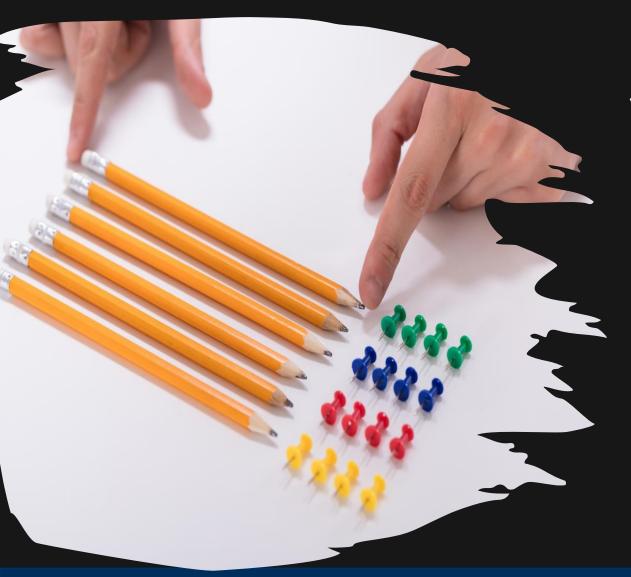


Obsessive Compulsive Disorder Redefined

A Functional & Integrative Medicine Approach

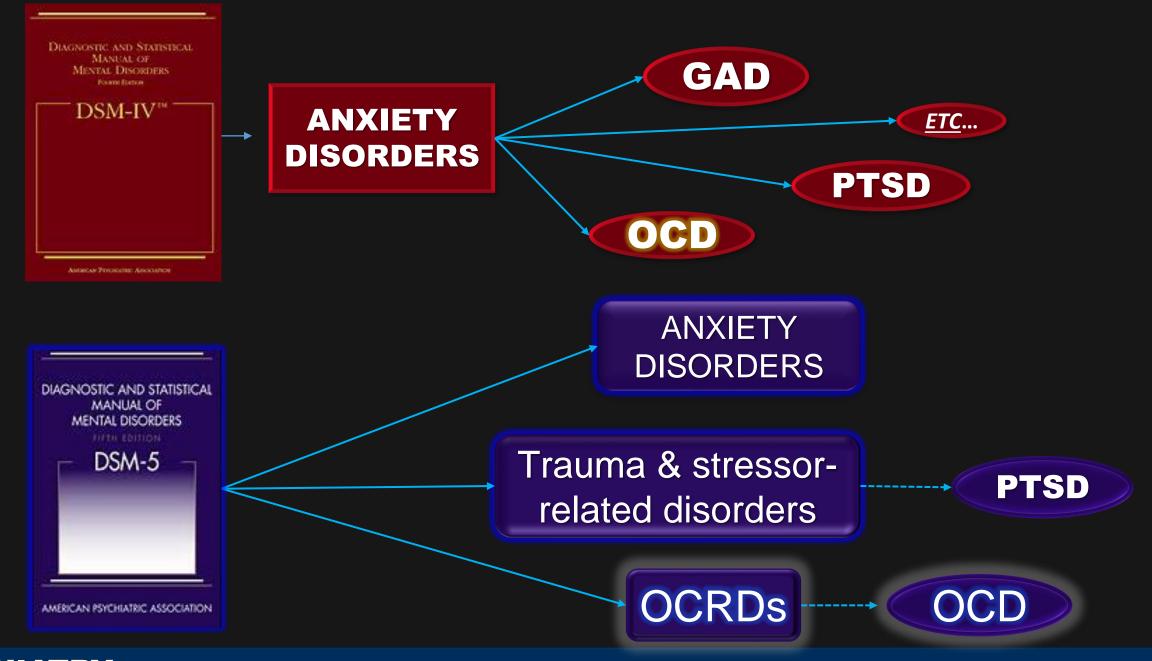
Dr. James Greenblatt





"I ...took sleeping pills to fall asleep, as this was the only way to not perform the rituals."

- Chandler



OCD

Body Dysmorphic Disorder

OCRD due to another medical condition

OCRDs

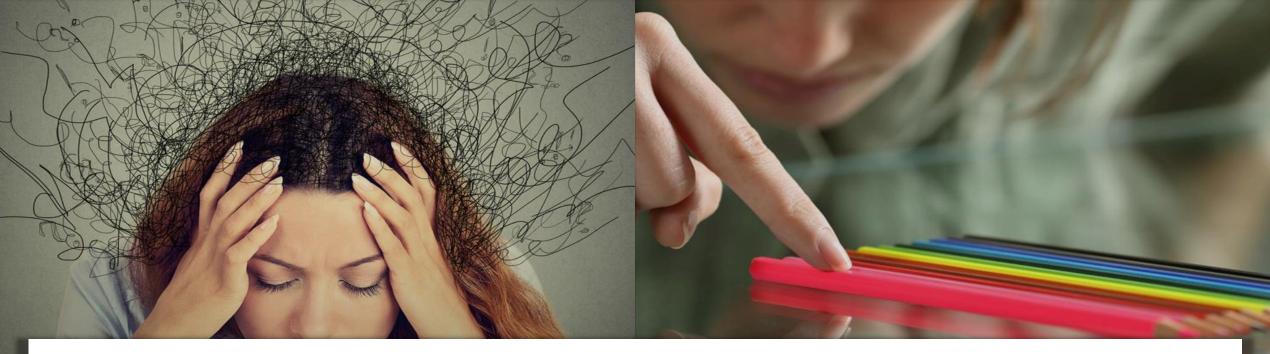
Hoarding Disorder

Substance/Medication Induced OCRD

Excoriation Disorder

Trichotillomania

OCD is characterized by intrusive & unwanted thoughts that elicit anxiety – also known as <u>obsessions</u>.



To alleviate anxiety from the obsessions, sufferers often engage in specific and repetitive behaviors –known as <u>compulsions</u>.



Common OCD Obsessions



- An intense need for symmetry
- Fear of dirt or germs
- Pathological doubt
- Intense religious / spiritual convictions
- Aggressive impulses
- Sexual impulses
- Concerns about feelings in or appearances of the body

Common OCD Compulsions

Excessive washing & cleaning

Repetitive checking (locks, etc.)

Pathologic doubt

Intense religious, spiritual convictions

Aggressive impulses

Sexual impulses

Concerns about feelings in / appearances of the body

At its most extreme, OCD can make it difficult to navigate school, hold down a job, or even leave the house



While OCD can occur at any age, there are generally two age ranges within which symptoms first manifest:



Between the ages of 8-12 years

Between late teens – early adulthood

"Angel": 12 year-old female

Symptom onset:

age 4

Obsessions:

not throwing away garbage

Compulsions:

hoarding garbage



Family History:

- Mother
- 2 maternal aunts
- Mother's cousin
- Maternal greatgrandmother

...ALL had OCD!

OCD Prevalence*



1 in 40 adults

1 in 100 children

Lifetime: 1.6 - 2.3% in the community

PSYCHIATRY REDEFINED Brock H, Hany M. Obsessive-Compulsive Disorder. [Updated 2022 Feb 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-Available from: https://www.ncbi.nlm.nih.gov/books/NBK553162/?msclkid=84e20acfc0b211ec8679786753aac9b6 Beyond OCD. BeyondOCD.org. https://beyondocd.org/ocd-facts. Nd. Accessed April 20, 2022.

Factors Contributing to Misdiagnosis / Non-diagnosis



Outward symptoms are often indistinguishable from those of other disorders



Many OCD sufferers feel compelled to hide their disorder

MISSING THE MARK

The average OCD sufferer will go an average of 11 years before being treated

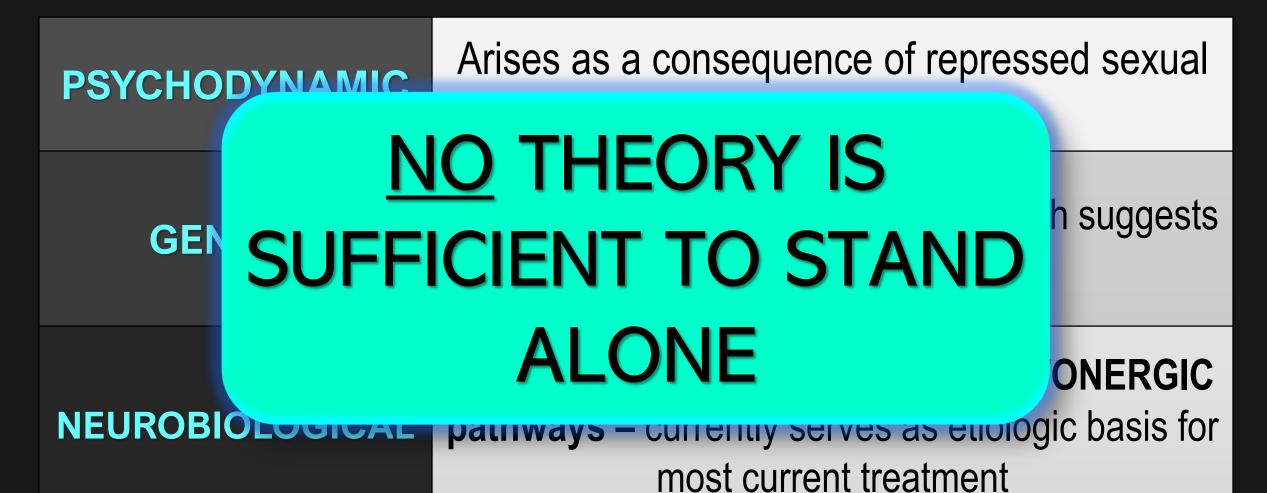


It's estimated that less than 10% of all sufferers receive ANY treatment at all



Brock H, Hany M. Obsessive-Compulsive Disorder. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-Available from: https://www.ncbi.nlm.nih.gov/books/NBK553162/?msclkid=84e20acfc0b211ec8679786753aac9b6′ Fenske JN, Schwenk TL. Am Fam Physician. 2009;80(3):239-45.

Etiologic Theories



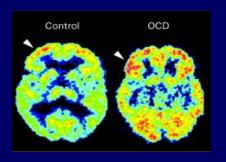
There is compelling evidence for a biological basis of OCD



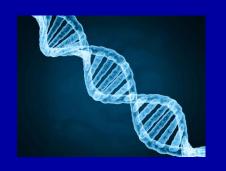
Common in several medical conditions



40-60% of patients respond to SSRIs

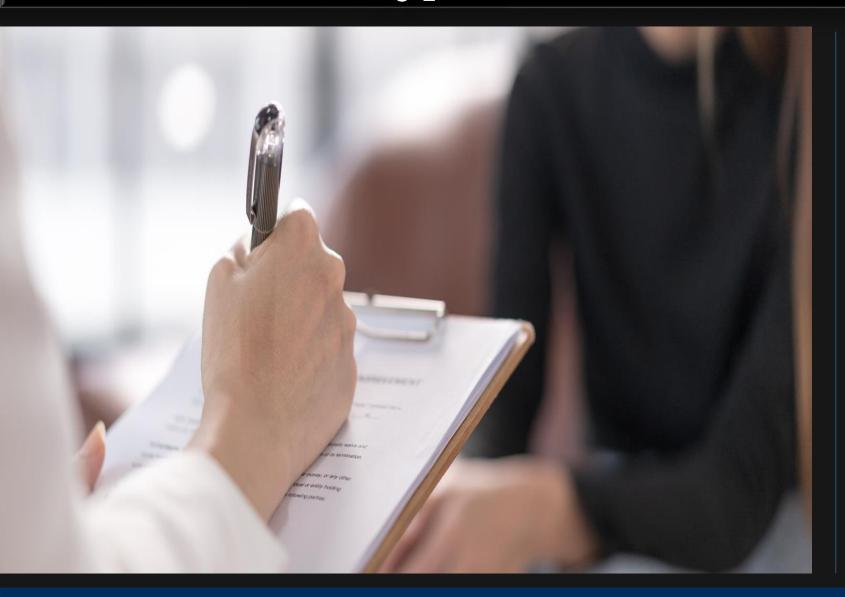


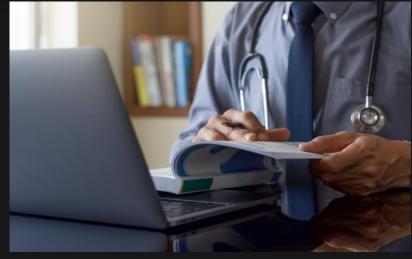
Distinct brain abnormalities

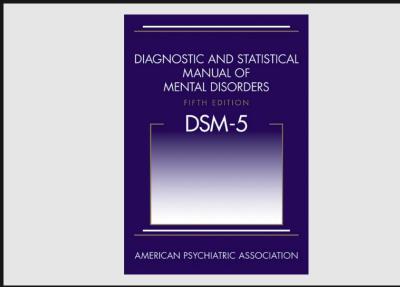


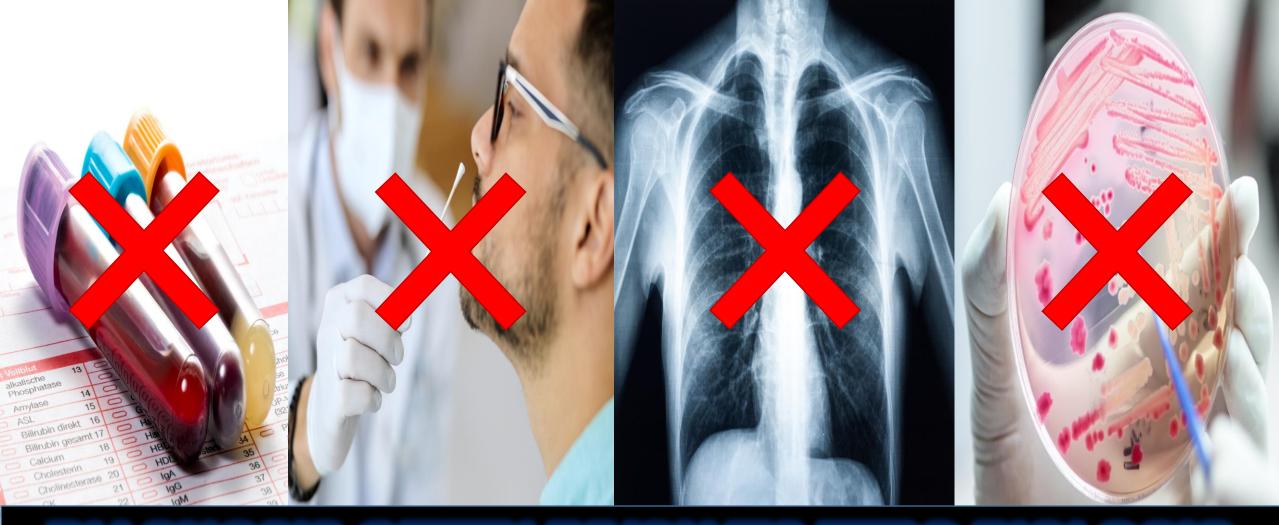
Heritability estimate of 45% - 65%!

A Typical Evaluation for OCD









DIAGNOSIS OFTEN INVOLVES ZERO BIOLOGIC TESTING OF ANY KIND



Pillars of Mainstream OCD Treatment



P.A.N.S. / P.A.N.D.A.S.



A clinical condition defined by acute onset of OCD and/or severe eating restrictions AND at least two concurrent cognitive, behavioral, or neurologic symptoms



Is this the best we can do for our patients?

....really?



FUNCTIONAL BIOMEDICAL ANALYSIS

<u>Urine Test</u>



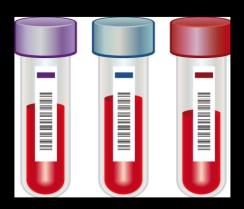
- Opiate peptides
- HPHPA
- Yeast
- Organic Acids
- Amino Acids

<u>Hair Test</u>



- Copper
- Zinc
- Lead
- Magnesium
- Lithium

Blood Test



- Amino Acids
- Food Allergies
- Hormones
- Fatty Acids
- Vitamins
- Trace Minerals

Saliva Test



- Genetics
- Hormones



If you don't test...

...how do you know?

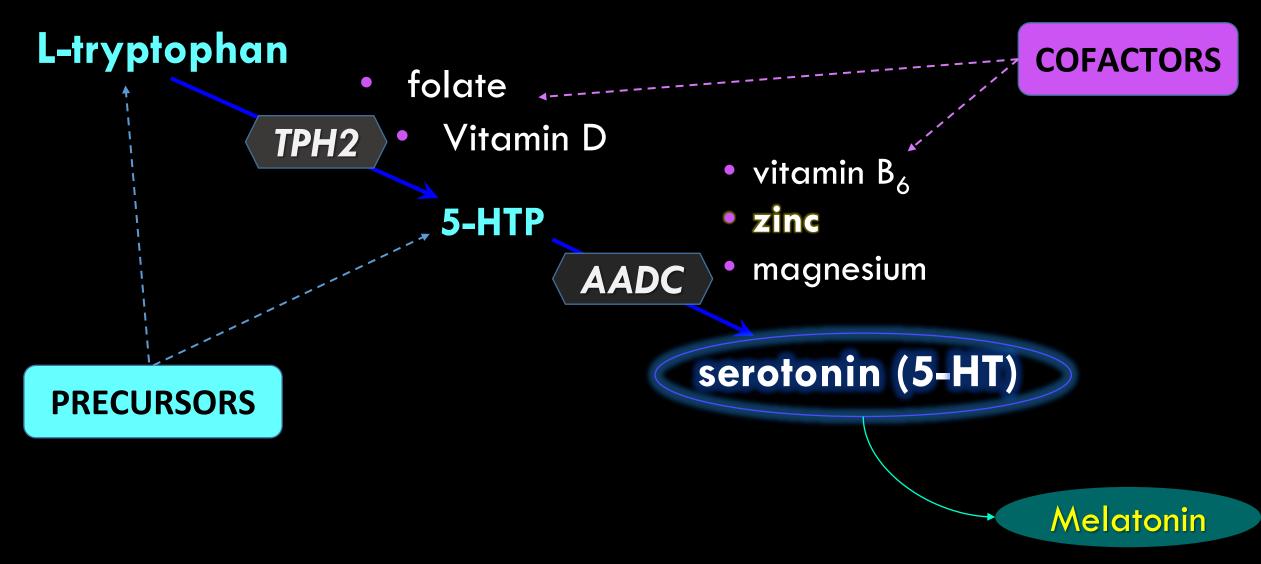
SSRIs & SRIs can reduce OCD symptoms





Nutritional interventions influencing SER activity

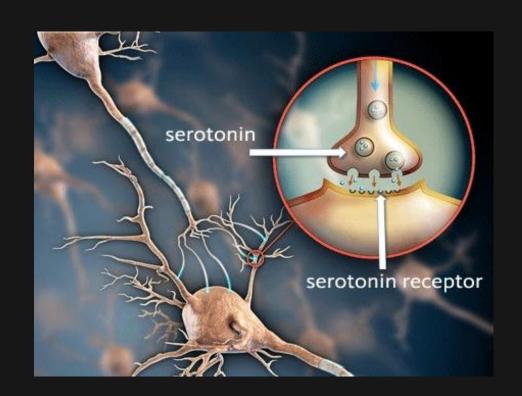
Serotonin Synthesis



OCD Redefined

Serotonin Synthesis

- Genetics
- Dietary intake
- Digestion/Absorption of Amino Acids (Amino Replete)
- Target Amino Acids 5-HTP,Tryptophan
- Zinc
- Folate
- Vitamins B6, B12, C, D
- Magnesium

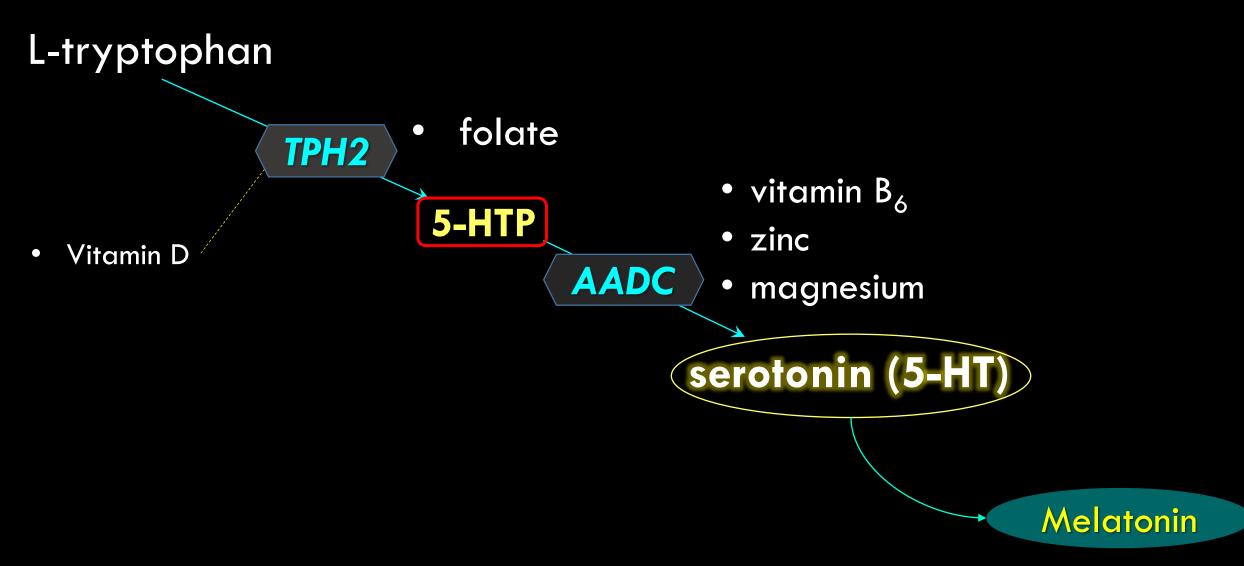


Neurotransmitters from Amino Acids

| Amino Acid | Neurotransmitter | Roles in Mental Health |
|---------------|----------------------------|---|
| • | Dopamine Norepinephrine | Alertness, cognitive performance, positive mood |
| | | IN ANY NORMAL OR VEGETARIAN |
| Tryptophan | Serotonin | DIET, TRYPTOPHAN IS THE *LEAST* |
| | Glycine | PLENTIFUL OF THE AMINO ACIDS! |
| Glycine | | Sieep, relaxation |
| Glutamic acid | Glutamate | Learning, memory |
| Arginine | Nitric Oxide | Modulation of other neurotransmitters |



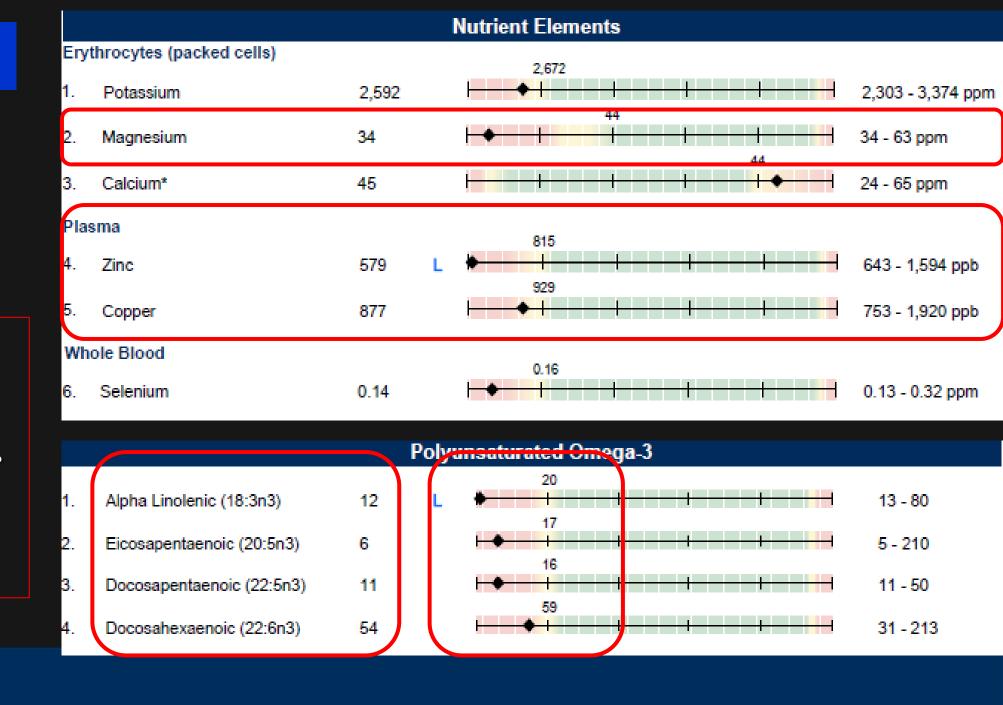
Serotonin Synthesis



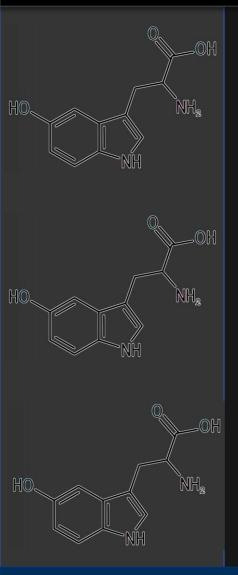
Case SE

ION Testing

- Low Mg
- Low Zinc
- Low Copper
- Low EPA, DHA, GLA



5-Hydroxytryptophan (5-HTP)



- A metabolite of tryptophan & a precursor for serotonin
- Effectively crosses the blood-brain barrier
- Is not incorporated into other proteins; is utilized exclusively for serotonin synthesis
- Can reliably increase brain / CSF serotonin

SeroPlus

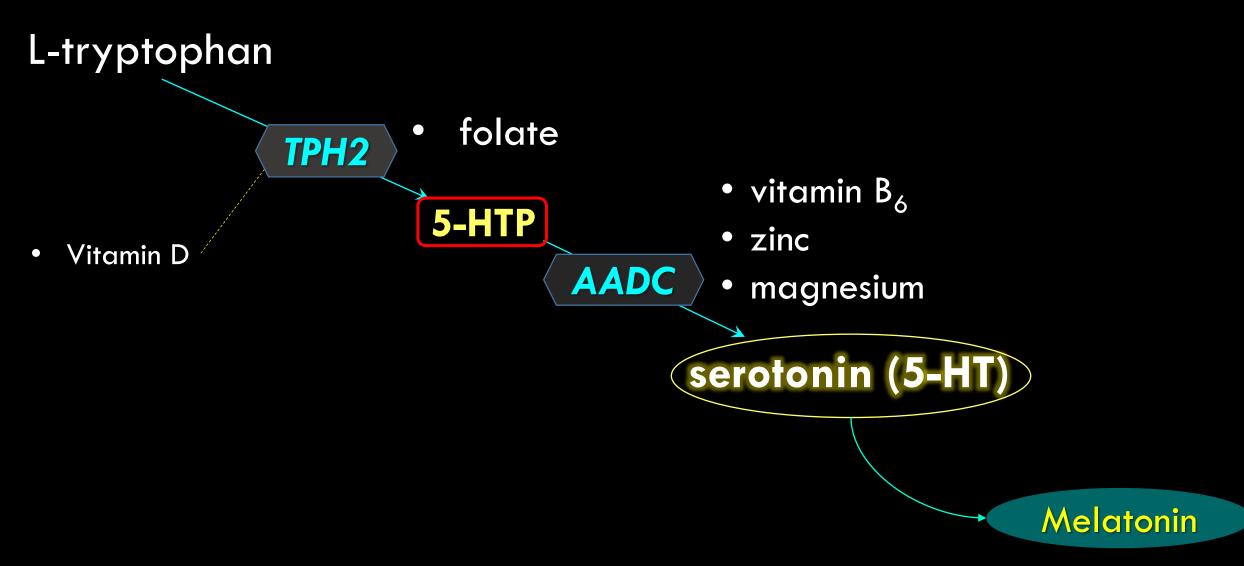
| Servings per container 60 | Amount Per Serving | %DV |
|--|----------------------------------|-------|
| Vitamin C (as ascorbic acid) | 100 mg | 111 % |
| Niacin (as niacinamide) | 20 mg | 125% |
| Vitamin B ₆ (as pyridoxal 5' phosphate) (activat | 6.7 mg ted B ₆) | 394% |
| Folate (as Metafolin®, L-5-MTHF) | 833 mcg DFE (500 mcg L5-MTHF) | 208% |
| Magnesium (as di-magnesium malate) | 100 mg | 24% |
| Zinc (as zinc picolinate) | 10 mg | 91% |
| 5-Hydroxytryptophan | 100 mg | * |
| Inositol (as myo-inositol) | 500 mg | |
| Taurine (free-form) | 200 mg | |

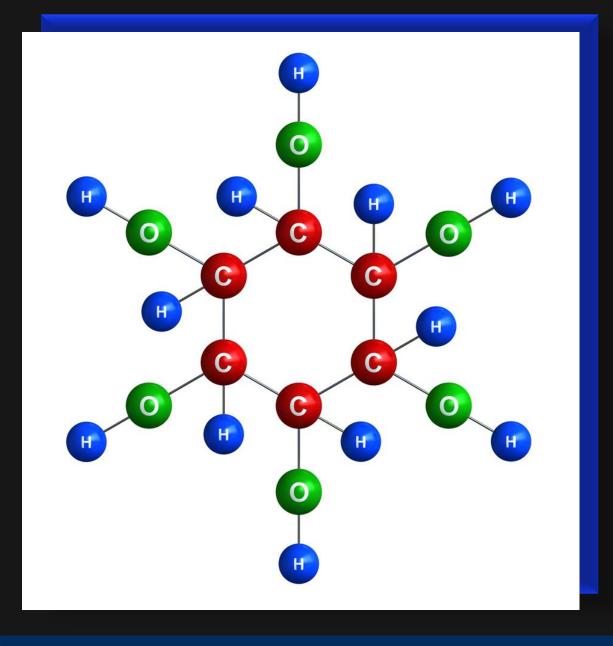


Supports serotonin production

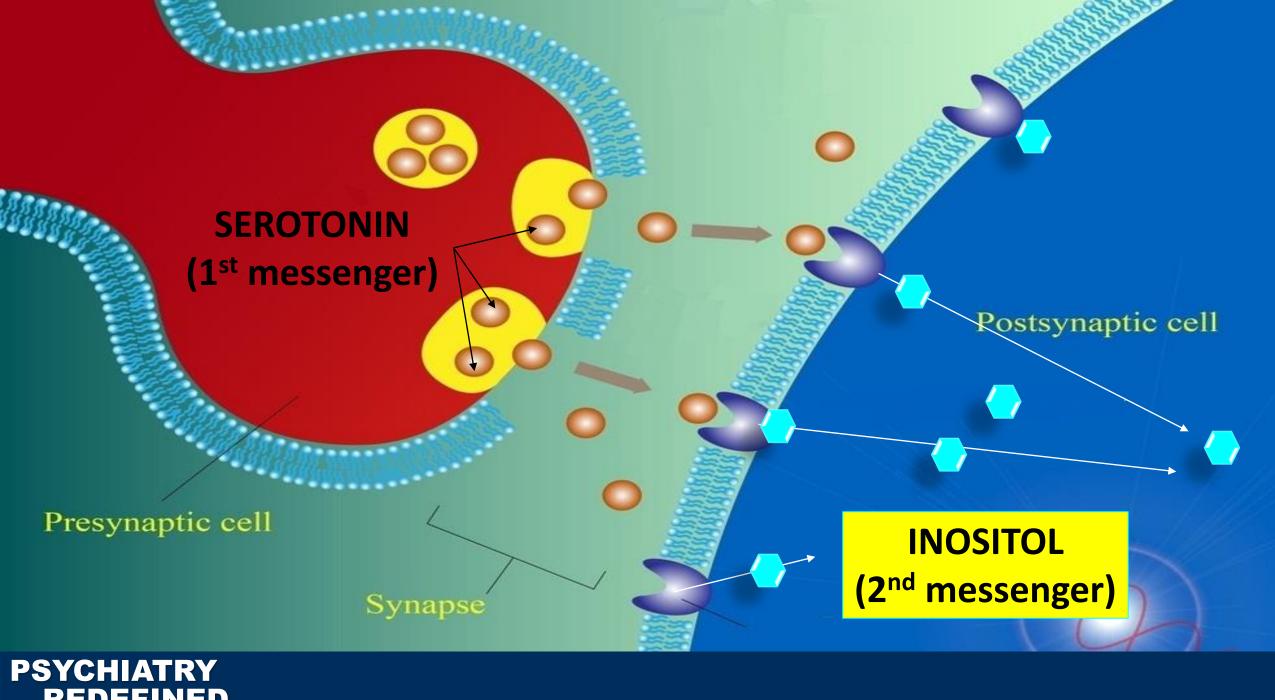
- Folate (5-MTHF)
- P5P (Vitamin B₆)
- 5-HTP
- Zinc
- Inositol

Serotonin Synthesis

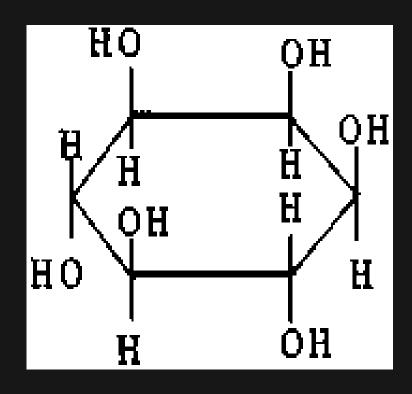




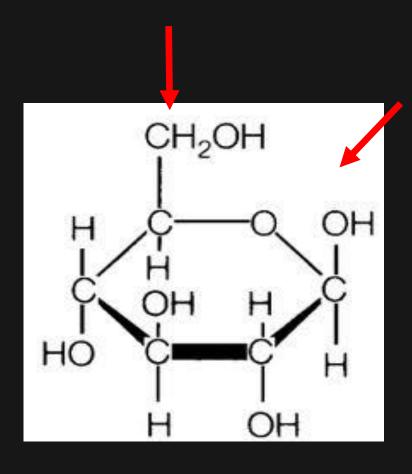
INOSITOL



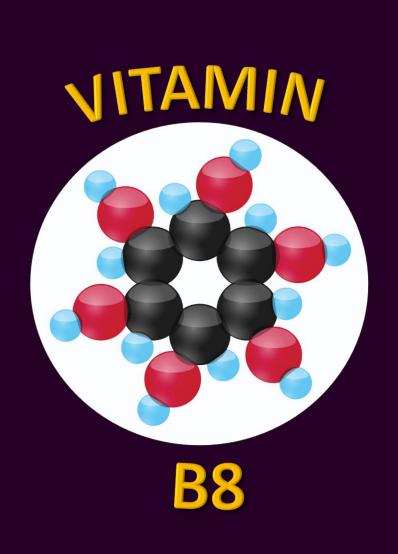
REDEFINED







Glucose



Helps to form healthy cell membranes

Maintains proper electrical energy and nutrient transfer between cells

Part of the second messenger system for the 5HT2 serotonin receptor

PSYCHIATRY REDEFINED

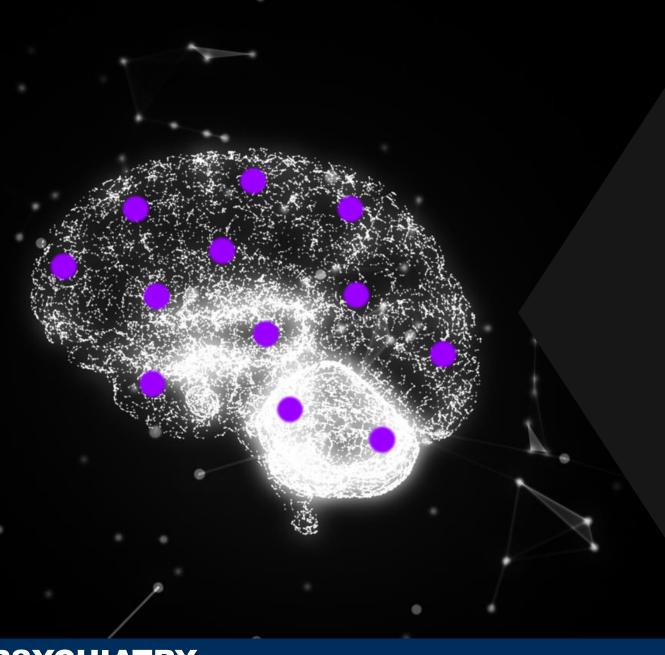
Inositol in Psychiatry

Reports of reduced CSF inositol levels in depressed patients

12g/day of Inositol raised CSF inositol levels by 70%

11
treatment
resistant
patients
responded
to inositol

Double-blind, placebo-controlled trial of inositol



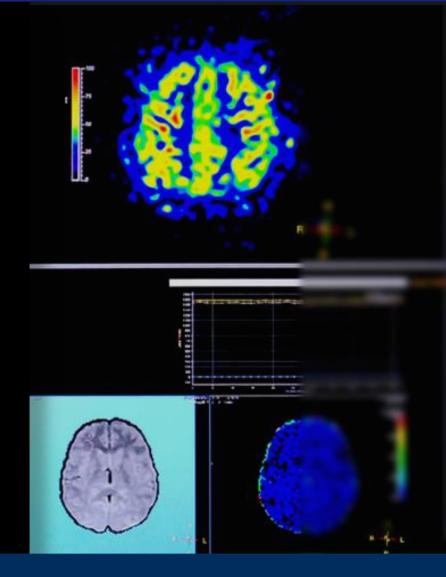
7-fold higher in cerebrospinal fluid relative to plasma...

...and ~50- to 200-fold higher in the brain

Neuroimaging Studies Have Documented...

Reduced myo-inositol (MI) levels in the frontal cortex of patients with depressive and sleep disorders

 Negative correlations between MI levels and depression severity



Inositol may have therapeutic effects in the spectrum of psychiatric illnesses responsive to SSRI medications, including:



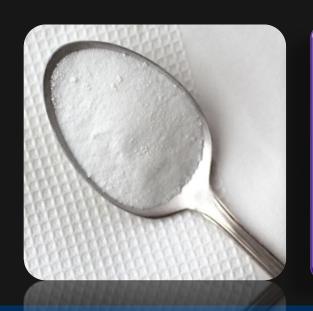
Adjunctive treatment for OCD; frequently the sole treatment for children



Double-Blind, Controlled Trial of Inositol Treatment of Depression

Levine, Joseph et al. Am J Psychiatry, Vol 152(5) May 1995. 792-794

28 unmedicated subjects with MDD or Bipolar Disorder experiencing depressive symptoms



Significant benefit for Inositol group at 4 wks

Side effects:

- Placebo insomnia, agitation, tension headache
- Inositol nausea, Gl upset



Inositol Treatment of Obsessive-Compulsive Disorder

Fux, Mendel, et al.; Am J Psychiatry, Vol 153(9) Sept. 1996. 1219-1221

Significant treatment effect of Inositol treatment vs. placebo at 6 weeks

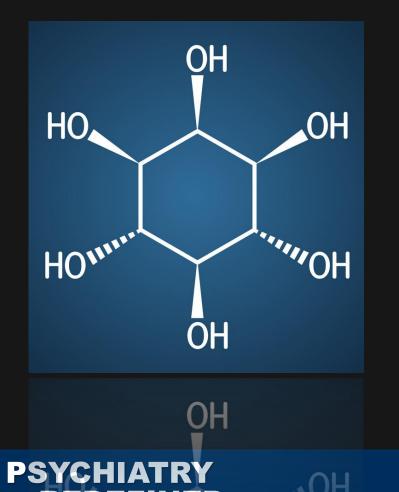
No reported side effects



Inositol augmentation of serotonin reuptake inhibitors in treatment-refractory obsessive-compulsive disorder: an open trial

S. Seedat and D.J. Stein

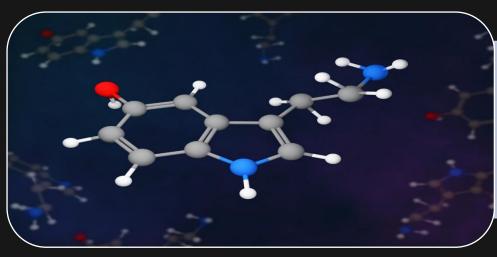
International Clinical Psychopharmacology 1999, 14: 353-356



Inositol augmentation 18 g/day did not lead to significant improvement in a majority of patients

3 patients did report a clinically significant response on the CGI improvement

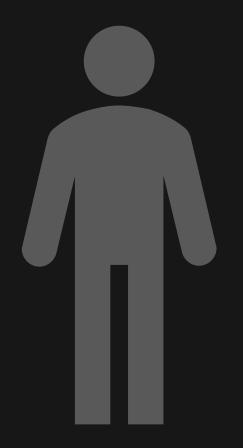
Inositol



- May have therapeutic effects for SSRI-responsive disorders
- ◆Depression ◆OCD ◆ Panic Disorder ◆ Bulimia



 Adjunctive inositol frequently the sole treatment for pediatric OCD



11 y/o male with increasing anxiety, worries that began at age 4

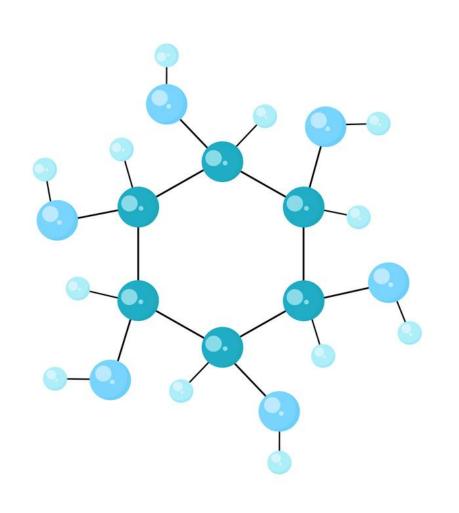
- > Fears of fire
- Contamination
- "Bad" things will happen to family
- Complete social withdrawal

Treatment: Inositol ½ tsp 3x/day (4.2 g)

"AMAZING. . . A DIFFERENT CHILD."

INOSITOL

RECOMMENDATIONS



1-12 grams daily

Start with 1,000 mg/day; titrate as needed

INOSITOL

KEYS TO SUCCESS



Inositol can cause GI upset or nausea in some individuals.



To minimize the risk of GI side effects, start at 1,000mg/day and titrate gradually.

Supplements can also be taken with food to further reduce stomach upset.

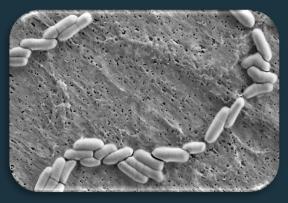


1014 friends you didn't know you had

Probiotics and Bipolar?



L. rhamnosus strain GG



B. animalis subsp. lactis

66 patients recently hospitalized for mania

After discharge:

- L. rhamnosus GG
- B. lactis

24 weeks

73% VS 24%



Probiotics Affect Neurotransmitters

Oral administration of probiotics:

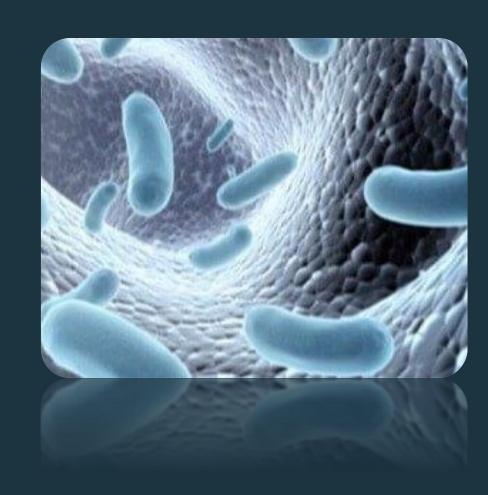
- Increased plasma tryptophan levels
- Decreased serotonin metabolites concentrations in the frontal cortex
- Increased dopamine metabolite concentrations in the amygdaloid cortex
- Increased acetylcholine levels
- Increased GABA levels

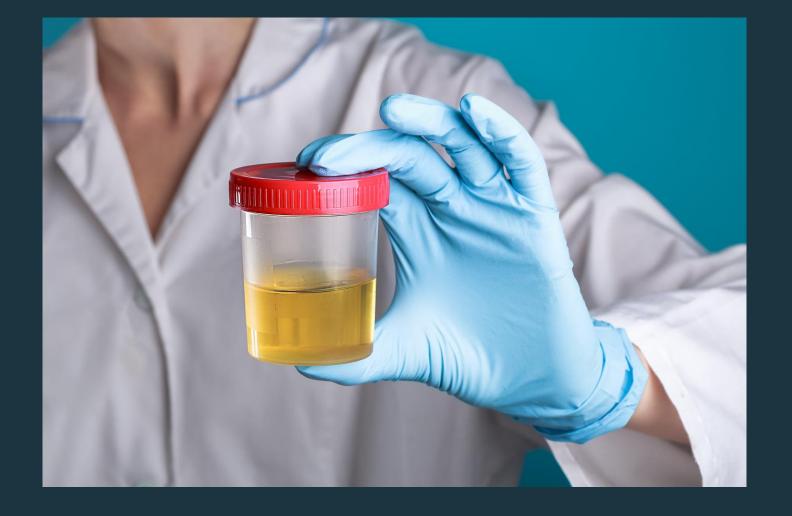
"I went to a psychiatrist, one of the most talented psychiatrists in the field, and he told me that there was nothing that psychiatry could do for me."



"I continued taking the 'Brand X' 30 Billion probiotics every day... I have not pulled even one hair since mid-January. Not only have I been symptom free, but I never had to apply any will power or focus on stopping the hair pulling...

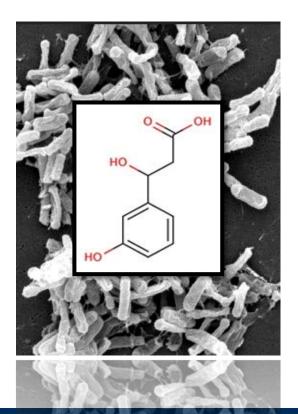
...the urges did not need to be fought off, they simply dissipated by themselves..."





16 HPHPA ≤ 220 173 (C. sporogenes, C. caloritolerans, C. botulinum & others)

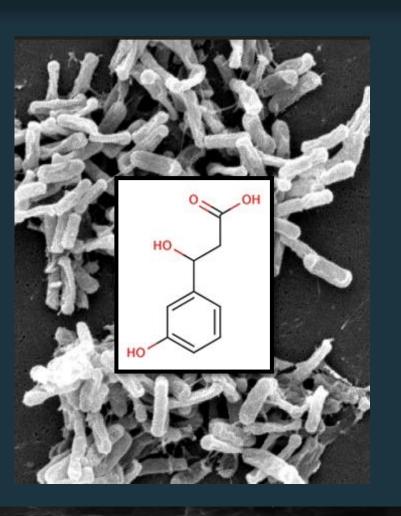
3-(3-hydroxyphenyl)-3-hydroxypropionic acid Otherwise known as: HPHPA



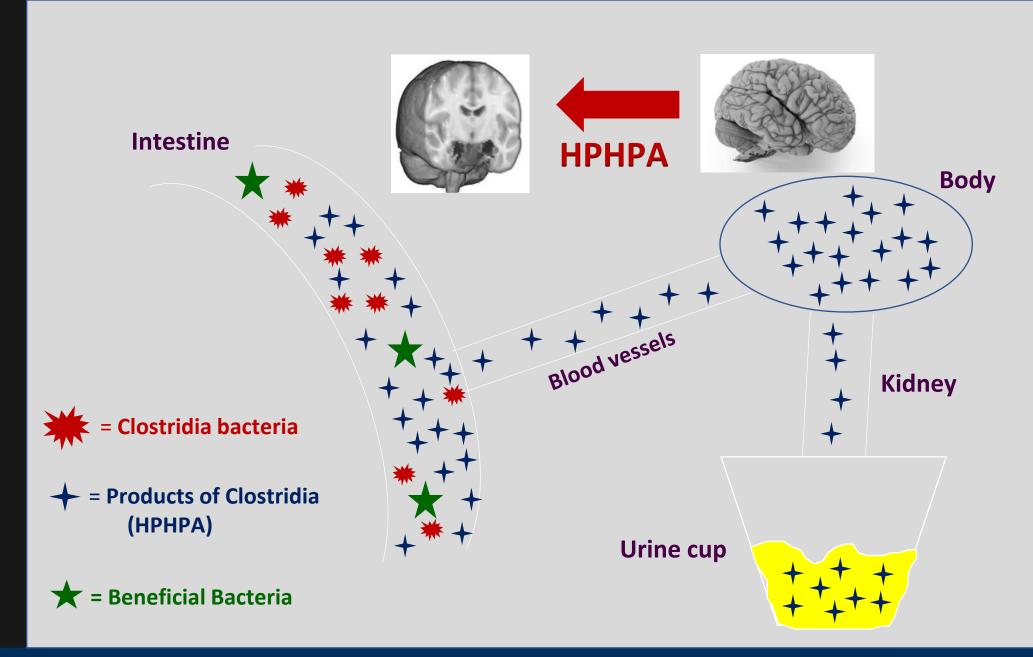
Neurotoxic byproduct of some* species of CLOSTRIDIA bacteria

* not all

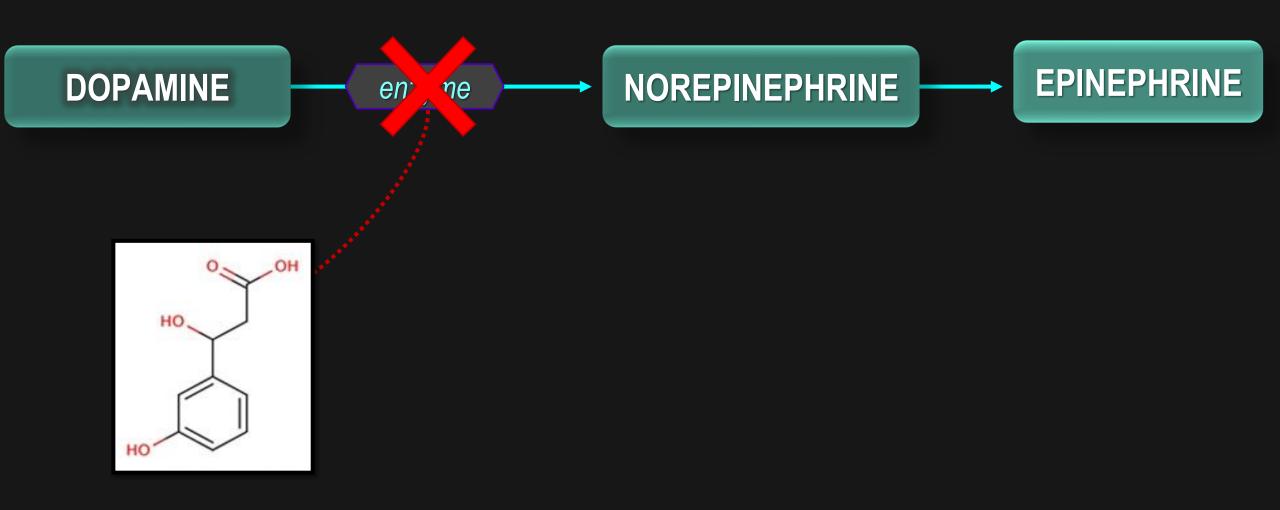
3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA)



- Made by anaerobic bacteria of the Clostridium genus
- •High HPHPA associated with behavioral, gastrointestinal, and/or neuropsychiatric effects
- •GI symptoms may include diarrhea *or* constipation



How HPHPA Disrupts the Dopamine Pathway





DOPA

3,4 dihydro phenylalar









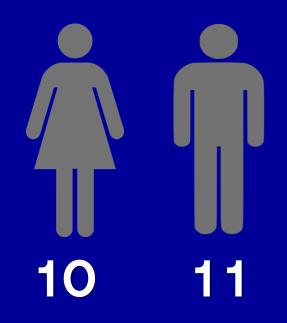
Benzodiazepine Use Benzodiazepine Dependence





PSYCHIATRY REDEFINED

Subject Characteristics





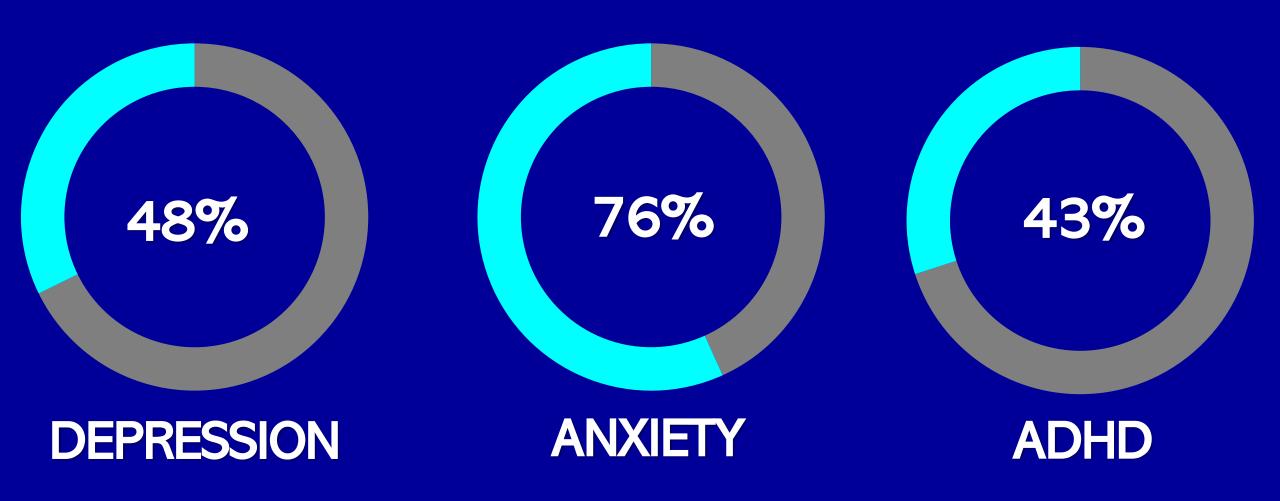
5 subjects

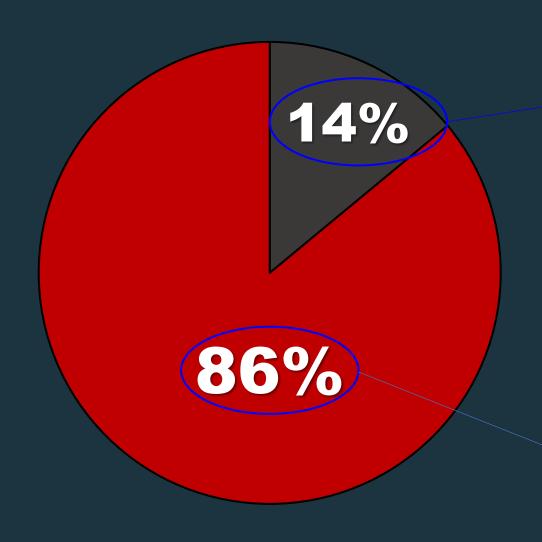
Age range

4 – 70 years



Dx Prevalance





Subjects with 1 clinical psychiatric diagnosis

Subjects with ≥2 clinical psychiatric diagnoses

OCD

BULIMIA NERVOSA

BIPOLAR DISORDER

ASD

MAJOR DEPRESSIVE DISORDER

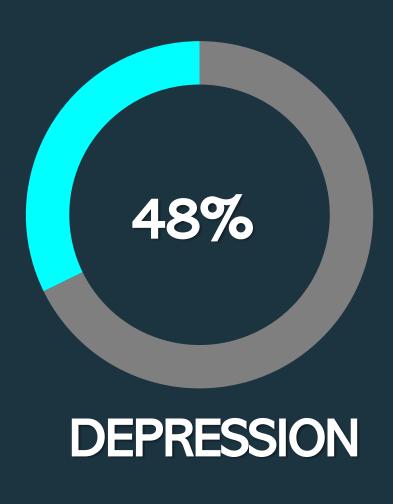
ADHD

GENERALIZED ANXIETY DISORDER

ANXIETY UNSPECIFIED IMPULSE CONTROL DISORDER

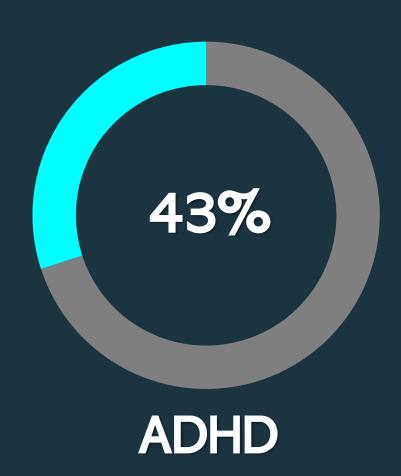
PTSD

PSYCHIATRY REDEFINED









Aggression and impulsivity

Daily worry, panic attacks

Fatigue, low energy

Low frustration tolerance

Anxiety with panic attacks

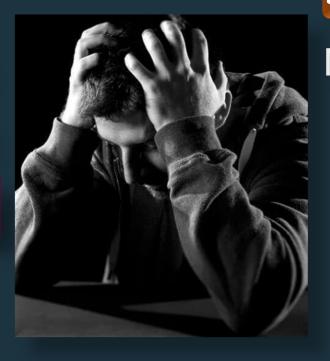
Inattention with impulsivity

Severe OCD, anxiety

Obsessive worries

OCD, rumination

PDisruptive bx, aggression



Anxiety, rumination, worry

Struggles with listening

Skin picking, restlessness

Mood dysregulation, rage

Difficulty focusing

Binge eating, compulsive exercise

Racing thoughts

OCD, rumination

Outbursts, impulsivity

Folate/B12 Food Allergies Thyroid Vitamin Deficiencies Vitamin D Mineral Deficiencies Zinc/Magnesium **LITHIUM HPHPA** Copper Acids Celiac Disease Heavy Metals Homocysteine **Fatty Acids** Infections Dysbiosis Cholesterol 13% **DHEA**

PSYCHIATRY REDEFINED

ONE SOLUTION...



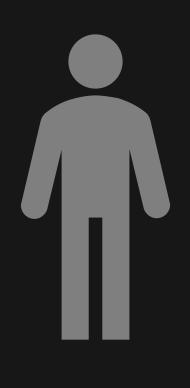
"JP": 21 year-old male

Presentations:

- Anxiety
- Inattention, auditory learning issues
- Trauma

Diagnoses:

ADHD; Anxiety (unspecified); Depressive Disorder



Symptom Duration:

5-7 years

History of Abx Use:

none reported

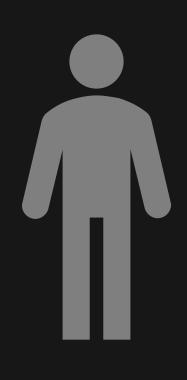
Birth: vaginal

3/9/18 OAT HPHPA level "193"

"JP": 21 year-old male

Recommendations:

- Multi-strain probiotics, 50 Billion CFU
- 1 cap twice daily w/meals
- Increase to 2 caps daily after two weeks



7/1/18 OAT

Patient states his mood is better overall... "less stressed, and less anxious"

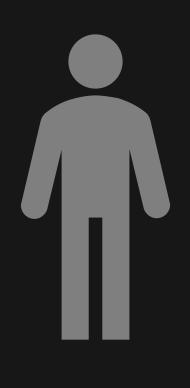
"JP": 21 year-old male

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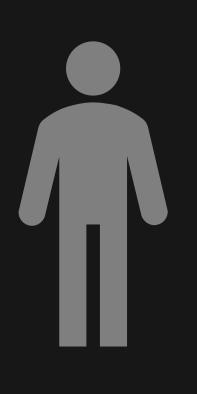
Birth: vaginal

3/9/18 OAT HPHPA level "193"

"CF": 26 year-old male

Presentations:

- Significant history of anxiety, irritability,OCD traits
- Multiple somatic complaints
- GI symptoms: steatorrhea, diarrhea



Diagnoses:

GAD, MDD, ADHD, OCD

Symptom duration: 14 yrs

History Abx use?: YES

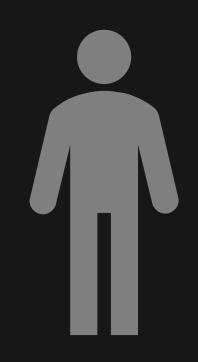
3/18/18 OAT HPHPA level "167"

PSYCHIATRY REDEFINED

"CF": 26 year-old male

Recommendations:

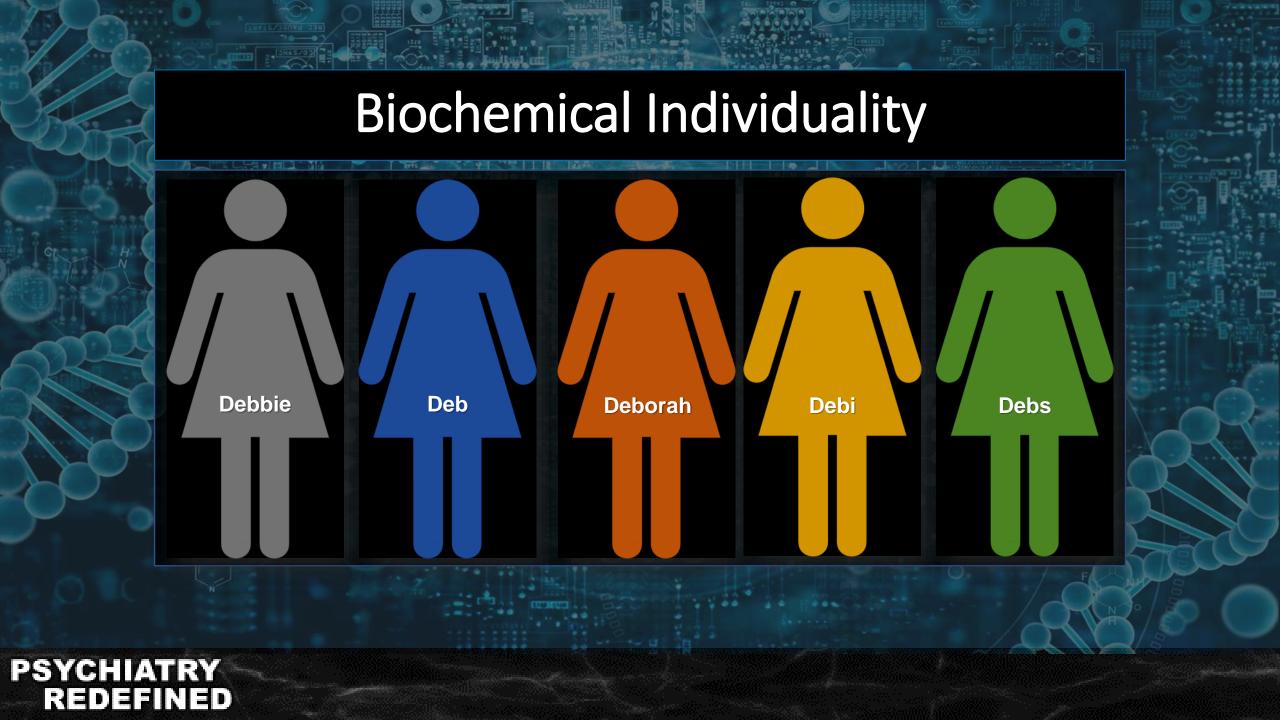
- Multi-strain probiotics, 50 Billion CFU
- 2 caps / day
- If tolerated, add 1cap/day in PM after meal



8/3/18 MOAT HPHPA level "61" 8/30/18 Follow Up:

Patient: "anxiety is low, I haven't had this level of anxiety in a long time."

- states GI symptoms nonexistent; NO physical anxiety symptoms





Depression

"Even after a few days' treatment, one is able to notice a difference in the appearance of the patient. The complexion is clearer and he wears a happier expression. The dry, furred tongue becomes moist and clean, and an increasing desire for food gradually appears. The feces increase in quantity, become softer, and of regular consistency, and the offensive smell diminishes."

The Treatment of Melancholia by the Lactic Acid Bacillus. (1) By J. George Porter Phillips, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital.

[July, 1910.]

Probiotics and Psychological Symptoms

2017 meta-analysis of 7 human RCTs

Measured depression, anxiety, and stress in healthy samples pre- and post-supplementation

2016 meta-analysis of 10 human RCTs

Measured depression & anxiety in healthy + clinical samples preand post-supplementation

Significant improvement in depression, anxiety, and perceived stress

Over 50% of studies concluded that interventions regulating intestinal flora helped reduce anxiety.



 2019 meta-analysis comparing interventions designed to alter gut microbiota + their effects on anxiety

• 21 studies, n = 1,503

Many Diagnoses...



HPHPA Treatment: Probiotics



High-dose probiotic (50 billion CFUs) for 2-3 months; 2-4 capsules daily

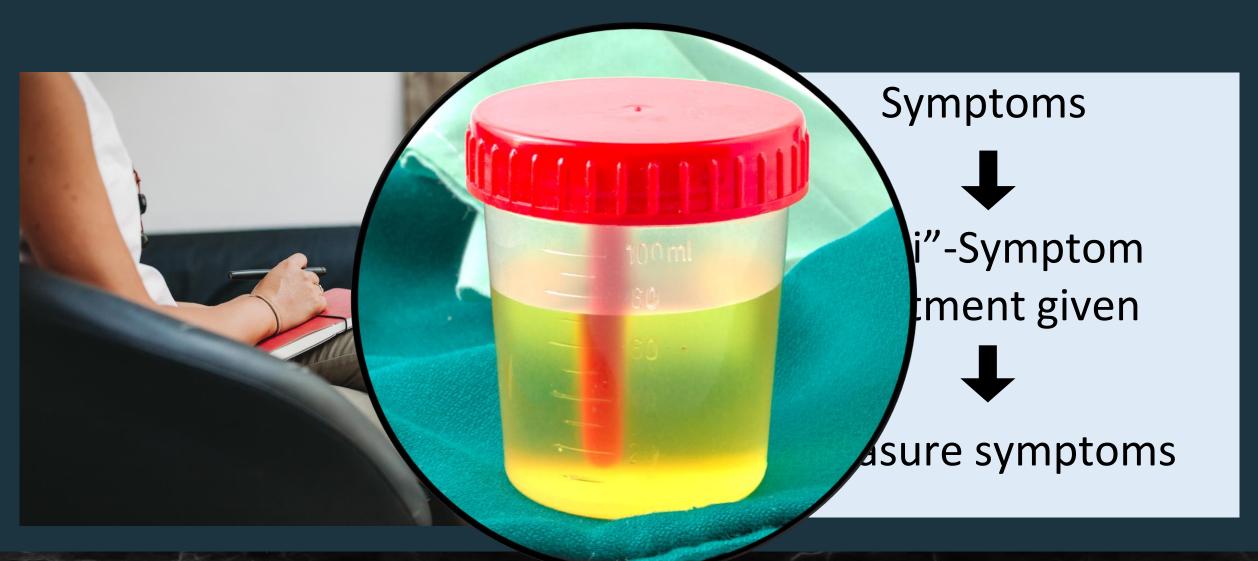
HPHPA Treatment: Vancomycin

30 days, in three 10-day courses: [1 day on, 2 days off]



- Day 1: Antibiotic/Probiotic
- Day 2: Probiotic
- Day 3: Probiotic
- Day 4: Antibiotic/Probiotic
- Day 5: Probiotic
- Day 6: Probiotic
- Day 7: Antibiotic/Probiotic
- Day 8: Probiotic
- Day 9: Probiotic
- Day 10: Antibiotic/Probiotic

Measureless Medicine?

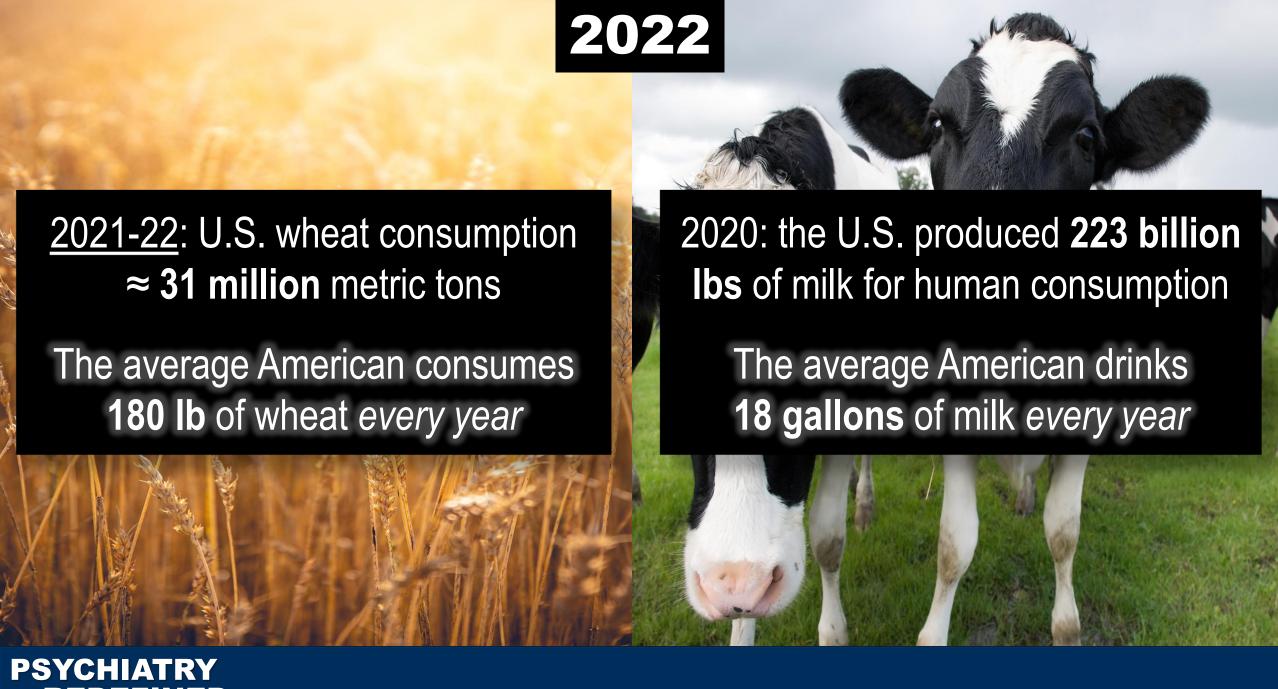


"The patient began eating flour when she was 16 years old. She recalls being depressed at that time but could not pinpoint specific thoughts that led her to eat flour, except that she enjoyed the taste of it. Currently, the patient associates eating flour with feeling relaxed and soothed.



...She currently eats from 1 to 2 lbs of flour daily, with a maximum of 4 lbs in one day."

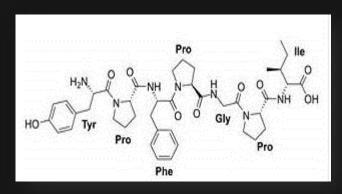




REDEFINED

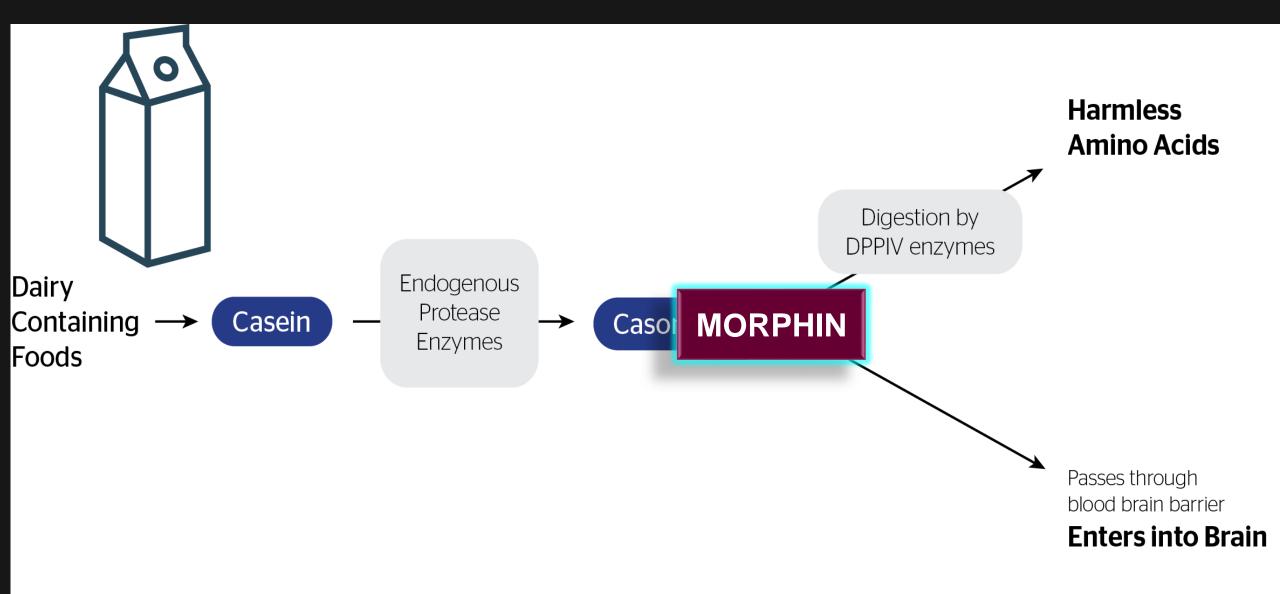


Casein — Casomorphin





→ Gluten → Gliadorphin



Understanding OPIOIDS**





Fun Fact: Your body makes its own opioids!

Like other signaling molecules, these endogenous (internallyproduced) opioids play critical roles in many biological processes

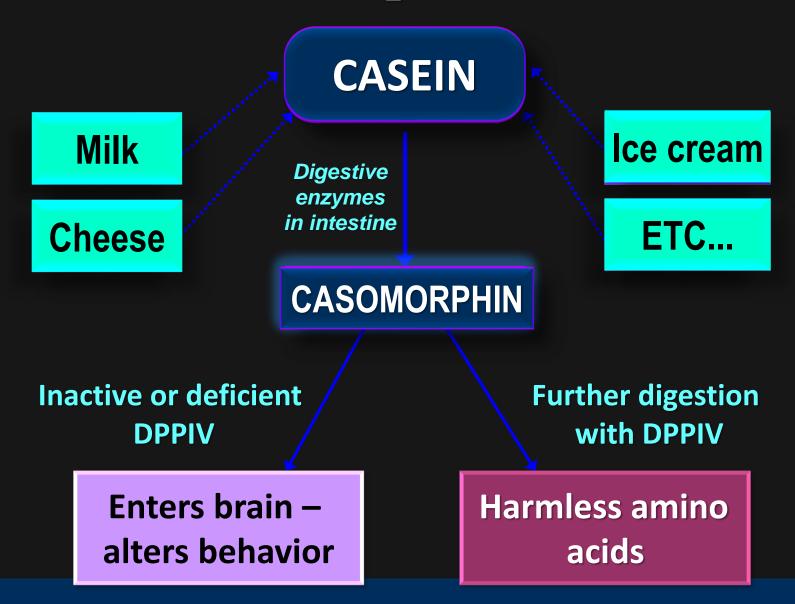
OPIOIDS & HUMAN BIOLOGY

ENDORPHINS:

opioid peptides produced internally by the body

EXORPHINS: opioid peptides produced from the incomplete digestion of foods originating outside the body

Formation of Opiates from Food







Dipeptidylpeptidase-4 (DPP-IV):

An enzyme responsible for breaking down complex proteins into smaller peptides that can be used by the body or further broken down into amino acids

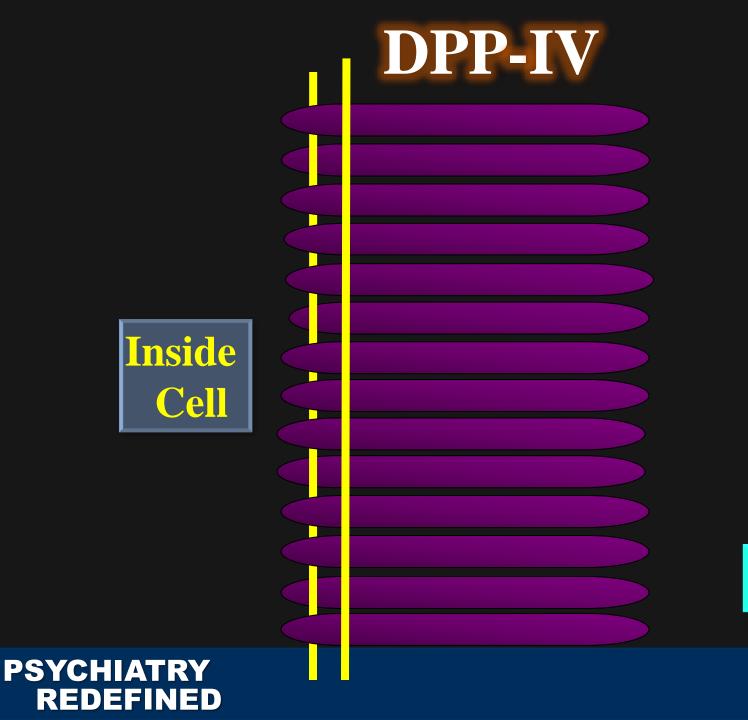
DPP IV
Activity

Gliadorphin: tyr-pro-gln-pro-gln-pro-phe

Casomorphin: tyr-pro-phe-pro-gly-pro-ile

N-terminal

Removes a dipeptide-two amino acids from the N-terminal end of peptides which have the amino acid proline or hydroxyproline in second position



Gluten, casein

Pancreatic enzymes

Gliadorphin Casomorphin

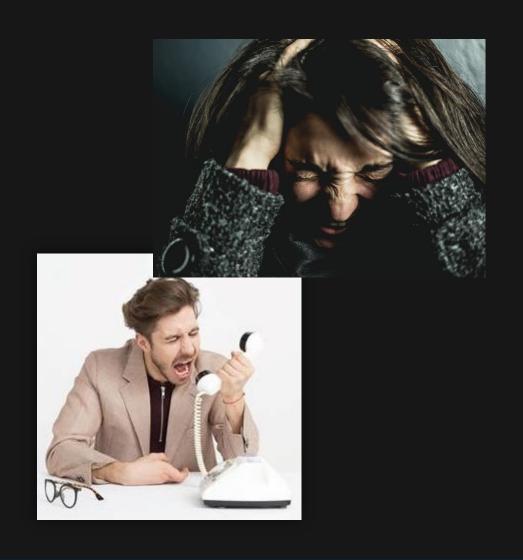
Dipeptide

Lumen of intestine

Morphine Variable Response







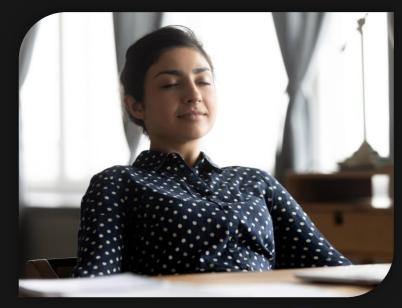
Symptoms of Elevated Casomorphin or Gliadorphin



Interse obsessions or interse obsessions or



Excessive consumption
of dairy / wheat to the



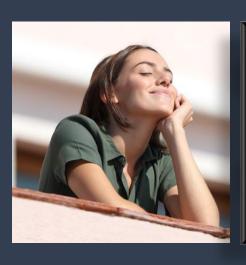
Intense feeling of

WITHDRAWAL IS COMMON

nterventions



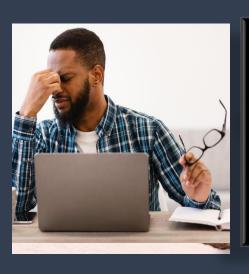
Clinical Indicators of High Dietary Exorphins



Strong sense of relief or calm after eating [bread / cheese / cookies ice cream / etc.]



Urge to eat dairy and/or wheat when stressed or irritable



Symptoms of withdrawal if haven't eaten dairy and/or wheat



Can't sleep without pre-bedtime ice cream / crackers / etc.



Take digestive enzymes containing dipeptidyl peptidase-IV (DPP-IV)

1-2 capsules at the start of a meal

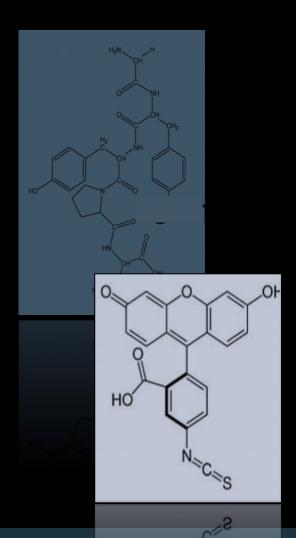
Incomplete gluten / casein digestion creates morphine-like molecules called **exorphins**

Casomorphin (from casein) and gliadorphin (from gluten) have proven opiate effects

Excess casomorphin and/or gliadorphin have been documented in patients with schizophrenia, autism, OCD, dyslexia, and other disorders

Urinalysis can detect these peptides; removal of gluten and/or dairy from the diet can improve psychiatric symptoms

DIETARY EXORPHINS



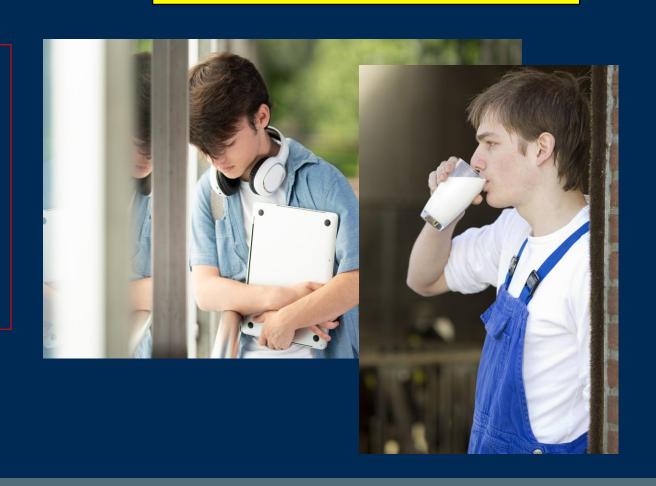


16-year-old

Drinks ½-1 gallon of milk per day

<u>Diagnoses:</u>

- ADHD
- Anxiety/Panic Disorder
 - Depersonalization –
 feeling out of his body





Screen Time & OCD Risk

- 9,208 children between the ages of 9 10 years
- Screen use, health outcomes tracked for 2 years



...and by 11% for every hour per day spent playing watching videos



Screen Time & Disruptive Behavior Disorders

Data from Adolescent Brain Cognitive Development (ABCD) Study (*n* = 11,875)

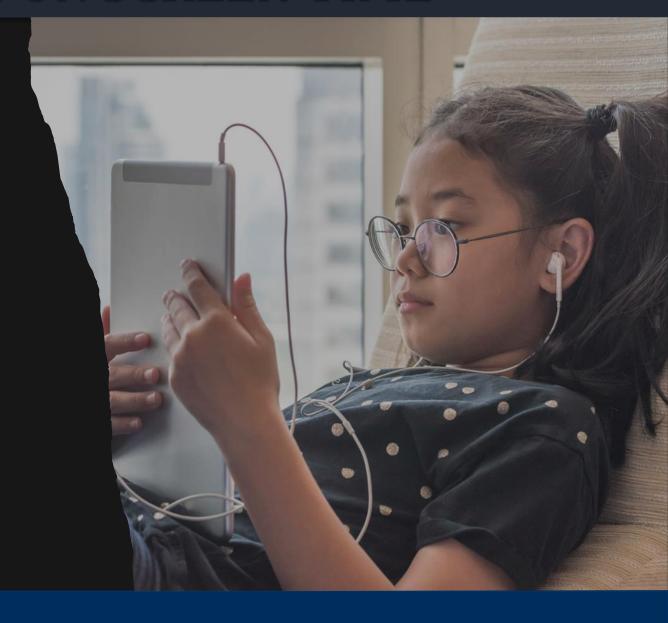
Analysis: baseline screen time ←→ CD or ODD diagnosis at 1 year



>4 hrs/day total screen time was associated with a higher prevalence of Conduct Disorder (69%) & Oppositional Defiant Disorder (46%)

CUTTING DOWN ON SCREEN TIME

The average U.S. child aged 8-12 years spends up to 6 HOURS PER DAY watching or using screens



FUNCTIONAL MEDICINE FOR MENTAL HEALTH

2023 CONFERENCE

OCTOBER 7-8, 2023



Day 1: The Impact of Ketogenic and Low Carb Diets on Mental Health

Day 2: Infections and Mental Health: Mold, Lyme, PANDAS, COVID, and Beyond

Featured speakers: Eric Westman, Terry Wahls, Georgia Ede, Iain Campbell, Robert Lustig, Bret Scher, James Greenblatt, Nancy O'Hara, Dan Kinderlehrer, Jaquel Patterson, Neil Nathan, and Mary Ackerley

All Details and Registration Coming Soon!

Other adds?

One diagnosis. . . Multiple Potential Causes / Etiologic Contributors

Neurotransmitter Cofactors

- Vitamin D
- Vitamin B12
 - Folate
- Vitamin B6

Infections / Immunologic

- HPHPA
- PANS / PANDAS
 - Lyme

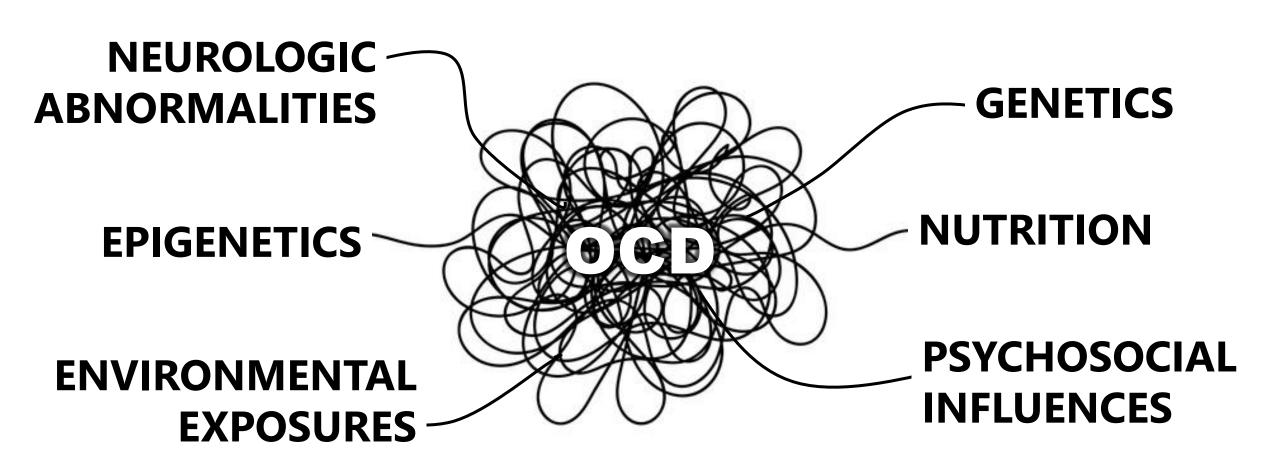
Nutritional /
Dietary

- Omega-3 deficiencies
- Neuropeptides (casomorphin, gliadorphin)

Misc.

- Trauma
- Pyroluria (B6, Zn deficiency)
 - Starvation

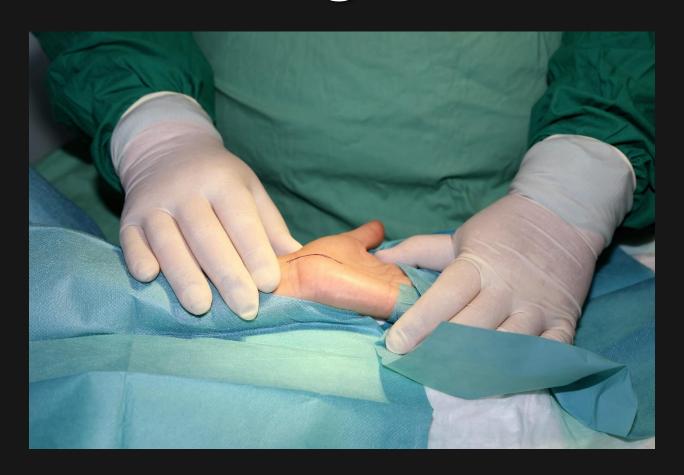
One diagnosis. . . Multiple Potential Causes / Etiologic Contributors



FOCUS ON ONE THREAD AT A TIME



Why I Should Have Been A Hand Surgeon



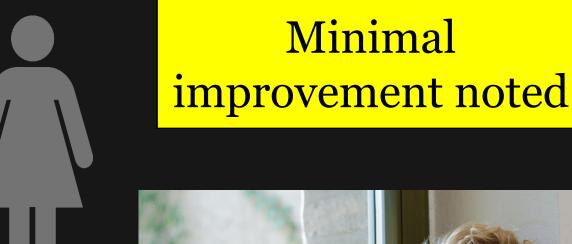
Previous Medication Trials:

- Celexa 10mg agitation
- Prozac 10mg aggressive thoughts of self-harm, attempted suffocation

! 40-lb weight gain on SSRI

Treatment:

inositol ½ tsp TID (4.2g/day)







One diagnosis. . . Multiple Potential Causes / Etiologic Contributors

Neurotransmitter Cofactors

- Vitamin D
- Vitamin B12
 - Folate
- Vitamin B6

Infections / Immunologic

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Nutritional /
Dietary

- Omega-3 deficiencies
- Neuropeptides (casomorphin, gliadorphin)

Misc.

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- Pyroluria (B6, Zn deficiency)
 - Starvation

PSYCHIATRY REDEFINED

OCD may be seen as a reflection of multiple errors in physiology

If we understand the causes, we will understand the cures.



We can do better.