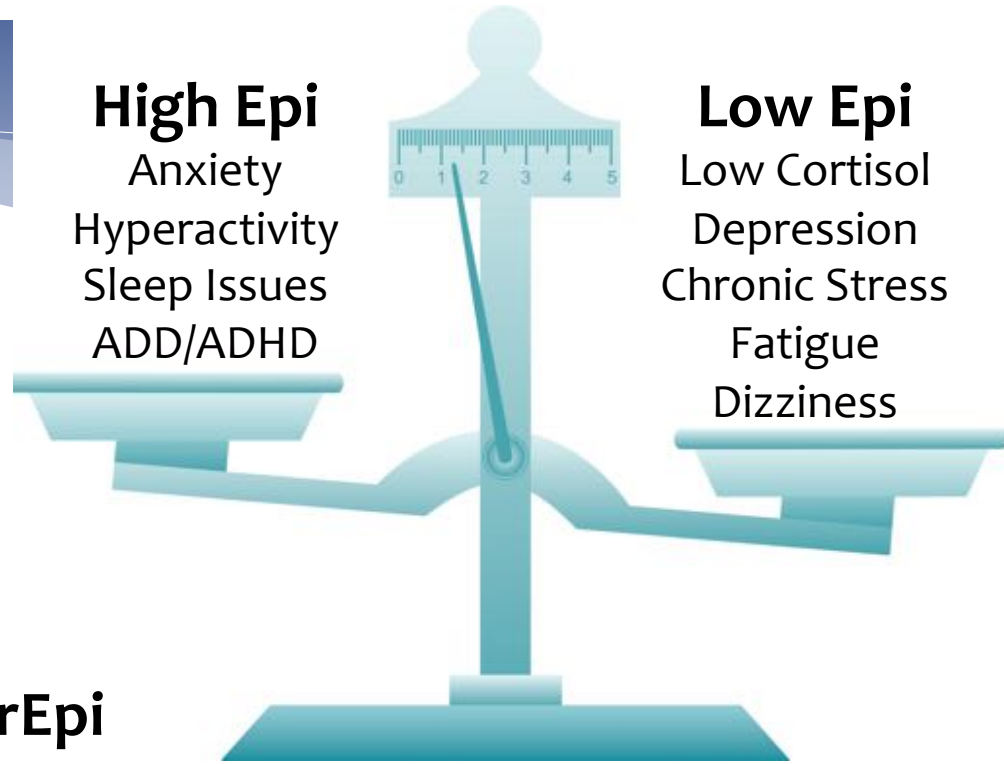
T<sub>4</sub> (thyroxine)

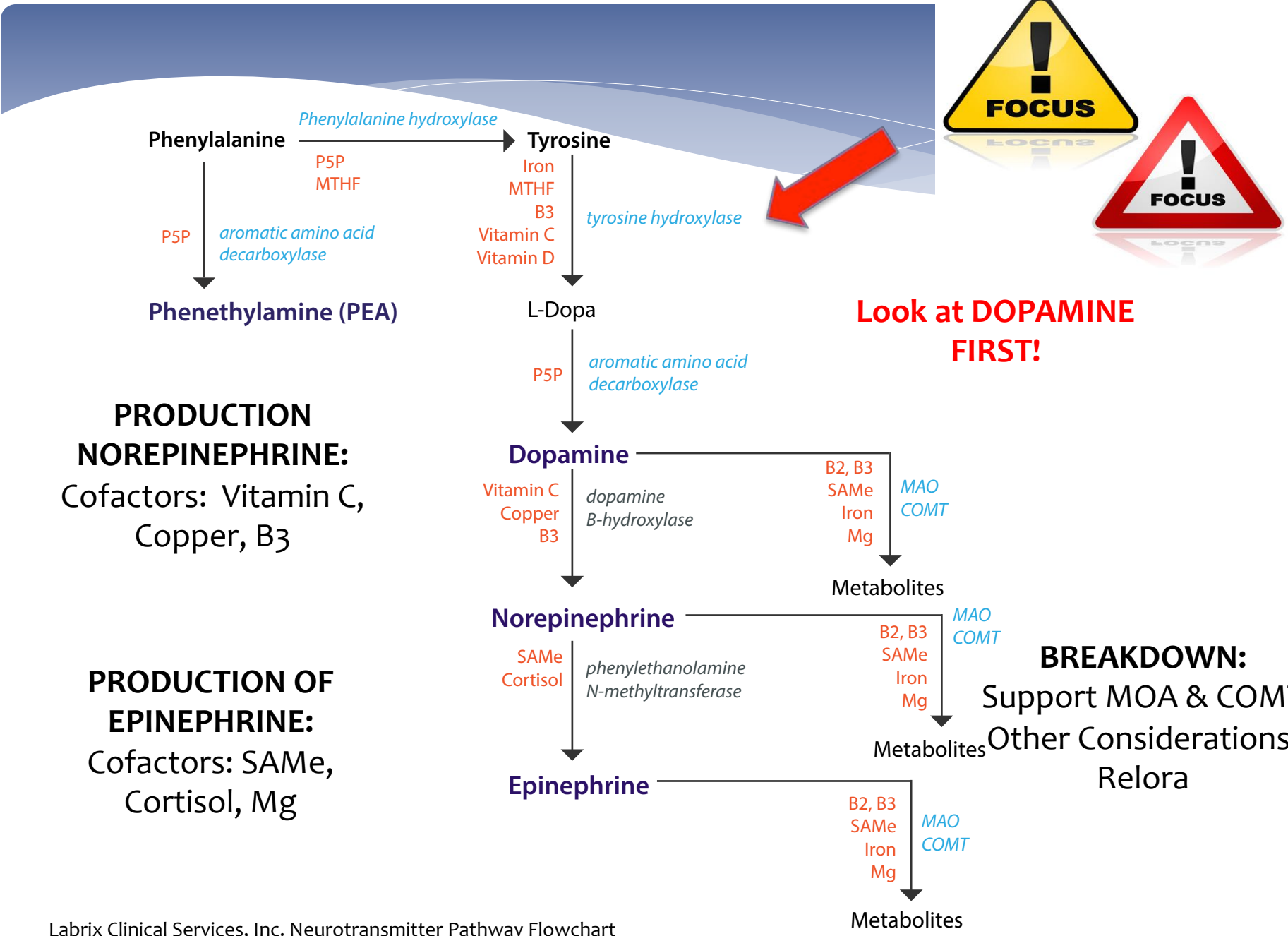
T<sub>3</sub> (triiodothyronine)

rT<sub>3</sub> (reverse T<sub>3</sub>)

# Flight or Fight

More Catecholamines





**PRODUCTION NOREPINEPHRINE:**  
Cofactors: Vitamin C, Copper, B3

**PRODUCTION OF EPINEPHRINE:**  
Cofactors: SAmE, Cortisol, Mg

**Look at DOPAMINE FIRST!**

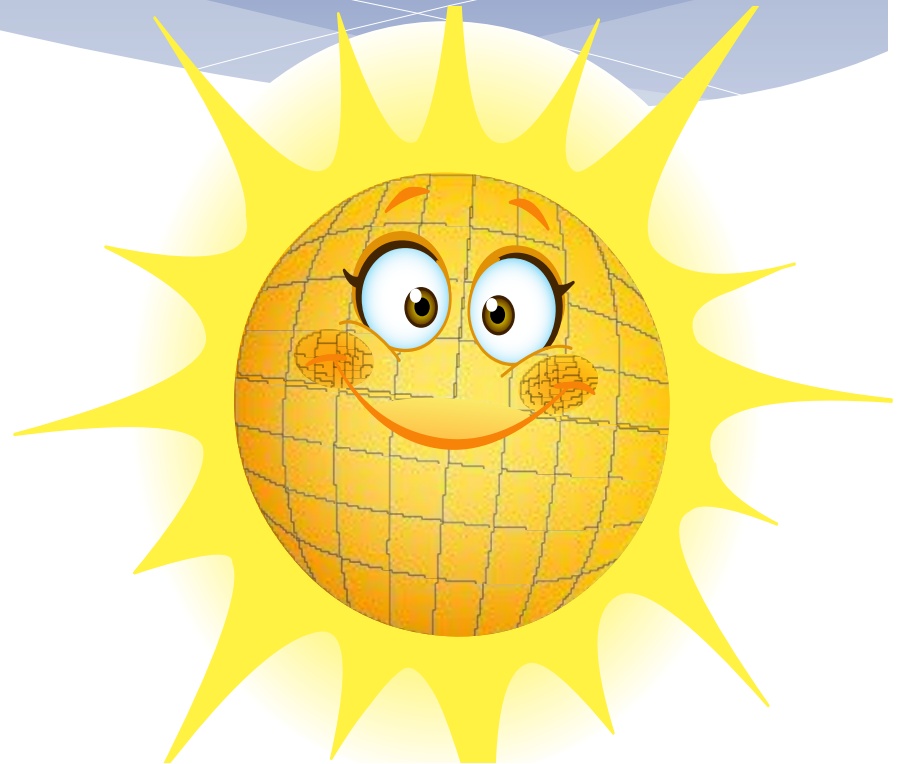
**BREAKDOWN:**  
Support MOA & COMT  
Other Considerations:  
Relora

# Vitamin D

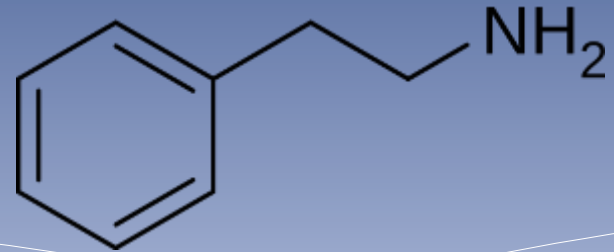
## Vitamin D is needed to Make CATECHOLAMINES

- Vitamin d activates gene expression of tyrosine hydroxylase
- Tyrosine hydroxylase is the rate limiting step in creation of catecholamines

Achieve Blood Levels of 25-OH  
Vitamin D between **50-80 ng/mL**



# Phenylethylamine

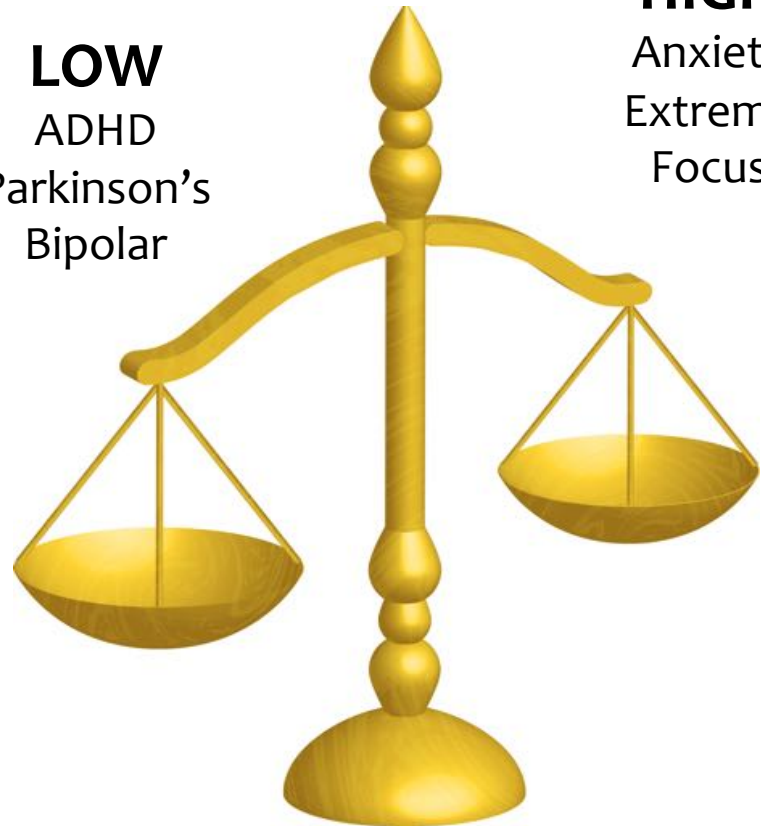


## The “Study” Neurotransmitter

- Synaptic neuromodulator – slows down reuptake of Dopamine & Norepinephrine
- Biomarker for ADHD
- Excitatory action by favoring glutamate activity

**LOW**  
ADHD  
Parkinson's  
Bipolar

**HIGH**  
Anxiety  
Extreme  
Focus



# How to Balance PEA

## PRODUCTION:

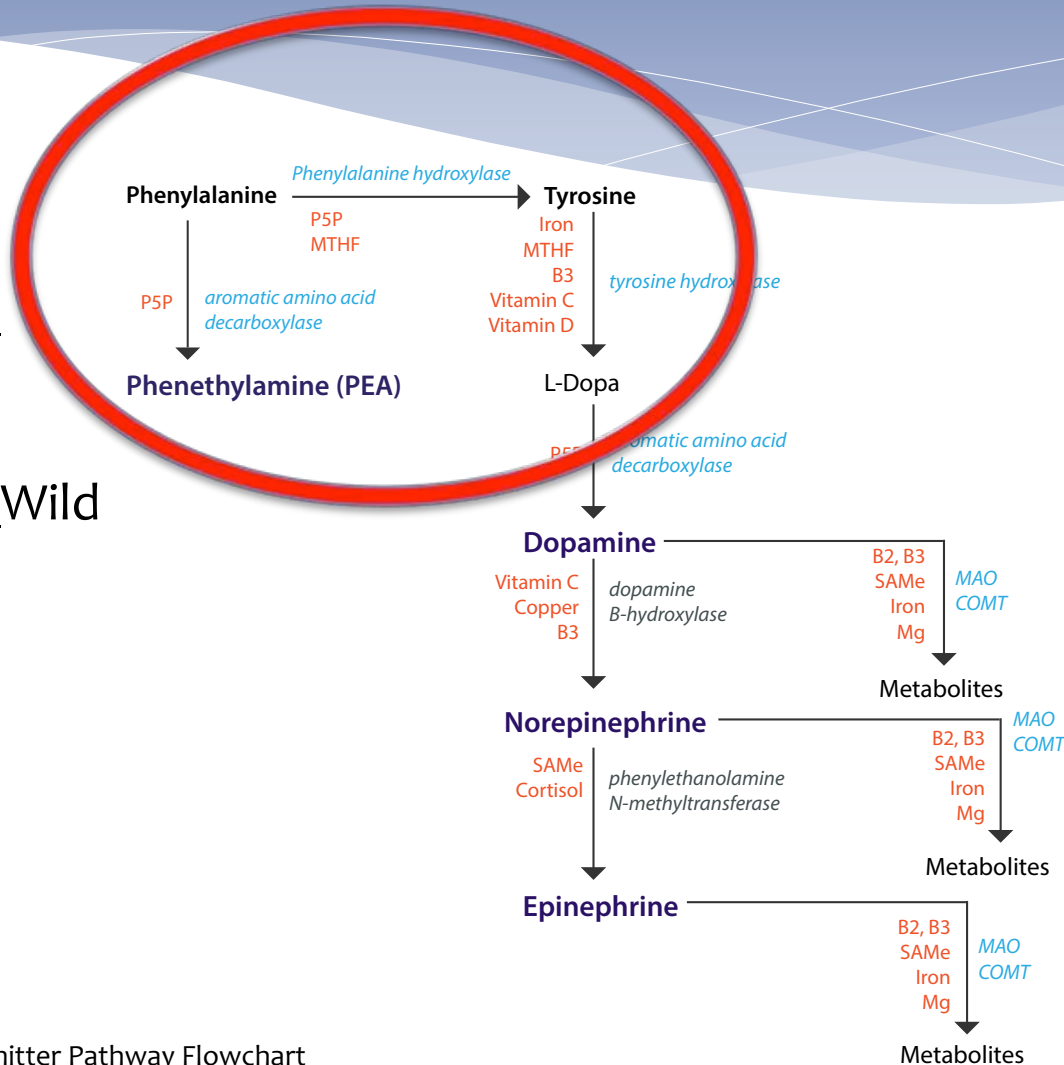
Amino Acid precursor:

Phenylalanine

Cofactors: B6

Other considerations: Wild

Green Oat, Rhodiola



## BREAKDOWN:

MAO-B: B2, B3, Iron

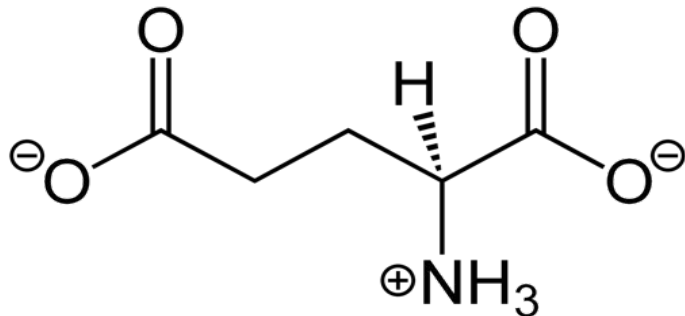
PNMT: SAME, Mg

# Glutamate & GABA

## Glutamate

### Major Excitatory Neurotransmitter

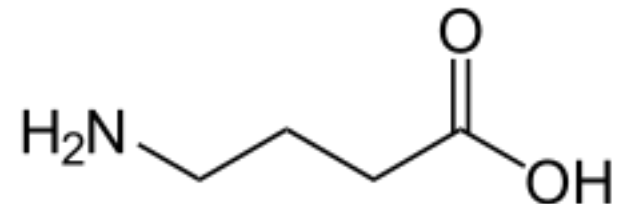
- Most abundant in nervous system
- Is involved in most aspects of normal brain functioning
- Required for learning & memory



## GABA

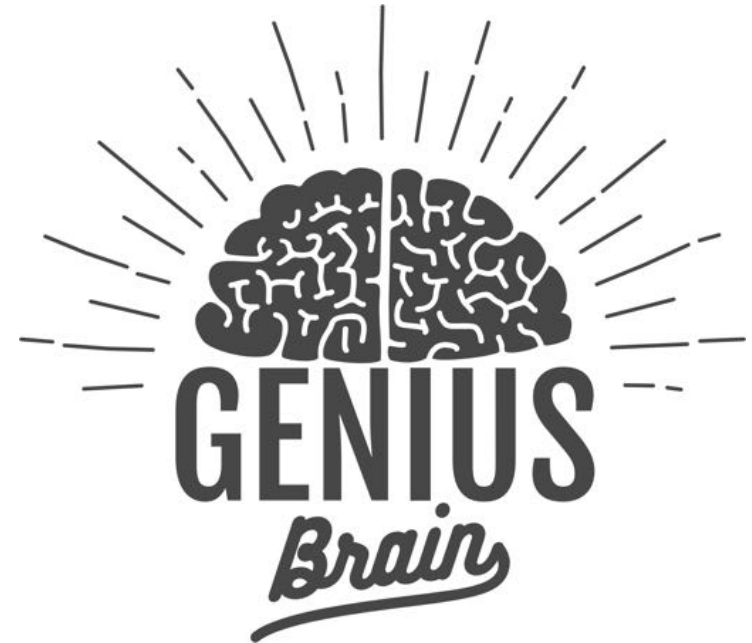
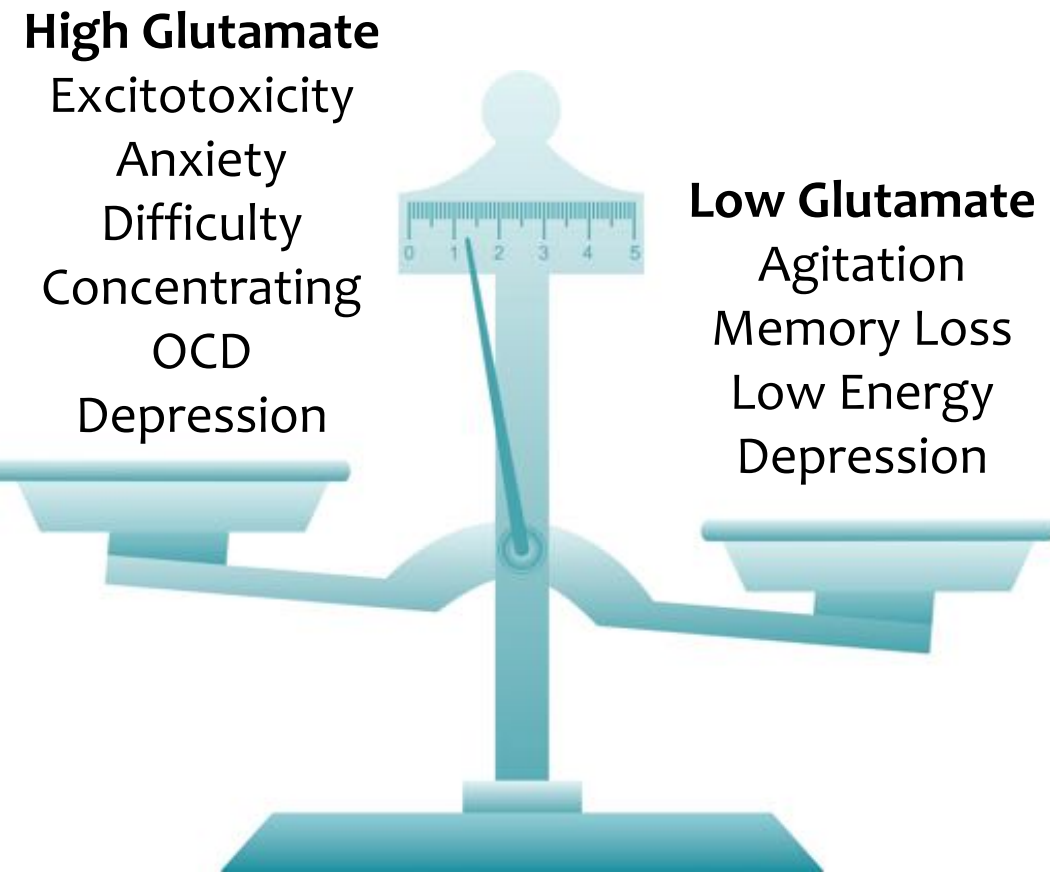
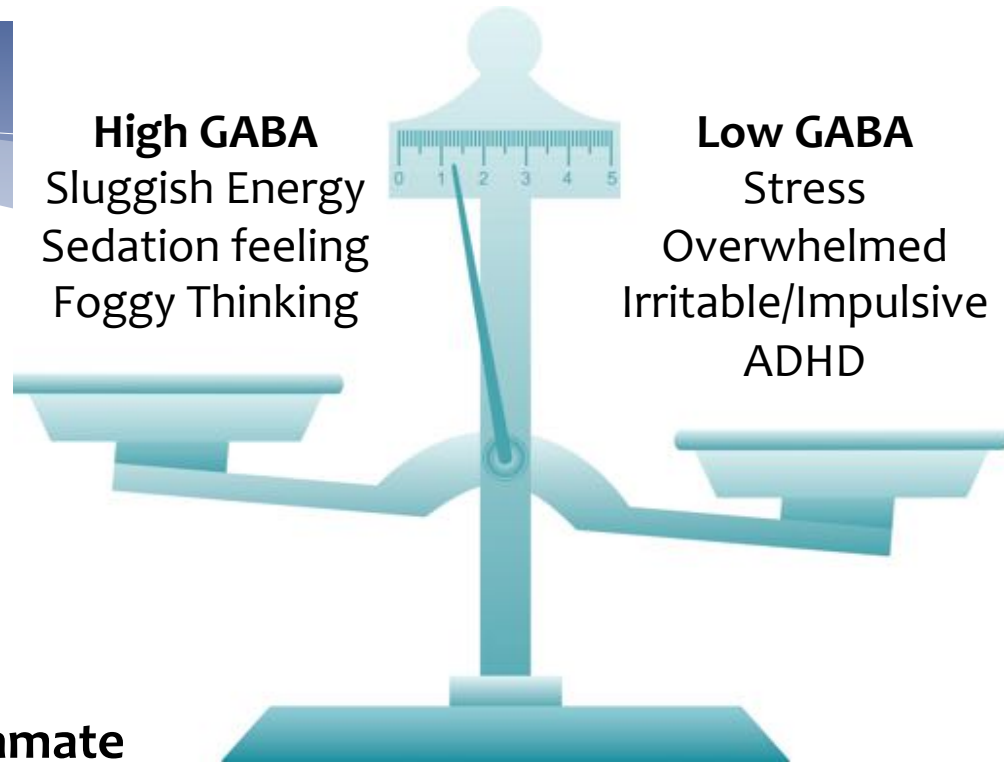
### “Mother Nature’s Xanax”

- Major Calming Neurotransmitter
- Balancing excitatory action of other neurotransmitters





# Major CNS Neurotransmitters



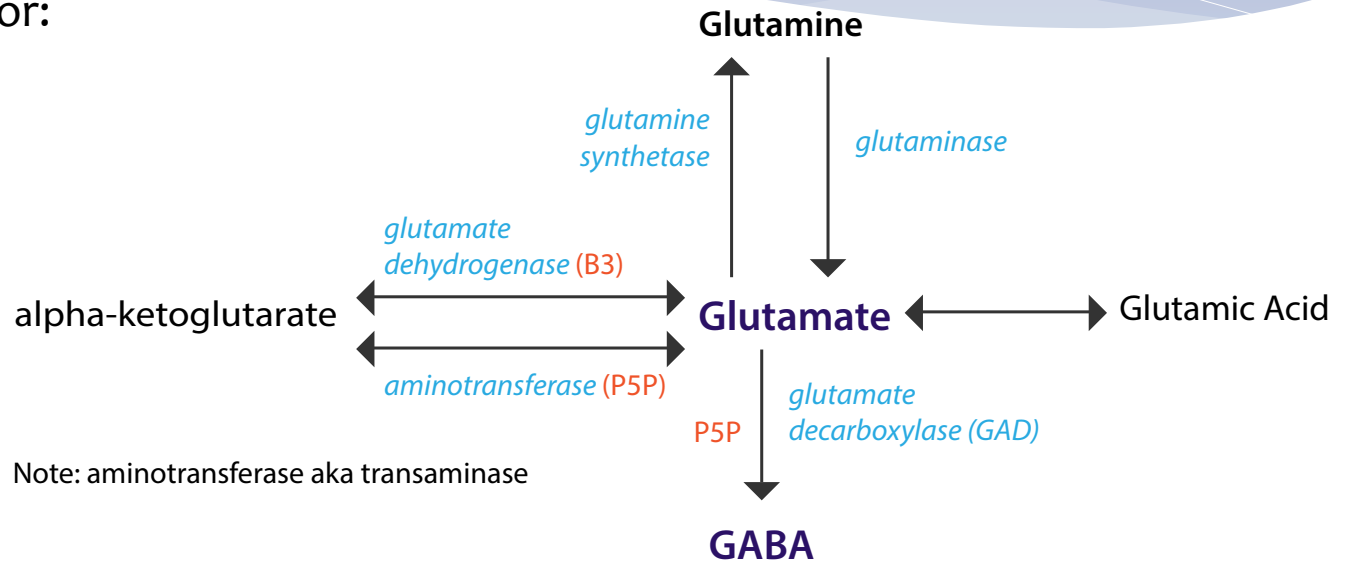
# How to Balance Glutamate & GABA

## PRODUCTION:

Amino Acid precursor:

**Glutamine**

GABA cofactor: B6



## BREAKDOWN:

Glutamate – convert into GABA (need B6)

Glutamate – other considerations: Theanine, Low Glutamate diet (ex no MSG)

GABA other considerations: Coffee

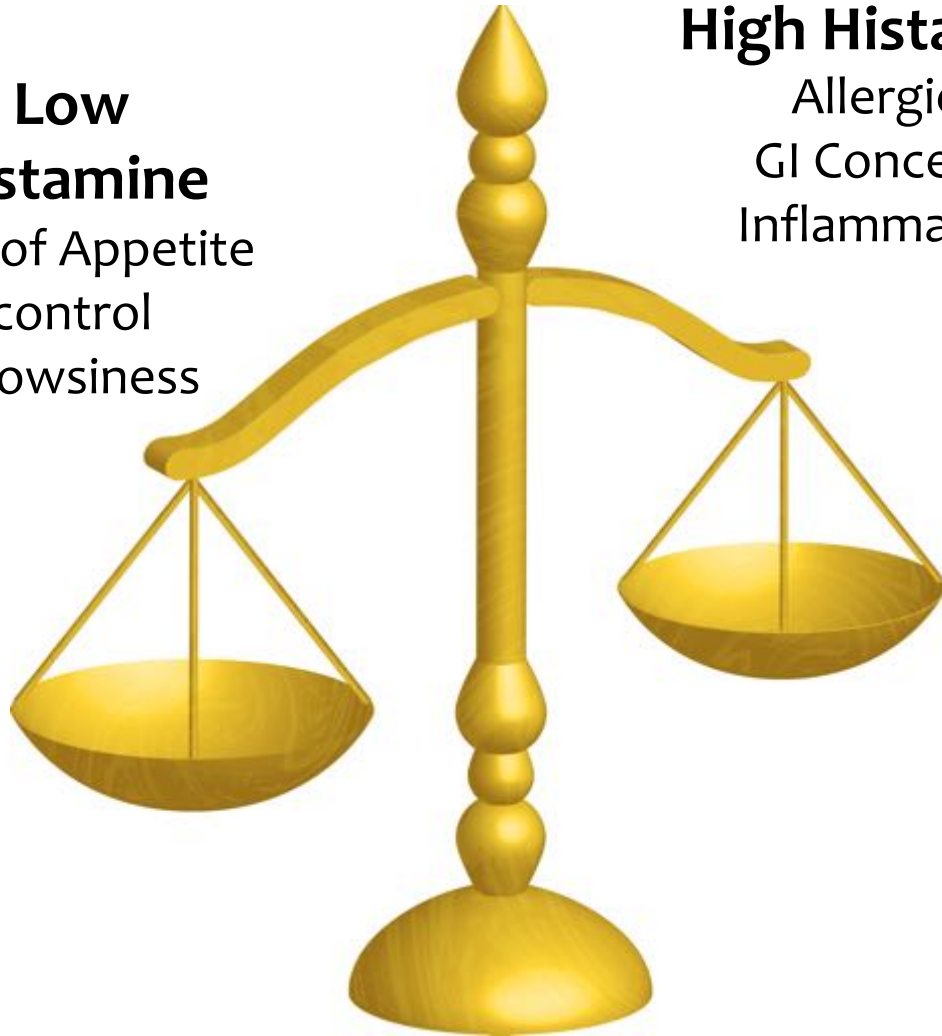
# Ahh Choo...Histamine

## Allergy Neurotransmitter

- Associated with Allergic & Inflammatory Response
- Controls sleep-wake cycles
- Affects digestion & appetite control

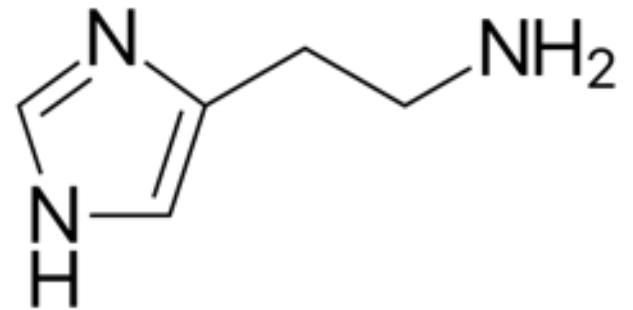


**Low  
Histamine**  
Loss of Appetite  
control  
Drowsiness

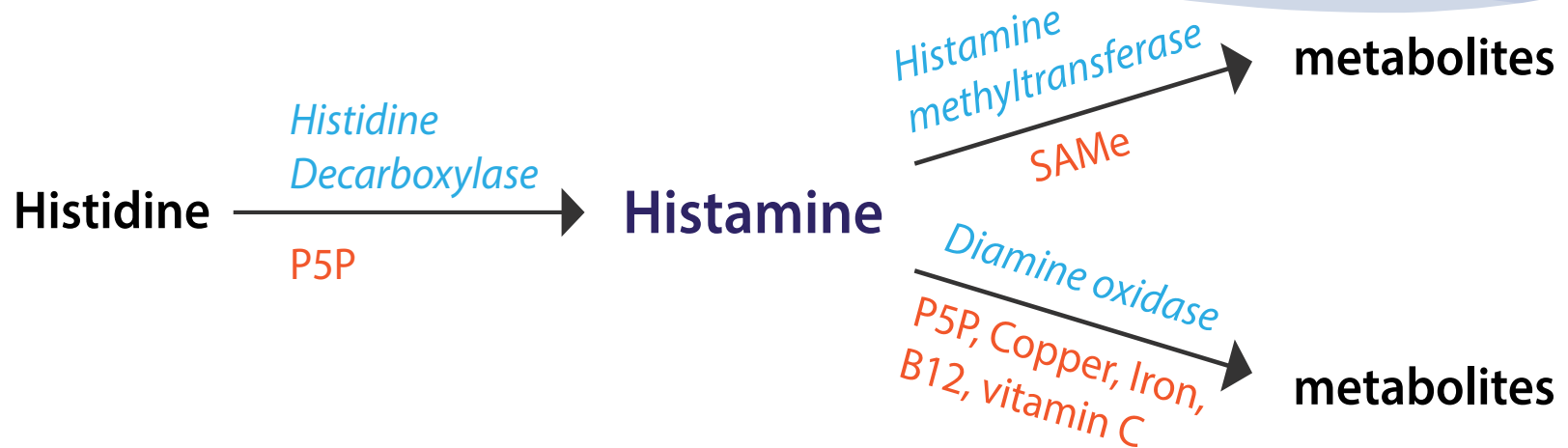


**High Histamine**

Allergies  
GI Concerns  
Inflammation



# How to Balance Histamine



## PRODUCTION:

Amino Acid precursor: Histidine

Cofactors: B6

Other consideration: Carnosine

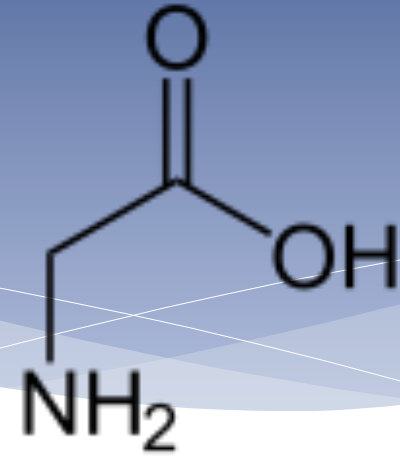
## BREAKDOWN:

Cofactors: DAO: B6 & Copper

Cofactors: HNMT: SAmE & Copper

Other consideration: Forskolin, Low Histamine Diet

# Glycine



## Simplest Amino Acid



- **Improves sleep**
- Eases inflammation
- Calms aggression
- Typically acts as inhibitory NT
  
- However, is a co-agonist for NMDA receptors, so can be excitatory

# How to Balance Glycine

## Low Glycine

Poor Sleep  
Poor Cognitive  
function  
Memory Issues

## High Glycine

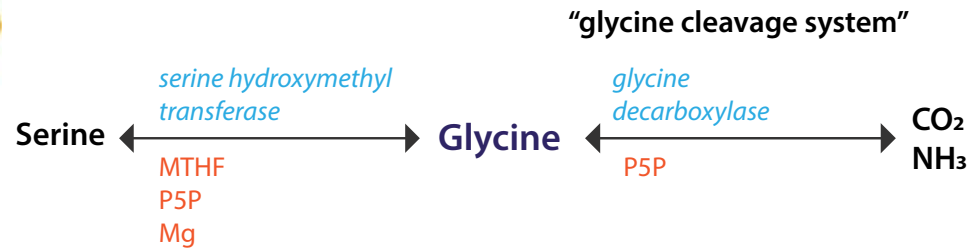
Compromised  
Cognitive  
Processing

## PRODUCTION:

Precursor: Serine & Glycine  
Cofactors: B6

## BREAKDOWN:

Cofactors: NAD<sup>+</sup>, folate, B6, B2



# Neuro-Endocrine Connection

Hormone  ne



# Hormonal Influences on Neurotransmission

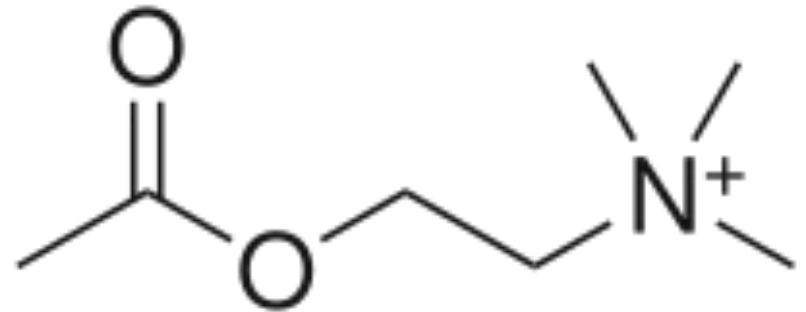
Hormone	Influence	Mechanism
Progesterone	GABA receptor sensitivity	<ul style="list-style-type: none"><li>• Enhances GABA receptor sensitivity</li></ul>
Estrogen	Increase Serotonin activity  Increase Dopamine Activity	<ul style="list-style-type: none"><li>• Increases tryptophan hydroxylase. Shown clinically to increase serotonin levels</li><li>• Inhibits MAO (decreases serotonin and catecholamine breakdown)</li><li>• Increases serotonin receptors</li></ul>
Testosterone	Increase Dopamine activity	<ul style="list-style-type: none"><li>• Testosterone increases dopamine synthesis</li><li>• Dopamine also supports testosterone production by stimulating LH and inhibiting prolactin</li></ul>

**Note:** Increasing the effect of a neurotransmitter does not always mean you will see an increase in that neurotransmitter upon testing

# Acetylcholine

- Most unstable neurotransmitter; therefore difficult to measure on routine testing
- Typically Cognitive Questionnaires are used if suspect imbalances

- Memory Neurotransmitter



**Need  
Choline**

**Choline  
+  
Acetyl-CoA**

**Choline  
acetyltransferase**

**Acetylcholine**

**Acetylcholinesterase**  
(target for  
pharmaceutical  
intervention)

**Choline  
+  
Acetate**

# Take Away



- Testing of Neurotransmitters & Steroid Hormones should be a part of Routine Screening
- Need to balance Serotonin & Dopamine Together
- Don't forget the importance of protein in diet (amino acids)
- Don't forget cofactors for neurotransmitter production
- NEED for steroid hormone balance



# More On Testing Neurotransmitters:

**Life Extension offers Neurotransmitter testing**

<http://www.lifeextension.com>

**For Questions, call the Wellness Specialists at 1-800-226-2370**

**Labrix/Doctors Data**

<https://www.labrix.com>

**Neuroscience**

<https://www.neuroscienceinc.com>

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# Thank You!!

Any Questions?

thank you!

