

# **Clinical Utility of Neurotransmitter Testing**

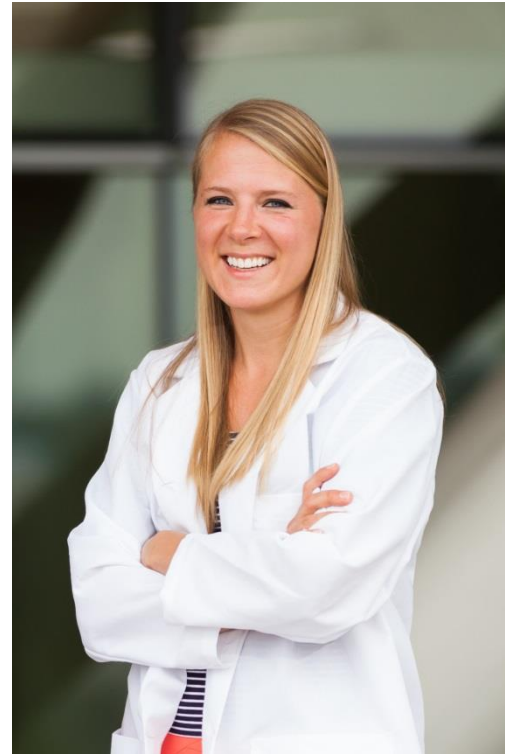
Kate Placzek, PhD

David Zava, PhD

# Today's Presenters

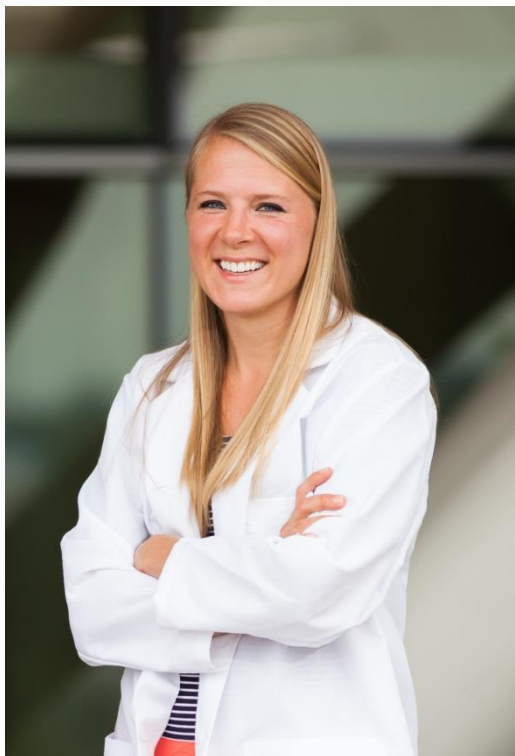


David Zava, PhD



Kate Placzek, PhD

# Meet Kate Placzek, PhD



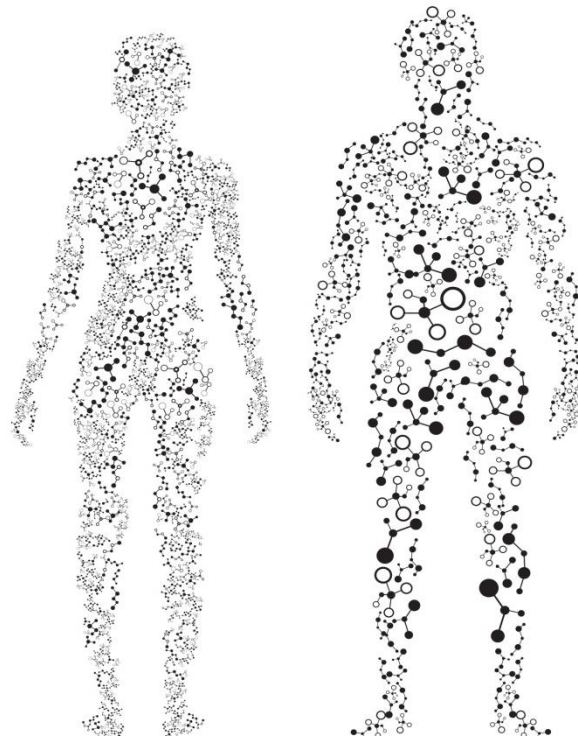
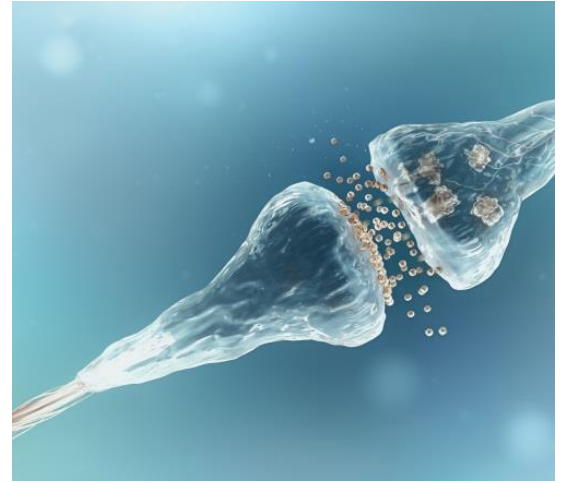
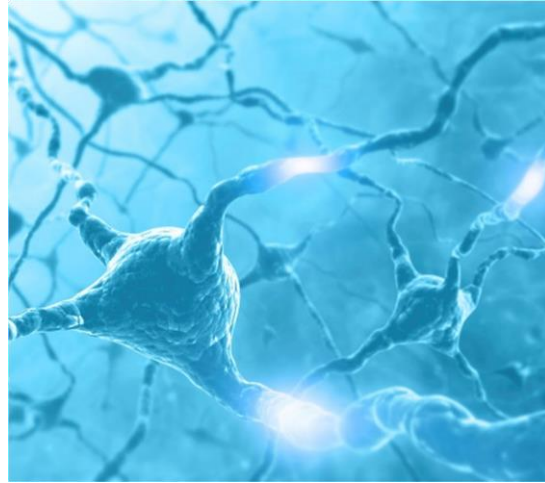
Dr. Placzek is the Senior Research Scientist at ZRT Laboratory.

She received her doctorate from Purdue University in Medicinal Chemistry and Molecular Pharmacology; and performed her postdoctoral studies at Oregon Health and Science University.

At ZRT Laboratory, Dr. Placzek is spearheading the neurotransmitter project.

# Disclosure

Neurotransmitter test is not intended to diagnose, treat, cure, or prevent any disease. Statements regarding supplementation have not been evaluated by the Food and Drug Administration.



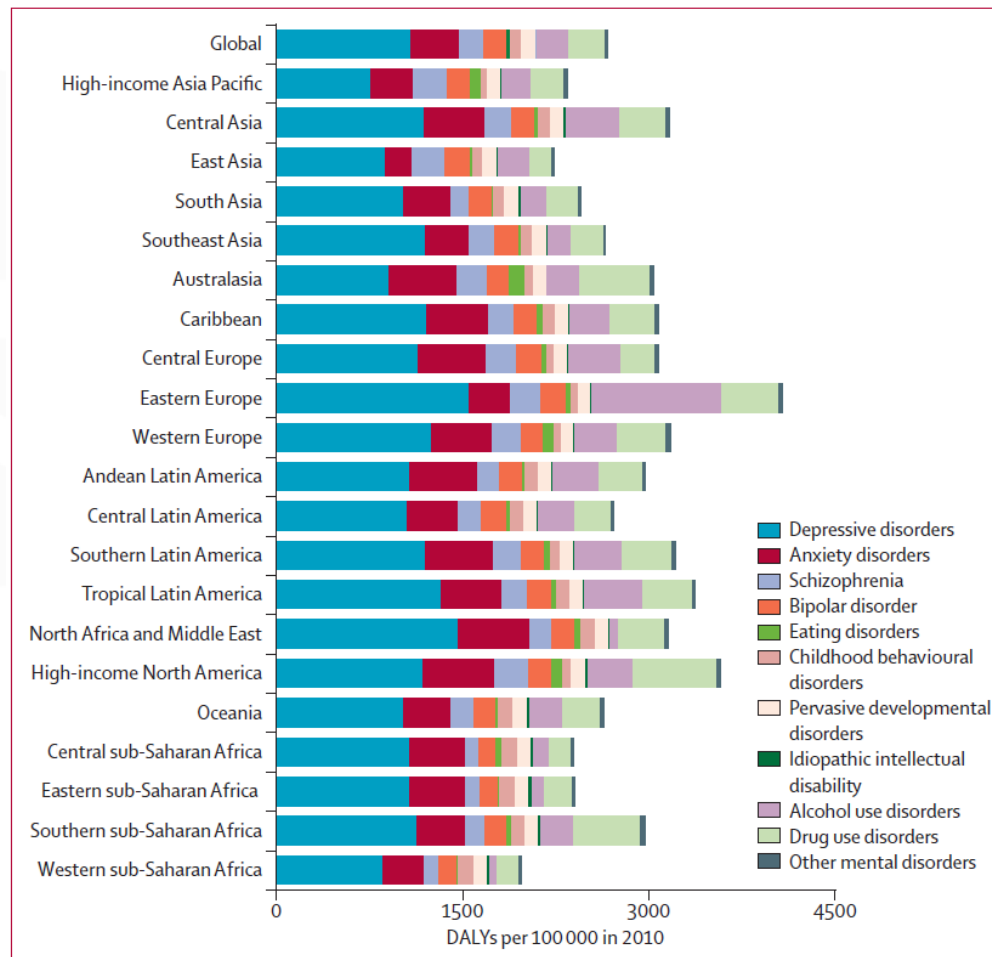


# Staggering Statistics for American Adults

- 7% live with major depression
  - 18% live with anxiety disorders (panic, OCD, PTSD, phobias)
    - Mood disorders are the 3<sup>rd</sup> most common cause of hospitalization for individuals aged 18-44

# Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010

Harvey A Whiteford, Louisa Degenhardt, Jürgen Rehm, Amanda J Baxter, Alize J Ferrari, Holly E Erskine, Fiona J Charlson, Rosana E Norman, Abraham D Flaxman, Nicole Johns, Roy Burstein, Christopher J L Murray, Theo Vos



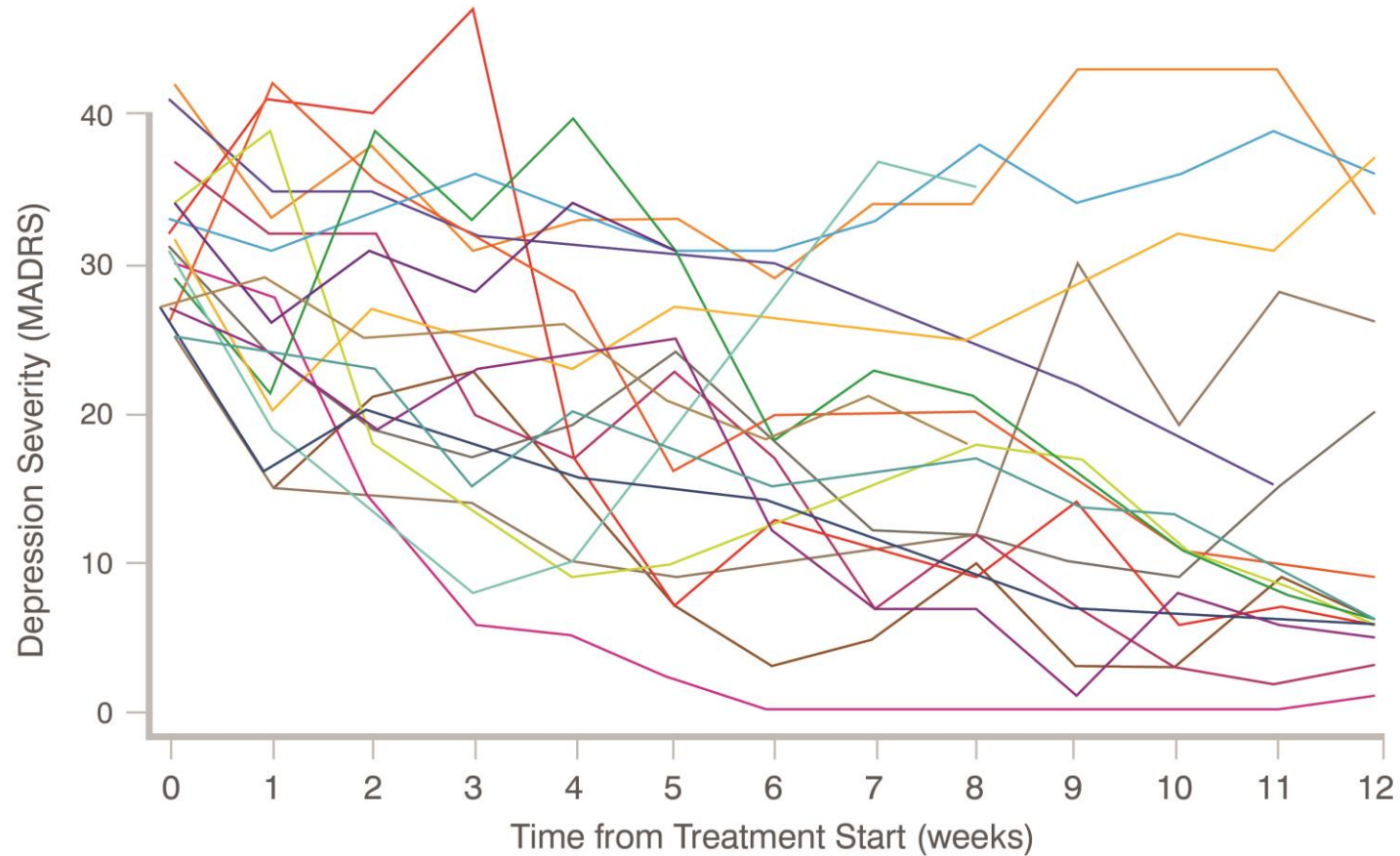


# Top-prescribed and Top-selling Prescription Drugs in the US

- Antipsychotics
- Antidepressants
- Attention-deficit  
disorder drugs



# Vast Individual Variability Response to Treatment of Depression



Adapted from Uher, R. 2011 Genes, Environment, and Individual Differences in Responding to Treatment for Depression. *Harv Rev Psychiatry*. 19(3): 109.

# Proximal Causality of Mood Disharmony

- Thyroid hormones
- Sex steroids
- Adrenal cortisol & DHEA
- Neurotransmitters



racing thoughts

DEPRESSION *fatigue*

HOPELESSNESS TREMBLING IRRITABILITY

*rumination* weight gain HEADACHES

ANGER OCD PANIC NERVOUSNESS

*DREAD* addiction fibromyalgia IMPULSIVITY

MANIA MALAISE FORGETFULNESS

ANXIETY phobia *RESTLESSNESS*

fear SWEATING HYPERVENTILATION AVOIDANCE

PTSD **BURNOUT** DOOM lethargy

INVASIVE THOUGHTS eating disorders

*mood swings* **WEIGHT LOSS** worry

INCREASED HEART RATE lack of

concentration  
INSOMNIA

# Diagnostics in Psychiatric Disorders



“We have convinced ourselves that we have developed cures for mental illnesses... when in fact we know so little about the underlying neurobiology of their causes that our treatments are often a series of trials and errors.”

# Benefit From Biomarkers in Psychiatry

- Objective peripheral physiological indicators
- Predict probability of onset or presence of disorder
- Stratify according to severity
- Indicate prognosis
- Track therapeutic intervention

Gururajan, et. al. (2016) *Neuroscience and Biobehavioral Reviews* 64  
Molecular Biomarkers of Depression.

# Urinary Neurotransmitter Analysis as a Biomarker for Psychiatric Disorders

by Amnon Kahane, MD

A biomarker is a measurement used as an indicator of biological actions. Biomarkers are prevalent in most branches of medicine. Measurement of specific biological features allows practitioners to determine diagnoses and prognoses and predict treatment

biomarkers in psychiatry to enhance patient management and ensure treatment success (Holsboer 2008; Keshavan et al. 2005; Peedicayil 2008).

In a recent article by Cook (2008), an outline of desirable characteristics

Urinary neurotransmitter analysis has a breadth of data to support its usefulness in clinical practice. In the late 1950s, publications revealed correlations of urinary catecholamine measures to various psychiatric symptoms (Bergman

*"If we consider the established criteria required for a biomarker to correspond to or indicate psychiatric symptoms, urinary neurotransmitter analysis meets these necessary requirements,"*  
*Dr. Amnon Kahane.*

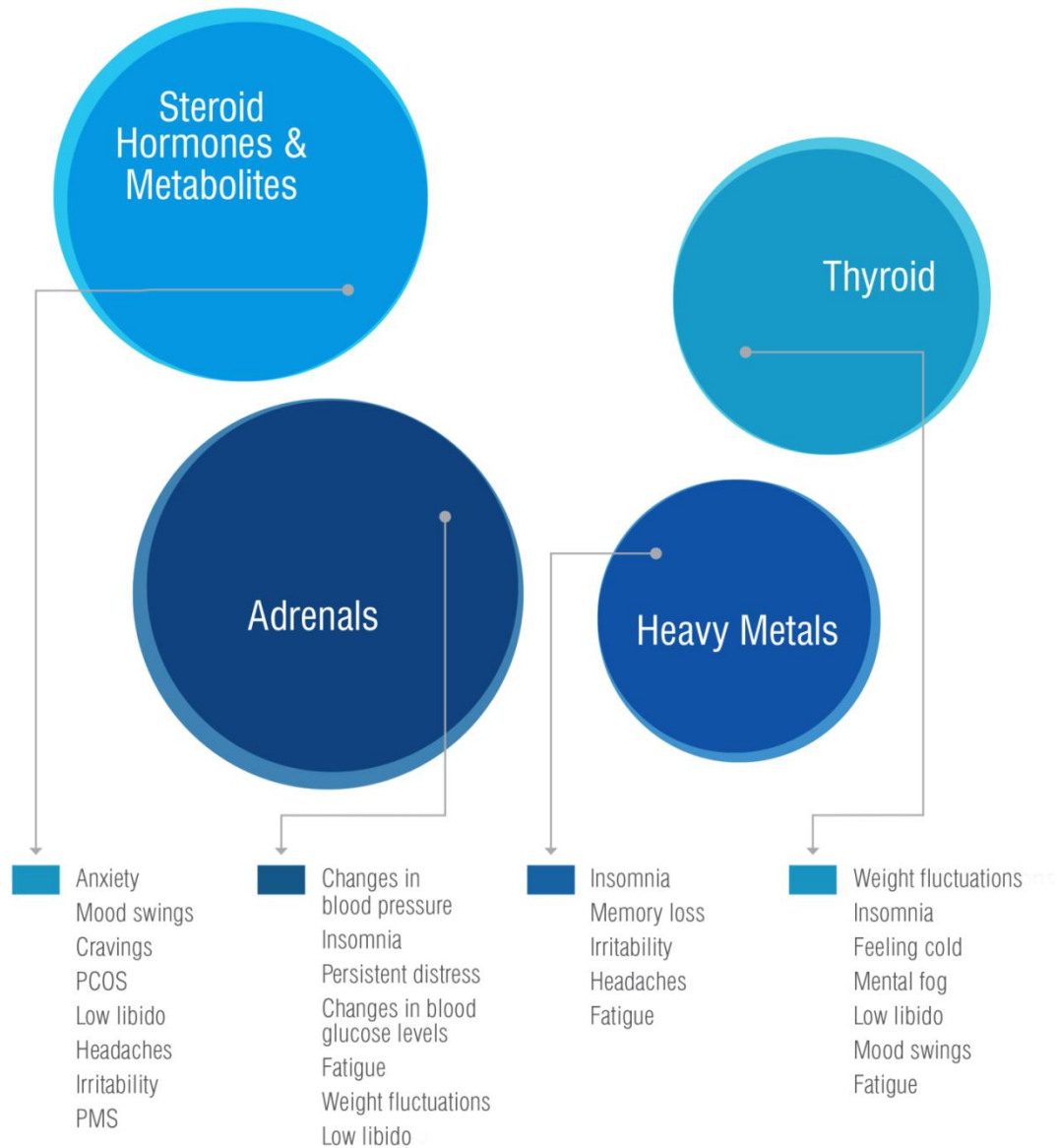
and symptoms that lack objectivity. That said, treatments for managing psychiatric symptoms are relatively effective. However, no single treatment works for everyone with a given disorder, and selection of the best treatment in mainstream psychiatry remains a challenge.

As in any other disease state, a primary goal in psychiatry is the identification of specific biomarkers that would permit a more precise definition of specific disorders and, in turn, enhance the ability to develop targeted patient treatments. In fact, research has highlighted a need for

than those that require a major change in the delivery of care. These criteria are mentioned here as a prelude for an innovative technology that both satisfies psychiatric biomarker requirements and significantly enhances initial treatment regimens for patients with psychiatric symptoms. In addition, this technology provides ongoing analysis of existing treatment strategies, thereby supplying valuable and relevant biological feedback to the psychiatric practitioner. This technology is urinary neurotransmitter analysis and has become an integral component of my psychiatric practice.

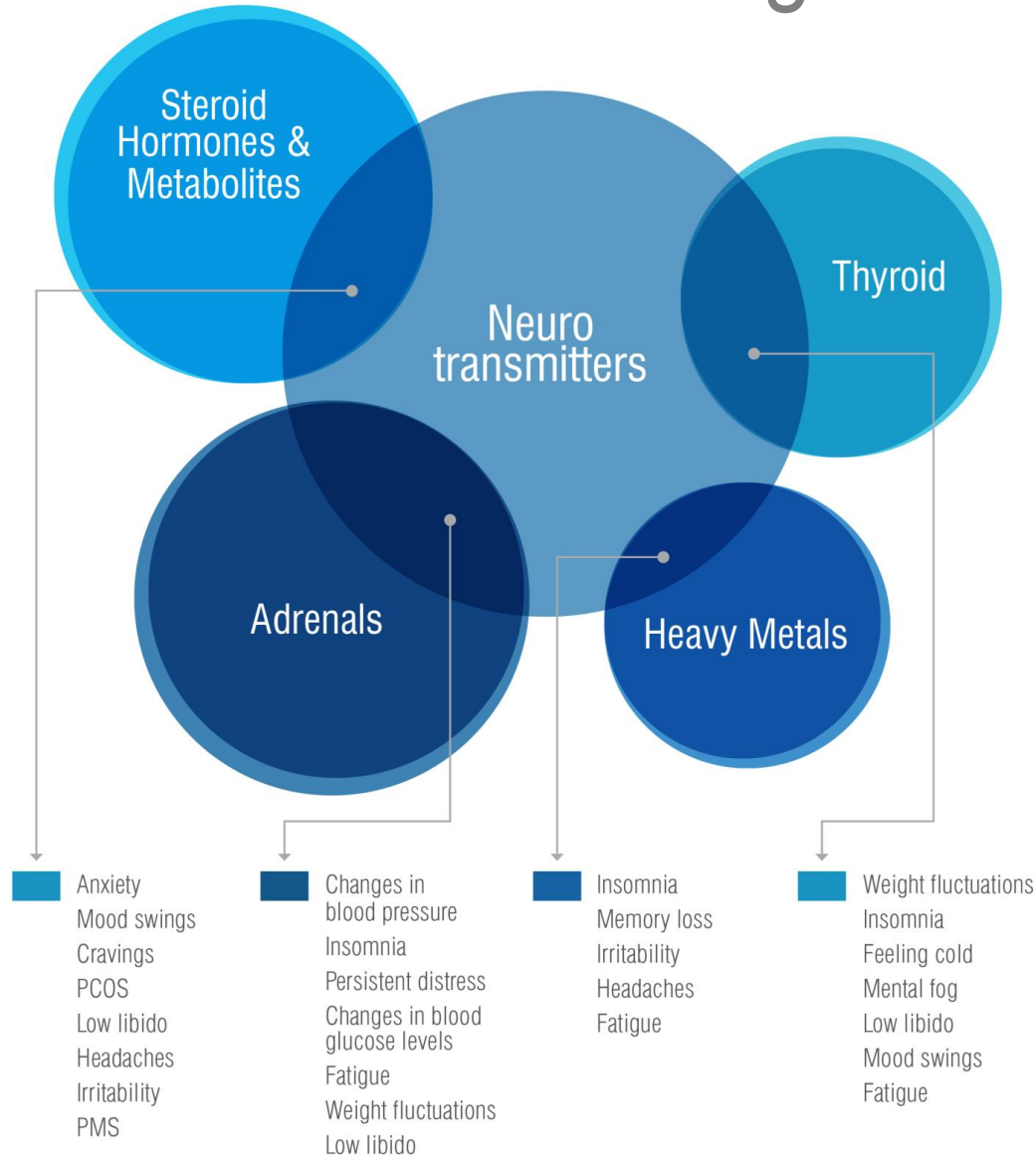
with pharmaceutical intervention. Roy and colleagues (1986) examined subsets of unipolar depressed patients and compared these subjects to non-depressed controls. Overall, depressed patients had high urinary norepinephrine and its metabolite normetanephrine, but lower urinary output of the dopamine metabolite dihydroxyphenylacetic acid (DOPAC) compared to controls. Subjects that met DSM-III criteria for a major depressive episode with melancholia, characterized by irrational fears, guilt, and apathy, exhibited significantly higher urinary outputs of normetanephrine than

# Current Tests Offered By ZRT





# Neurotransmitter Testing – Complementary Addition to the Existing Profiles



# ZRT Neurotransmitter Test

## Excitatory Neurotransmitters

- Glutamate
- Histamine
- PEA
- Epinephrine (adrenalin) and VMA
- Norepinephrine and Normetanephrine
- Dopamine, DOPAC and HVA

## Inhibitory Neurotransmitters

- Serotonin and 5-HIAA
- GABA
- Glycine

# Inhibitory Neurotransmitters

- Serotonin, generally regarded as the “happiness molecule,” contributes to the feelings of calm and well-being that eases depression and anxiety, supports sleep, and decreases appetite.
- GABA functions as the “off” switch in the brain as the major inhibitory neurotransmitter in the brain that improves mood, relieves anxiety, and promotes sleep.
- Glycine plays a dual role as a neurotransmitter and amino acid that serves as a building block to proteins, improves sleep quality, calms aggression, and serves as an anti-inflammatory agent.

# Serotonin

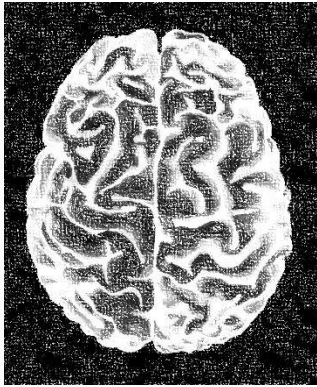
“happiness molecule”



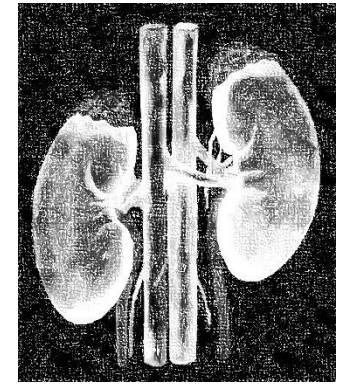
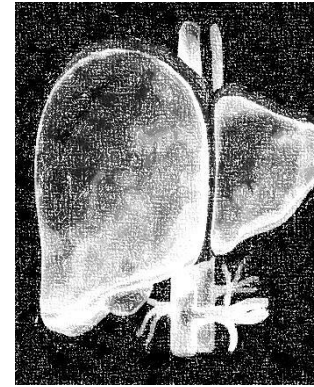
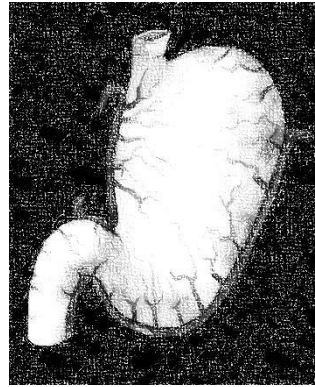
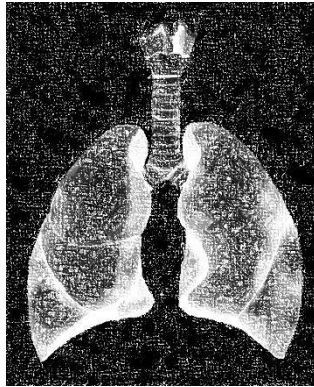
- Decreases anxiety
- Improves Sleep
- Modulates clotting
- Regulates cognition/learning/memory
- Stimulates gut motility
- Suppresses appetite and libido
- Controls thermoregulation and vasoconstriction/dilation

# Serotonin Biosynthesis, Storage & Elimination

brain ~ 10%



gut ~90%

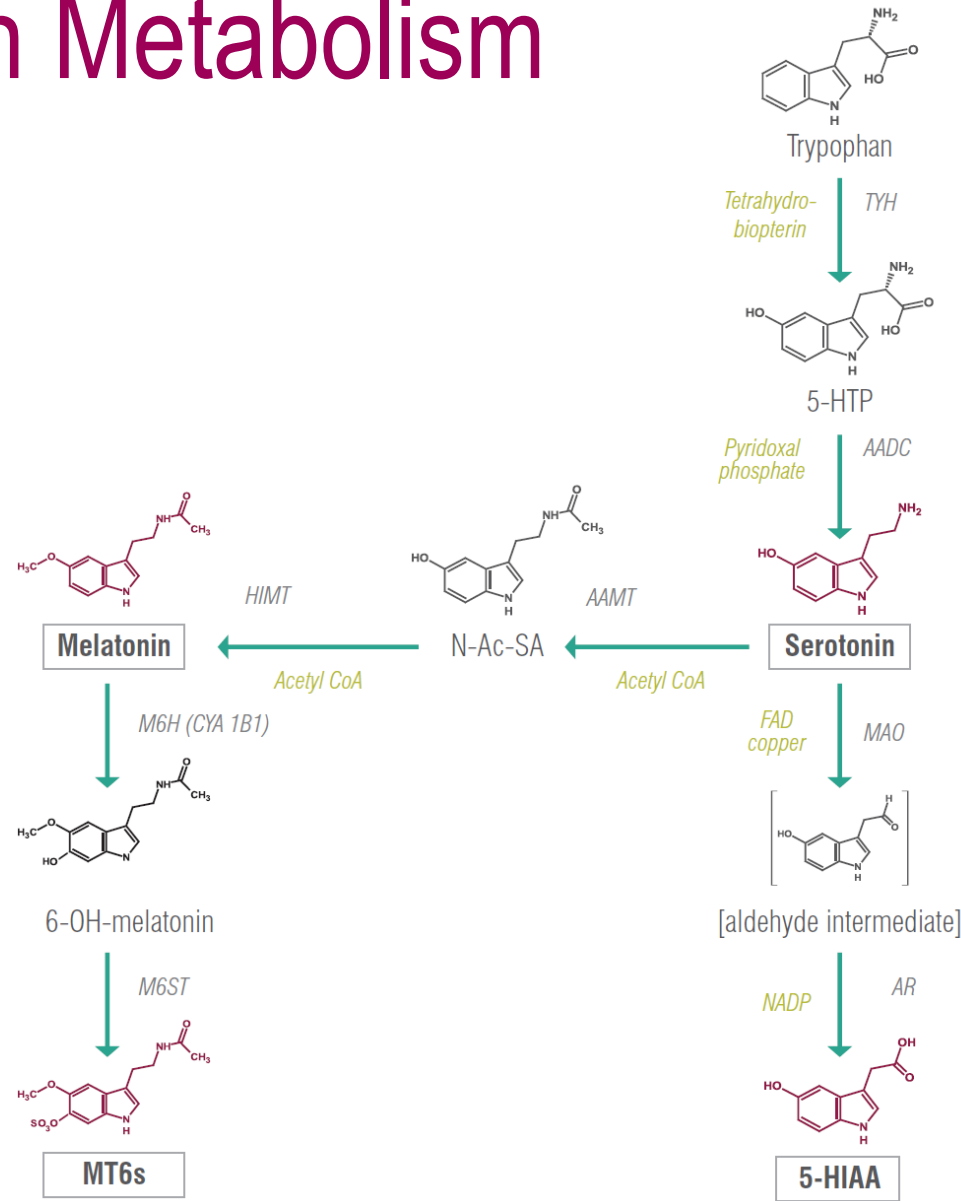


storage

metabolism

elimination

# Serotonin Metabolism



**AADC** = aromatic L-amino acid decarboxylase

**AAMT** = arylalkylamine N-methyltransferase

**AR** = aldehyde reductase

**HIMT** = hydroxyindole O-methyltransferase

**MAO** = monoamine oxidase

**M6H** = melatonin 6 hydroxylase

**M6ST** = melatonin 6 sulfotransferase

**TYH** = tryptophan hydroxylase

**MT6S** = 6-sulfatoxymelatonin

**5-HIAA** = 5-hydroxyindole 3-acetic acid

# High Serotonin in Urine Symptom Profile



- Anxiety
- Bone loss
- Carcinoid syndrome
- Celiac disease
- Diarrhea
- High blood pressure
- Hypercortisolism
- Irritability
- Low libido

# Low Serotonin in Urine Symptom Profile

- Anxiety
- Depression
- Change in appetite
- Cravings
- Excessive worry
- Hot flashes
- Hunger
- Insomnia
- Low mood
- Migraines
- OCD
- Sensitivity to pain



# Serotonin Support

- Cofactor support:
  - High serotonin: copper (with zinc), Acetyl Coa, SAMe
  - Low serotonin: vitamin B6
- Tryptophan, 5-HTP
- L-theanine
- Probiotics
- Bright light, diet, exercise, self-induced positive mood

# Food Sources of Tryptophan

- Avocadoes
- Bananas
- Beans
- Cantaloupe
- Chicken
- Corn
- Dairy
- Eggplant
- Eggs
- Fish
- Grains
- Grapefruit
- Kiwi
- Lentils
- Meats
- Nuts
- Pineapple
- Plantains
- Pork
- Rice
- Seeds
- Tomatoes
- Tuna
- Turkey
- Wheat

# Inhibitory Neurotransmitters

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# GABA

## the “off” switch

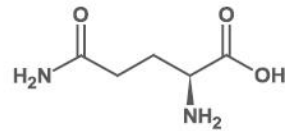


- Attention
- Blood flow/pressure
- Catecholamine release
- Cytokine and hormone production
- GI acid secretion
- Memory/mood/sleep
- Stress management

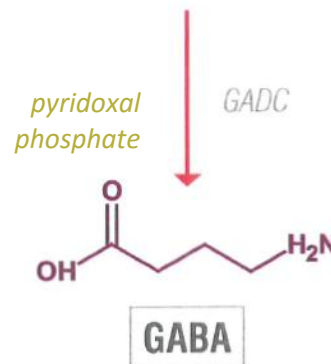
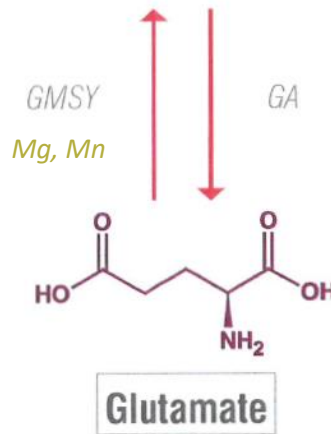
# GABA Metabolism and Imbalance Symptoms

## HIGH GABA IN URINE

- Anxiety
- Excessive need for sleep
- Lethargy
- Ovarian cancer



Glutamine



## LOW GABA IN URINE

- Anxiety
- Inability to focus
- Low energy
- Panic attacks
- ADHD
- Tourette syndrome

**GA** = glutaminase

**GADC** = glutamate decarboxylase

**GMSY** = glutamine synthetase

# GABA Support

- GABA
- L-theanine
- Vitamin B6
- Probiotics
- Yoga



## Herbal Supplements:

- Ashwagandha
- Ginko biloba
- Gotu Cola
- Kava kava
- Lemon balm
- Magnolia bark
- Phellodendron bark
- Skullcap
- Valerian root

## Food sources:

- Brewer's yeast
- Dairy
- Eggs
- Fish/seafood
- Fermented foods
- Legumes
- Nuts/seeds
- Whole grains

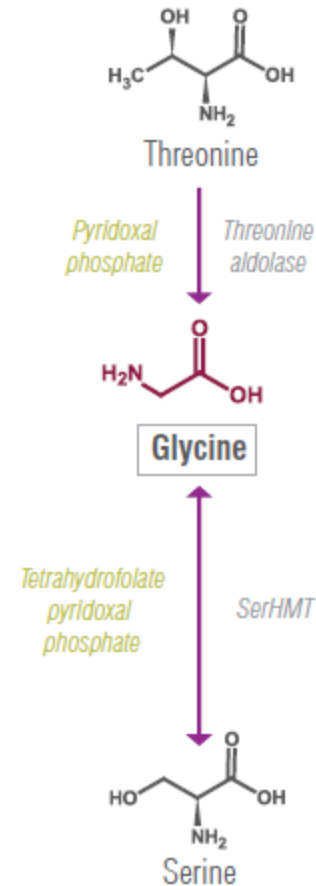
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# Glycine

amino acid and neurotransmitter

- Anti-inflammatory agent
- Calms aggression
- Improves sleep quality
- Regulates locomotion
- Stabilizes blood sugar



**SerHMT** = serine hydroxymethyl transferase

**ThrA** = threonine aldolase



# Excitatory Neurotransmitters

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- PEA promotes energy, elevates mood, regulates attention, aggression, and serves as a biomarker for ADHD.
- Epinephrine and norepinephrine function as neurotransmitters and hormones that regulate the “fight or flight” response and elevate blood pressure and heart rate, stimulate wakefulness, and reduce digestive activity.
- Dopamine generally regarded as the brain’s pleasure and reward center, plays the central role in addiction, improves attention, focus, and motivation, and modulates movement control.

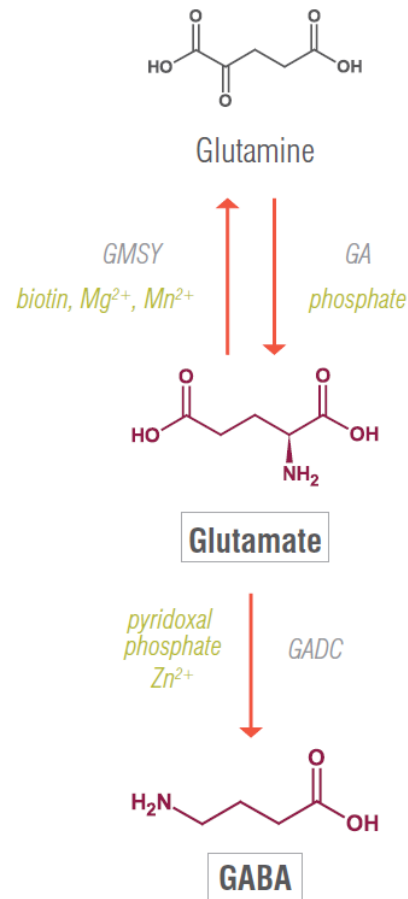
# Glutamate

## the “on” switch

- Regulates appetite
- Cognition/learning/memory
- Increases gut motility
- Improves libido
- Decreases sleep



# Glutamate Metabolism



**GA** = glutaminase

**GADC** = glutamate decarboxylase

**GMSY** = glutamine synthetase

# Glutamate Imbalance Symptoms

## HIGH GLUTAMATE IN URINE

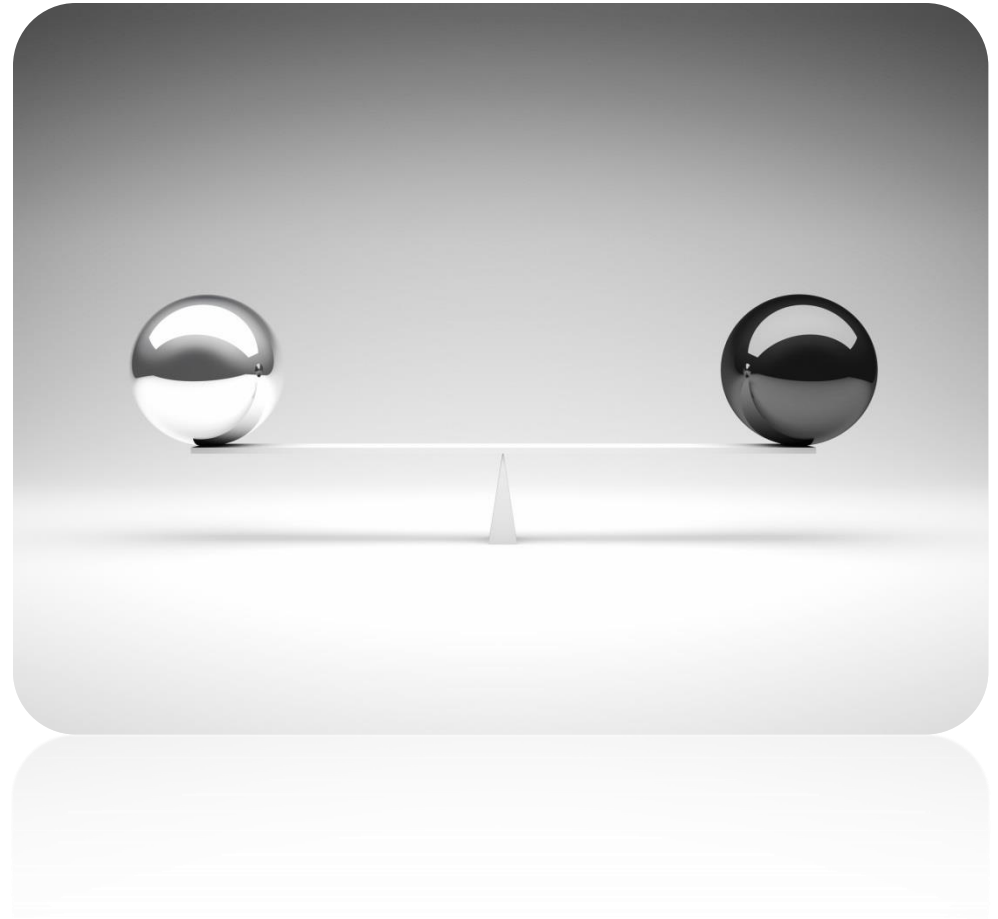
- Anxiety
- Autism
- Bipolar disorder
- Celiac disease
- Depression
- Hyperthyroidism
- Insomnia
- OCD
- Panic
- Stroke

## LOW GLUTAMATE IN URINE

- Agitation
- Chronic fatigue
- Depression
- Insomnia
- Lethargy
- Migraines

# Glutamate Support

- LOW GLUTAMATE:
  - L-glutamine
- HIGH GLUTAMATE:
  - GABA, L-theanine, taurine
  - Vitamin B6
  - Vitamin E
  - N-acetyl cysteine



# Excitatory Neurotransmitters

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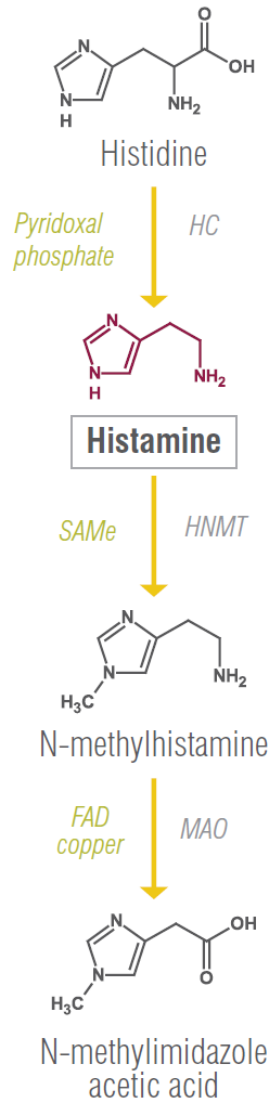
# Histamine

## neurotransmitter and immunomodulator

- Decreases sleep
- Increases metabolism
- Potent vasodilator
- Pro-inflammatory agent
- Prevents weight gain
- Stimulates gastric acid production
- Stimulates wakefulness
- Suppresses appetite



# Histamine Metabolism



**HNMT** = histamine N-methyl transferase

**MAO** = monoamine oxidase



# Histamine Imbalance Symptoms

## HIGH HISTAMINE IN URINE

- Allergies
- Burns
- Cystitis
- Depression
- Flushing disorder
- Food allergies
- Headaches/migraines
- Insomnia
- OCD

## LOW HISTAMINE IN URINE

- Easy frustration
- Lethargy
- Low libido
- Mild depression
- Tension headaches
- Weight gain

# Histamine Support

- LOW Histamine:

- Histidine

- HIGH Histamine:

- Flavonoids

- Low histamine diet

- Antihistamines

- Herbal Supplements:

- (flavonoids)

- Bilberry extract

- Citrus bioflavonoids

- Ginko biloba

- Grape seed extract

- Green tea extract

- Hawthorn extract

- Quercetin

- Food sources:

- Beer

- Champagne

- Cheese (aged)

- Eggplant

- Fish

- Meat

- Red wine (vinegar)

- Sauerkraut

- Spinach

# Excitatory Neurotransmitters

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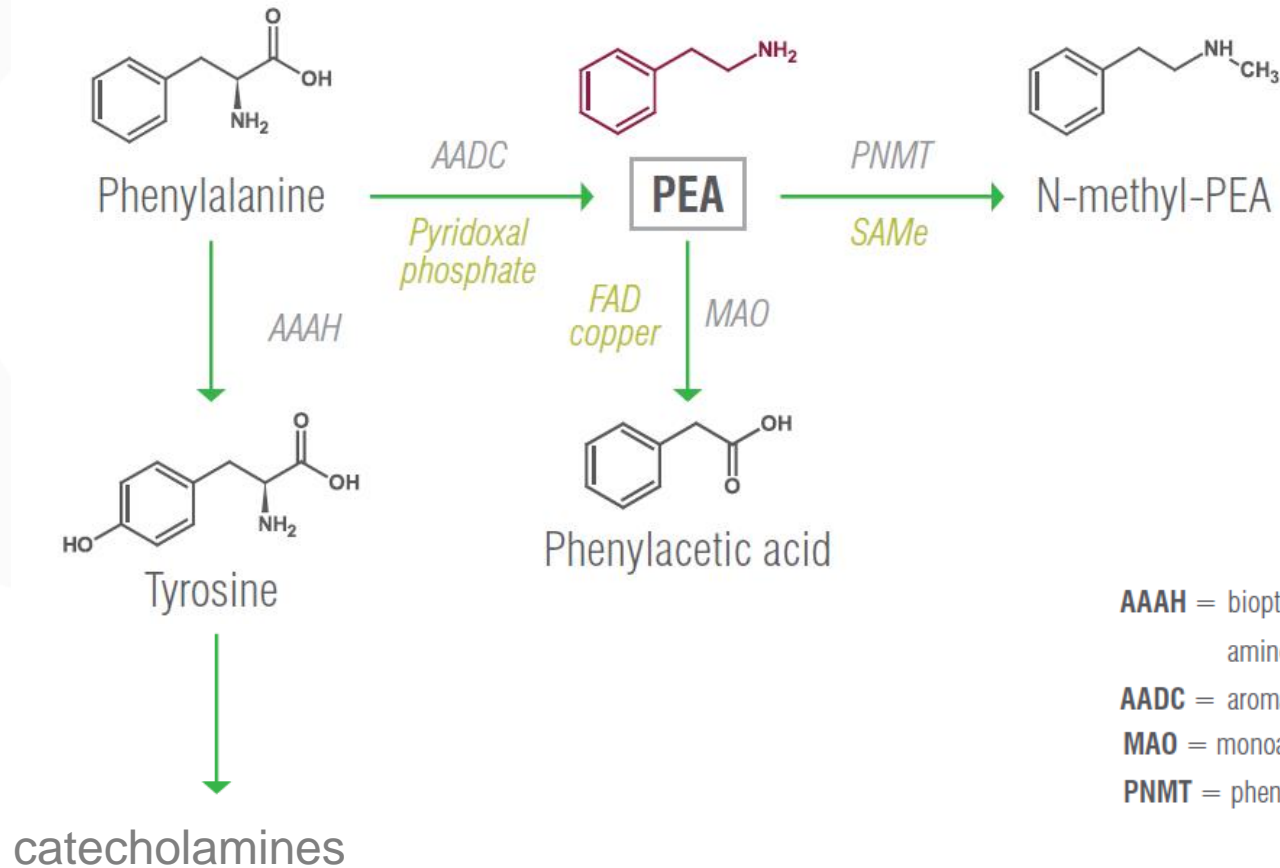
# PEA

promotes energy, elevates mood, regulates attention



- Biomarker for ADHD
- Inhibits dopamine, norepinephrine, and serotonin reuptake
- Regulates aggression

# PEA Metabolism



**AAAH** = biotin-dependent aromatic amino acid hydrolase

**AADC** = aromatic L-amino acid decarboxylase

**MAO** = monoamine oxidase

**PNMT** = phenylethanolamine N-methyltransferase

# PEA Metabolism and Imbalance Symptoms



## HIGH PEA IN URINE

- Amphetamine
- Anxiety and insomnia
- Bipolar disorder
- Exercise
- Schizophrenia
- Postpartum period

## LOW PEA IN URINE

- Autism
- ADHD
- Bulimia nervosa
- Depression
- Inattentiveness
- Memory issues
- Parkinson's disease
- Tourette syndrome
- Weight control difficulties

# PEA Support



- LOW PEA:
  - PEA
  - Phenylalanine
  - Vitamin B6
- HIGH PEA:
  - SAmE

## Food Sources:

- Beans
- Chocolate
- Cocoa nibs
- Eggs
- Natto
- Peas

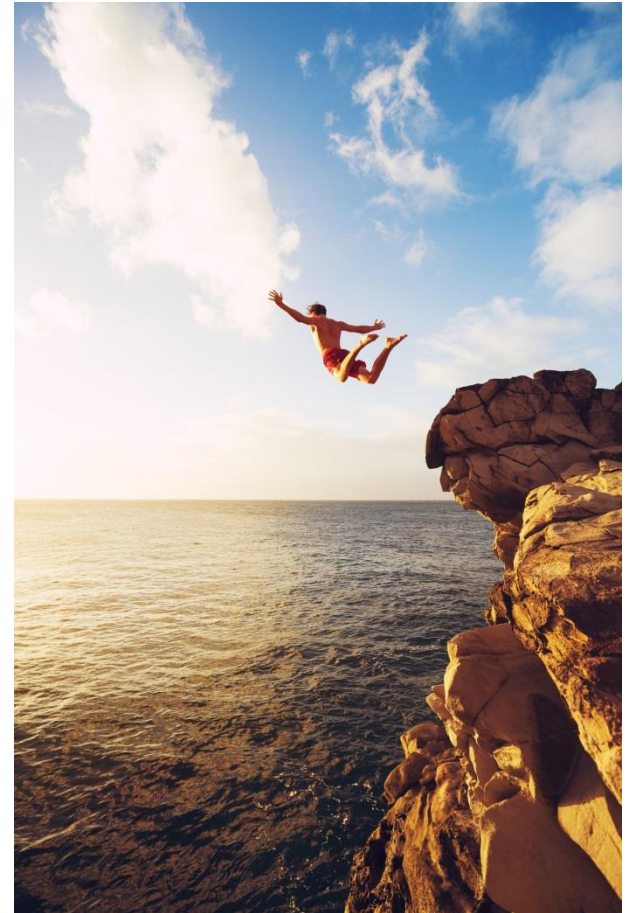
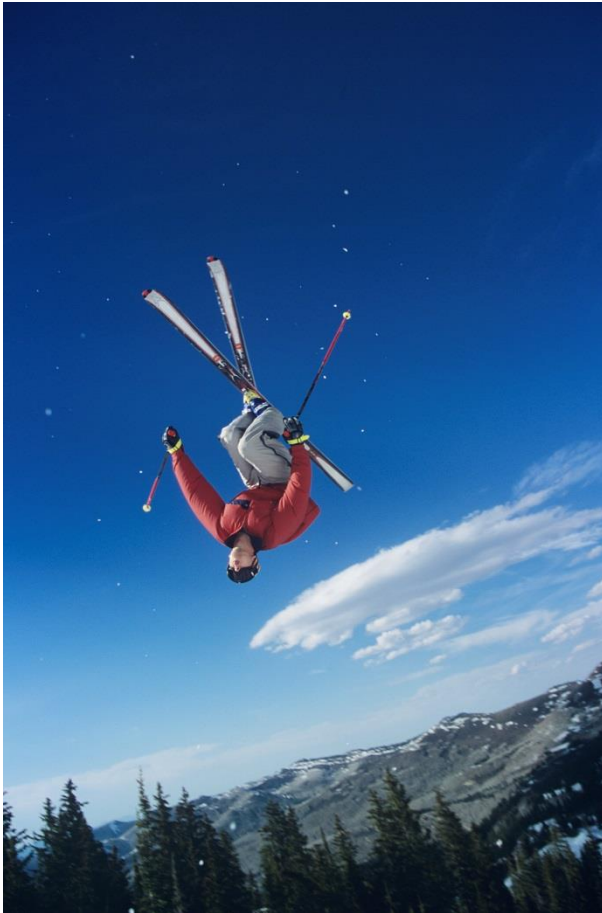
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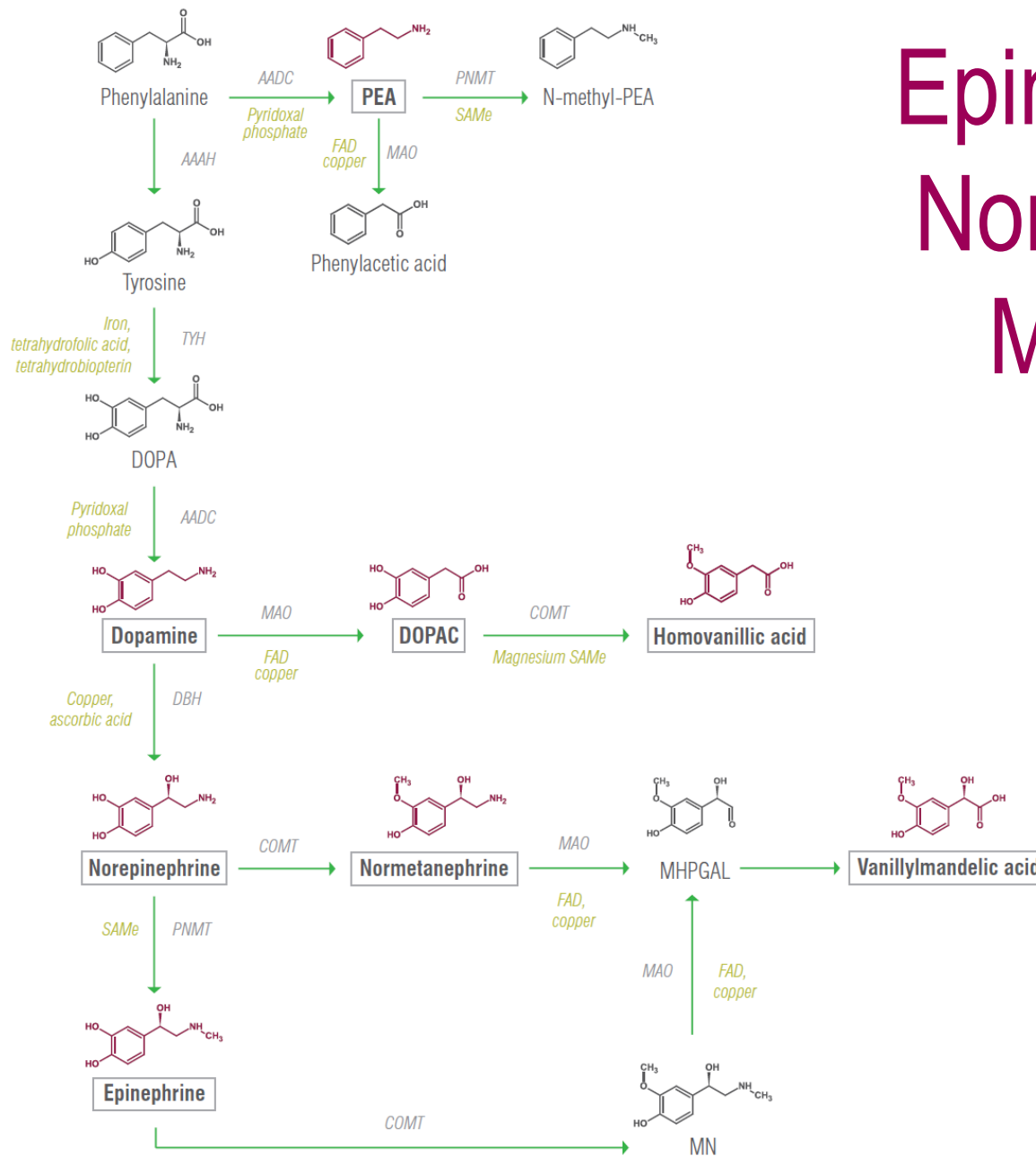


# Epinephrine and Norepinephrine

“fight or flight”



# Epinephrine and Norepinephrine Metabolism



AAAH = bipterin-dependent aromatic amino acid hydrolase  
 AADC = aromatic L-amino acid decarboxylase

COMT = catechol-O-methyltransferase  
 MAO = monoamine oxidase  
 PNMT = phenylethanolamine N-methyltransferase

DBH = dopamine beta hydroxylase  
 TYH = tyrosine hydroxylase  
 PEA = phenylethylamine

# Epinephrine and Norepinephrine HIGH Levels in Urine

- ADD
- Anxiety and depression
- Bipolar disorder
- Hyperglycemia
- Hyperinsulemia
- Obesity (norepinephrine only)
- Obstructive sleep apnea
- PTSD
- Stress



# Epinephrine and Norepinephrine LOW Levels in Urine

- Alzheimer's disease
  - Anorexia
- Attention impairment
  - Depression
  - Fatigue
- Hypotension
  - Low mood
- Obesity (epinephrine only)



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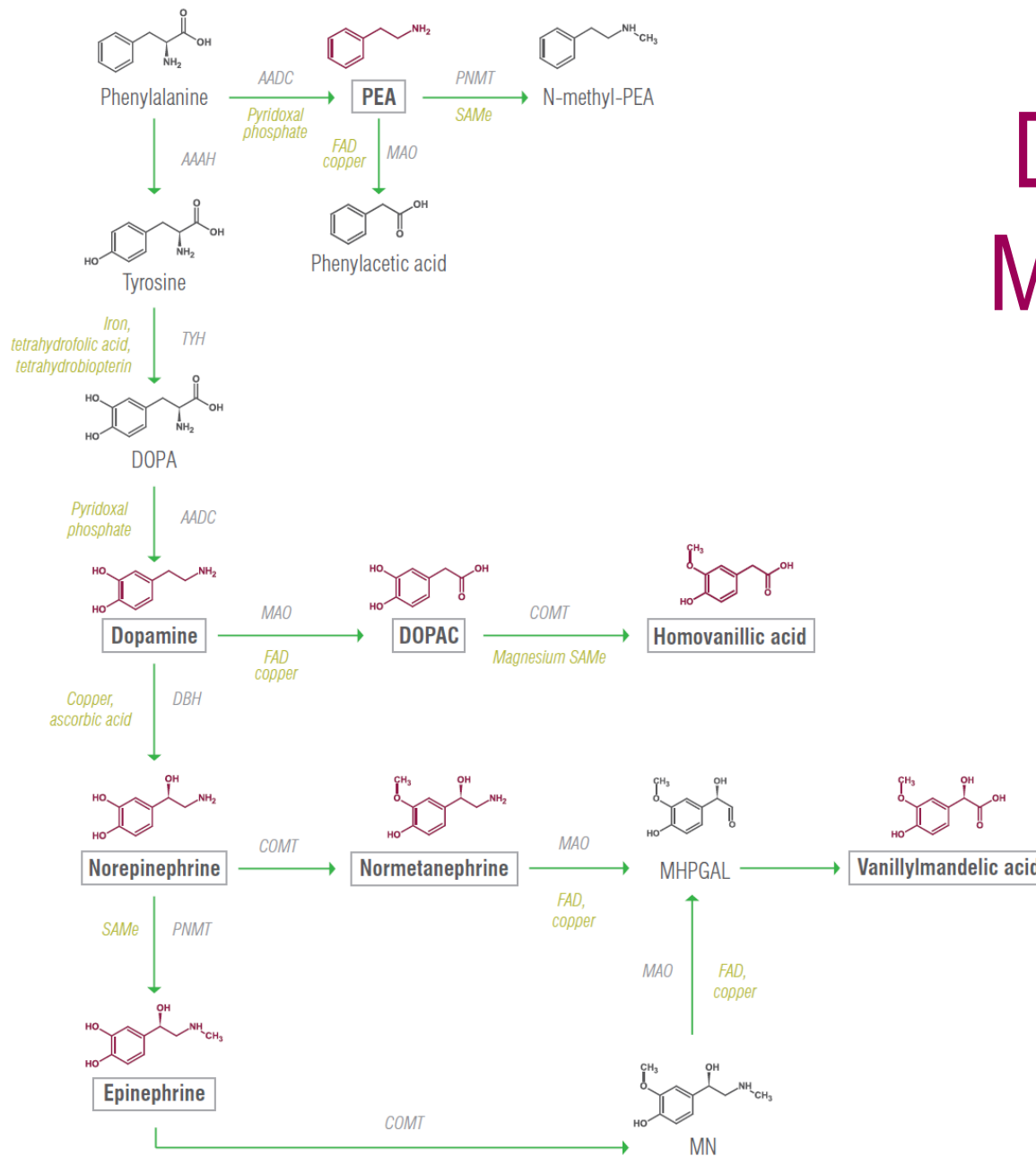
# Dopamine

“pleasure center”

- GI function
- Helps with decision making
- Improves attention
- Increases blood pressure
- Inhibits lactation
- Modulates immune function
- Promotes arousal
- Regulates sodium excretion



# Dopamine Metabolism

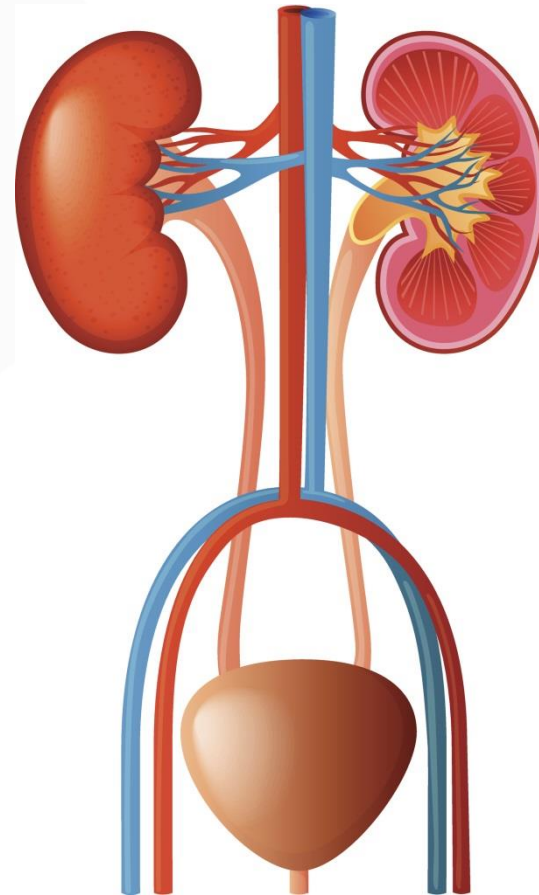


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# Urinary Dopamine is Biosynthesized in the Kidneys





# Dopamine Imbalance

## HIGH DOPAMINE IN URINE

- Anxiety
- Hyperactivity
- Inability to focus
- Increased sodium intake
- Insomnia
- Mercury toxicity
- Mood swings
- Pheochromocytoma
- PTSD
- Stress

## LOW DOPAMINE IN URINE

- Addiction
- Alzheimer's disease
- Anorexia nervosa
- Anxiety with depression
- Apathy
- Cravings
- Fatigue
- Fibromyalgia
- Impulsivity
- Insomnia
- Low libido
- Low mood
- Memory issues
- Periodic limb movement disorder

# Catecholamine Support

## Food Sources:

- Avocados
- Bananas
- Beans
- Chocolate
- Coffee
- Hazelnuts
- Oranges
- Pineapples
- Potatoes
- Spinach
- Tea
- Tomatoes
- Wine

- LOW:
  - Cofactor support
- HIGH:
  - Cofactor support
  - Tyramine
  - Tyrosine
  - Phenylalanine

# When to Test?

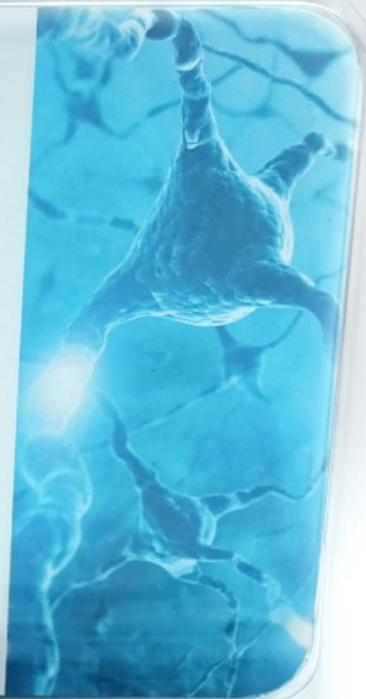
**persistent inability to cope with stress**  
**causes failure to thrive**

DEPRESSION *fatigue* HOPELESSNESS  
TREMBLING IRRITABILITY *rumination* weight gain  
HEADACHES ANGER OCD PANIC  
IMPULSIVITY MANIA MALAISE  
RESTLESSNESS *mania* SWEATING HYPERVENTILATION  
AVOIDANCE PTSD BURNOUT DOOM lethargy  
INVASIVE THOUGHTS eating disorders *mood*  
*swings* WEIGHT LOSS worry  
INCREASED HEART RATE lack of concentration  
INSOMNIA

zrtlab.com

# NEURO TRANSMITTERS

A home-collection test to assess neurotransmitter levels that affect overall health and well-being.



## Test Requisition

### 1 Individual Information

Please print clearly, placing one capital letter in each space.

First Name: \_\_\_\_\_  
Last Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
City: \_\_\_\_\_  
Day Phone: \_\_\_\_\_  
Email: \_\_\_\_\_  
Gender:  Female  Male

### 2 Current Menstrual Cycle

First day of last menstrual cycle:  
 Regular Cycle  
 Irregular Cycle  
 No Menstrual Cycle

Symptoms:  
or 3 (severe)

## Collection Instructions

Urine Specialty Profiles  
Please read this entire instruction pamphlet prior to sample collection. We strongly recommend you view our quick video collection instructions at [urinevideo.com](http://urinevideo.com) or [zrtlab.com](http://zrtlab.com)

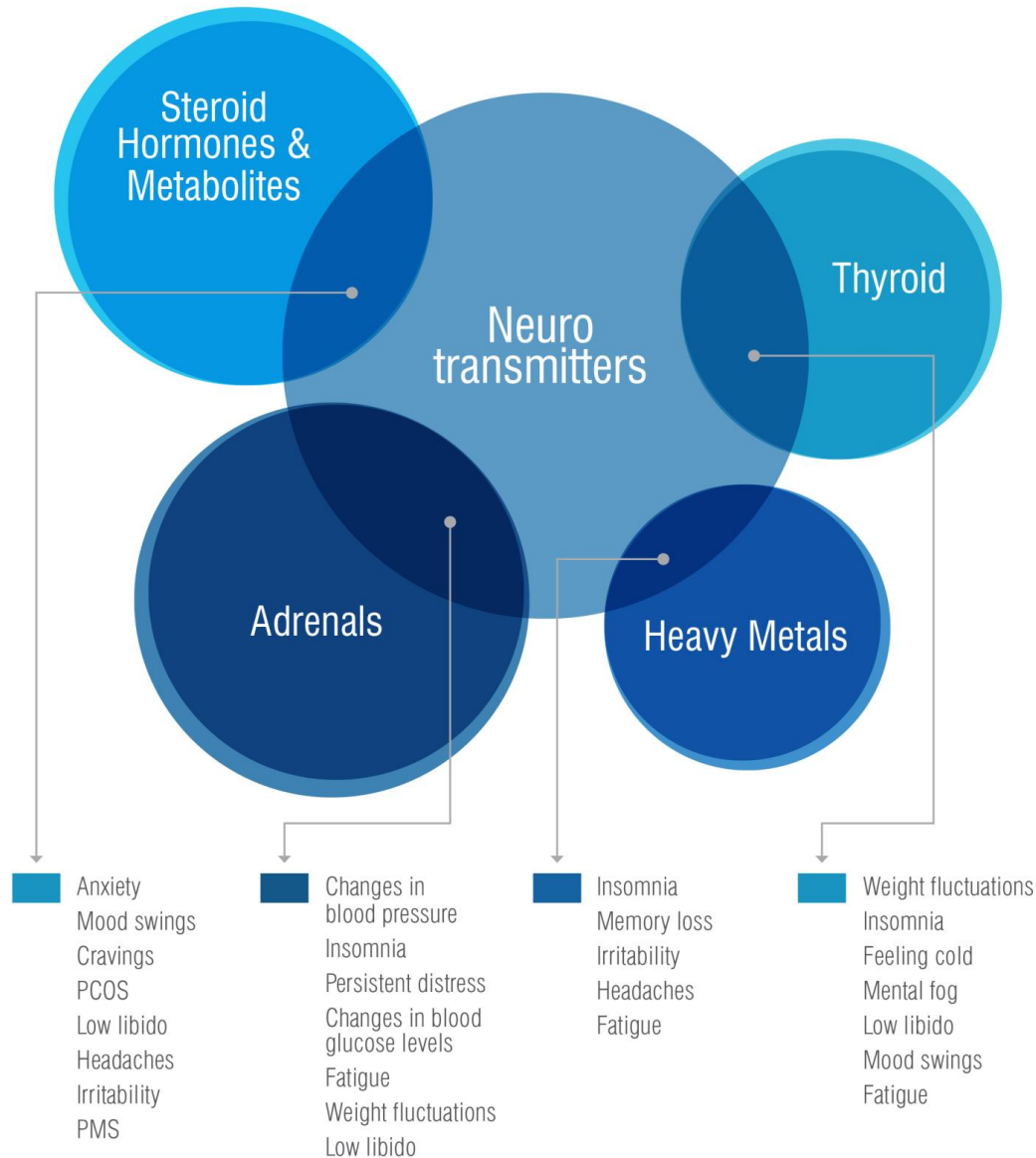
What day should samples be collected?  
 Women who no longer use birth control  
 Premier  
 21 or younger  
 Postmenopausal  
 Pregnant



Tuck Flap Under Here



# WHAT THE FUTURE HOLDS





THANK YOU!

QUESTIONS

*Please address any additional questions to Dr. Kate Placzek [kaplaczek@zrtlab.com](mailto:kaplaczek@zrtlab.com)*