

AN INTRODUCTION TO FUNCTIONAL MEDICINE FOR DEPRESSION

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How your
biochemistry
affects mood
and mind

MOOD DISORDERS: NIMH STATS

Mood disorders include: Major Depressive Disorder, Dysthymic Disorder and Bipolar Disorder

-Approx. 20.9 million American adults (9.5% of the US population 18 and older) in a given year have a mood disorder

-Depressive disorders often co-occur with anxiety disorders and substance abuse, and others

-In 2006, 33,300 people died by suicide in the US. 90%, related to depression and/or substance use

STANDARD OF CARE FOR DEPRESSION

-Psychotropic Medication

Antidepressants- Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

-Prozac, Zoloft, Paxil, Wellbutrin, Cymbalta etc.

-Psychotherapy

Addressing thoughts and feelings
variety of techniques-many schools of
thought in what helps alleviate emotional
Suffering. Good efficacy for a variety of therapies.



ANTIDEPRESSANT FACTS

-According to the CDC, **11%** of Americans over **12 years old** take antidepressant medication

-SSRIs are the second most prescribed class of drug after cholesterol lowering drugs, with **254 million** prescriptions written in the US in **2010**

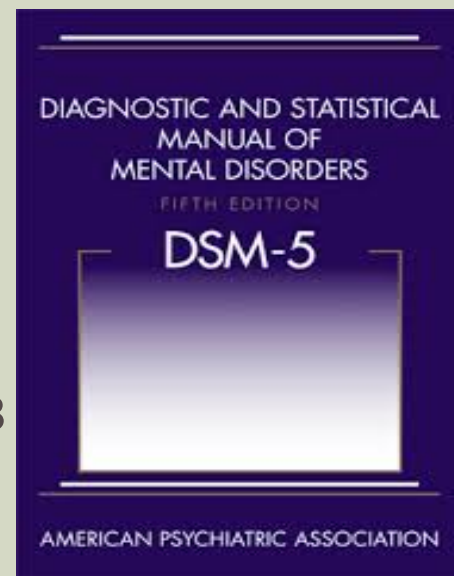


MENTAL HEALTH CARE AT A CROSSROADS

In 2013, just before the publication of DSM V, National Institute of Mental Health (NIMH) announced that it will no longer fund research based on the DSM symptom clusters because the manual provides no data about CAUSE of psychological problems.

“The weakness of the manual is it’s lack of validity. Unlike our definition of Lymphoma or AIDS, the DSM diagnoses are based on consensus about clusters of clinical symptoms, not any OBJECTIVE Laboratory measures....Patients with mental disorders deserve better.”

-Dr. Thomas Insel, Director of NIMH, April 2013



SSRI EFFICACY AND THE PLACEBO EFFECT

According to the research, how helpful are SSRIs?

In a 2010 meta-analysis of SSRI treatment of depression, including studies both published and unpublished, found the overall difference between antidepressants and placebo is NOT CLINICALLY SIGNIFICANT, except in cases of severe depression.

“In the majority of trials conducted by drug companies in recent decades, sugar pills have done as well---or better than—antidepressants. Companies have had to conduct numerous trials to get two that show a positive result, which is a minimum for FDA approval. The makers of Prozac had to run five trials to obtain two that were positive.”

Washington Post, 2002

“Placebo Effect” getting stronger over time.
Harder to show medication efficacy. Less new meds being developed.



FDA WARNINGS: SSRI

March 2004- FDA published a “Health Advisory” citing possible side-effects of SSRI meds including: “anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, hypomania, and mania”

September 2004- FDA issued a black box warning citing the connection between antidepressant use to suicide risk in children under 18

December 2006- FDA expanded to black box warning for suicide to include young adults under 25



SSRI: CONNECTION TO SUICIDE AND VIOLENCE

SSRIStories.com documents over 5,000 media reports that link SSRIs to violent, suicidal and homicidal acts since 2000.

Includes: at least 51 school shootings, 700 murders, over 200 murder-suicides and other acts including workplace violence

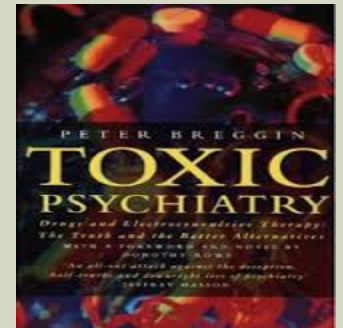
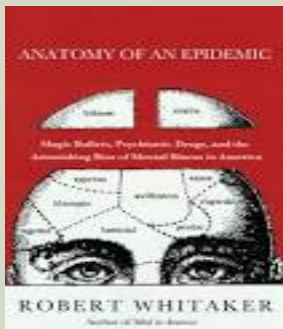
“In virtually every mass school shooting during the past 15 years, the shooter has been on or in withdrawal from psychiatric drugs,”

Lawrence Hunter, Social Security Institute

NEGATIVE LONG-TERM DANGERS OF PSYCHIATRIC MEDICATION

-In the last decade, many writers including Robert Whitaker in his groundbreaking book *Anatomy of An Epidemic* and Dr. Peter Breggin, in *Toxic Psychiatry* and others, have compiled data about the negative effects that all classes of psychiatric meds can have on the brain.

-Looking at longitudinal data and found medication (especially antipsychotics) seems to create chronic mental illness that may have been episodic illness leading to remission, had medications been used only during the psych. emergency



CURRENT STATE OF PSYCHIATRY

Business as usual for mental health treatment:

- Diagnosis based on symptoms, without testing to determine ROOT cause.
- Use medications as the main treatment tool that are often no more effective than placebo; That are dangerous for some in the short-term and and likely dangerous for many in the long-term

ARE THERE OTHER OPTIONS?



My desire to be well-informed is currently
at odds with my desire to remain sane.

IS IT TIME FOR A PARADIGM SHIFT IN PSYCHIATRY?

-The mainstream medical literature is FULL of peer reviewed studies that look at *underlying nutritional/biochemical factors* related to mental health issues.

-Laboratory testing is available to identify many of these **UNDERLYING FACTORS** so that they can be addressed using nutrition and/or medicine

Why doesn't psychiatry pay attention to the findings of it's own literature and the literature of the other medical disciplines in regards to factors influencing mental health??

FUNCTIONAL MEDICINE

“Functional medicine is the future of conventional medicine- available now. *It seeks to identify and address the ROOT cause of disease*, and views the body as one integrated system, not a collection of independent organs divided up by medical specialties. It treats the whole system, not just the symptoms”

- Mark Hyman, MD

Chairman, Institute for Functional Medicine

Functional Medicine may be just what's needed to expand treatment options beyond reliance of psych meds!

FUNCTIONAL MEDICINE FOR MOOD DISORDERS

Common biochemical issues related to depression:

- Neurotransmitter deficiencies
- Vitamin and Mineral Deficiency (Vit. D, B12, B6, Folic Acid, Zinc, Magnesium etc.)
- Gut issues (Bacterial and Yeast Overgrowth, parasites, celiac etc.)
- Food Allergies
- Systemic Inflammation

Functional Medicine would look to identify the UNDERLYING CAUSE each patient's depressive symptoms

Moving towards a system of **INDIVIDUALIZED MEDICINE**
Knowing the cause → specific treatment

PSYCHIATRY'S CURRENT FOCUS: NEUROTRANSMITTERS

Neurotransmitters: Chemical messengers that facilitate communication between brain cells

-Low level (and sometimes high) can cause mental health symptoms

Almost all psychiatric medications target one or more of three key neurotransmitters: 1) serotonin, 2) dopamine/norepinephrine, and 3) GABA

If a person has low levels of Serotonin, why is that the case?

Are there ways beyond medications to understand and address neurotransmitter issues?

ONE THING FOR SURE DEPRESSION IS NOT A PROZAC DEFICIENCY



CASE: JANE

- 42 year old female
- Longstanding depression, anxiety, fatigue
- Years of therapy and many psych meds over years with modest improvement
- Pt. eats a clean "mental health diet"- moderate high quality protein, relatively low carbohydrates and good quality fats (little processed foods, caffeine, sugar, or junk food)

Testing performed to answer the question why is Jane not getting better with med tx. :

Amino Acid Test:

Measures levels of breakdown product of protein in blood plasma, that are precursors to neurotransmitters

-Serotonin can ONLY be made from the amino acid Tryptophan

Organic Acid Test:

Urine test that measures many systems in the body including the levels of serotonin, dopamine and Norepinephrine metabolites

Jane Had low levels of multiple amino acids and low levels of breakdown products of Serotonin (5HIAA)

-This suggested that her digestion was weak and she was not able to breakdown proteins into amino acids to make serotonin (so that the meds could work)

OUTCOME FOR JANE

Treatment:

Free Form Amino Acid Blend between meals (including tryptophan, precursor to serotonin)

Digestive enzymes and Hydrochloric Acid (HCL, stomach acid) to break down proteins into needed amino acids

Outcome:

Within 2 weeks, her depressive symptoms had lessened by 75% and she was able to wean off of her medication.

SEROTONIN PRODUCTION

**Protein (from food)---> L-Tryptophan
-->5htp---> Serotonin --->Melatonin**

With the help of HCL, digestive enzymes, vitamins and minerals: including B6, Folate (B9), and zinc required to facilitate the enzymatic conversions (represented by arrows)

IMPORTANCE OF GASTRIC ACID (HCL)

The only way protein can only be broken down into amino acids (for neurotransmitter synthesis) is by digestive enzymes which are tuned on by Hydrochloric Acid in the stomach

-HCL TRIGGERS THE ENTIRE DIGESTIVE CASCADE

-Low HCL → poor digestion of proteins → low amino acids →

LOW NEUROTRANSMITTERS

Leading to:

-Depression

-Anxiety

-Other MH symptoms

VITAMIN AND MINERAL COFACTORS

Without any one of the needed cofactors neurotransmitter production will stop!

B6, Folic Acid, Zinc, Vit C, Copper

-Deficiency in any can cause depression

Commonly depleted as a result of dietary deficiency (junk food diet), medications (including psych meds), genetic mutations, and environmental factors like heavy metals, etc.

Vitamins and minerals important for MH but not cofactors:

Vitamin D, Magnesium, B12, Lithium

PSYCH SYMPTOMS OF B12 DEFICIENCY

- Irritability
- Apathy
- Personality changes
- Memory Loss
- Hallucinations
- Violent Behavior
- Depression
- Dementia

B12 DEFICIENCY SO COMMON, ESPECIALLY IN THE ELDERLY and vegetarian/vegans, BUT RARELY TESTED FOR!

“Lack of understanding of B12 is one of the greatest tragedies of modern medicine!”

-Dr. James Greenblatt, Integrative Psychiatrist

How many psychiatrists test for B12 levels?

FOLIC ACID AND DEPRESSION

Low Folate (B9) associated with:

- Increased incidence of depression
- Poor response to antidepressants
- High relapse rate for mental health patients

Supplementation with L-methylfolate (activated form of Folate) can enhance effectiveness of antidepressants

**HUNDREDS OF STUDIES SUPPORTING THE RELATIONSHIP
BETWEEN FOLATE AND DEPRESSION**

SERUM FOLATE AND RELAPSE

After 28 weeks of treatment with 40mg/day Prozac:

Relapse rates for patients with low folate (<2.5ng/mL) was **42.9%**

Relapse rates for subjects with normal folate was **3.2%**

WHY ISN'T IT STANDARD PRACTICE TO TEST EVERY DEPRESSED PATIENT FOR FOLATE LEVELS WITH A SIMPLE BLOOD TEST?

Papakostas GI et al. *J Clin Psychiatry*, 2004; 65: 1090-1095.

MTHFR AND DEPRESSION

Gene mutation that affects enzyme, Methyl-Tetra-Hydro-Folate Reductase (MTHFR)-needed to process folate into the activated form, called *L-Methyl Folate*, which is a co-enzyme in neurotransmitter production.

Up to 20% of the population have an MTHFR gene polymorphism:

Patients who have MTHFR C→T genotype have a 1.3 x greater chance of developing depression

The odds of having the T/T genotype is 2x more likely in depressed versus normals

Supplementation with L-methylfolate provides the body with a form of folate that skips the enzymatic/genetic problem in people with have either of these genotypes

Lewis S.J. et al. Mol Psychiatry. 2006; 11(4): 352-60.

ZINC AND DEPRESSION

Levenson, C. Nutritional Reviews, Vol. 11, No. 6, 694-700

-Low serum Zinc linked to Major Depression

-Zinc treatment has been shown to have an antidepressant effect (as it is a cofactor in serotonin and dopamine synthesis)

Swardfager W et al. Biol Psychiatry 2013 June

-Meta-analysis of 17 studies, 2400 subjects, showed low serum zinc correlated to depression in peripheral blood

Siwek et al. J Affect Disord 2009;118(1-3); 187-95.

-12 week study, 60 subjects w/ depression, previously unresponsive to antidepressants- took 25mg Zinc or placebo in addition to Imipramine—Zinc significantly reduced depression

LITHIUM

-Trace mineral (not a drug) essential for mental health and used in psychiatry at very high doses for mood stability/depression

-Very low levels (measured in hair) found in autistic children and their mothers.

-Levels of lithium in the public water correlates with depression and violence, so places that have high lithium in the water have lower levels of depression and crime, and vice versa

Mechanism of action:

-Lithium helps with brain inflammation by facilitating the use of the Essential Fatty Acids, and is needed to transport folate and B12 into the brain

Schrauzer GN, et. Al. Lithium in scalp hair of adults, students and violent criminals. Effects of supplementation of Lithium with Vitamin B and other trace elements. Biological Trace Element Research, 1992 Aug 34(2): 161-76

INFLAMMATION AND DEPRESSION

Scientists are beginning to hypothesize that depression is actually a “side effect” of chronic low grade inflammation of the body and brain---caused by chronic immune activation from a variety of sources: like physical injury, infection, allergies, or toxicities.

“Sickness Behavior” as an immunological model of depression

- Lethargy
- Decreased concentration
- Decreased interest in pleasurable things
- Malaise
- Decreased appetite
- Weakness

Sounds like depression doesn't it?

MEASURING INFLAMMATION (CRP)

C-Reactive Protein (CRP)- is a blood protein that has become a easy to measure lab marker for systemic inflammation

Depression has been associated with Elevated CRP levels

-508 healthy adults, data collected at baseline and quarterly intervals over 1 year

-Individuals with higher depression scores have higher CRP.

How many psychiatrists test for CRP?

CYTOKINES AND DEPRESSION

Cytokines- chemical messengers involved in immune response. Some are pro-inflammatory and others anti-inflammatory

-Research has shown that pro-inflammatory cytokines were significantly higher in patients with depression and anti-inflammatory cytokines were significantly lower.

-Zoloft led to a decrease in some pro-inflammatory cytokines and an increase in anti-inflammatory cytokines.

What if part of the efficacy of SSRIs is in affecting the immune system and targeting inflammation?

INFLAMMATION AND DEPRESSION

Pro-inflammatory cytokines activate an enzyme called IDO (indoleamine 2,3-dioxygenase) that degrades L-tryptophan and Serotonin

Tryptophan → 5HTP → **Serotonin**

Leads to less tryptophan available to make serotonin and less serotonin in the brain → depression

-One explanation for low levels of serotonin in depression

SOURCES OF INFLAMMATION

- Standard American Diet (SAD)
- Environmental toxins
- Low grade infection (candida, Lyme)
- Food and environmental allergies
- Stress
- Dysbiosis
- Nutritional def.
- Inadequate sleep

If Inflammation is a KEY factor in depression and there are multiple causes for inflammation, proper identification and treatment is essential---*this is the strength of functional medicine*

-If we identify the CAUSE we can treat the problem!

NATURAL TOOLS FOR TREATMENT OF DEPRESSION CAUSED BY INFLAMMATION

Curcumin (active ingredient in tumeric) has been shown to be as effective as prozac in treating depression--likely because of its anti-inflammatory properties.

Phytother Res. 2014 Apr; 28(4):579-85

Omega 3 Fish Oil- Dr. Stoll from Harvard has found high dose fish oil (more than 10g/day) is as effective as SSRIs in the treatment of depression

Omega 3 connection by Stoll, A 2001

Lithium- Recent research has suggests that lithium reduces brain inflammation by adjusting the metabolism of the omega 3 fatty Acid DHA

Basselin et al. Lithium modifies brain arachidonic metabolism in rat lipopolysaccharide model of neuroinflammation. Journal of Lipid Research, 2010; 51 (5) 1049.

FOOD ALLERGIES

-IgE—Common Food Allergies- Diagnosed by MD Allergists- cause histamine reaction directly after ingestion- know you have it because the allergic response is big and immediate

-IgG- Delayed food sensitivity- exposure one day then reaction a few days later- hard to diagnosis without testing- more important marker for chronic illness and mental health symptoms

Most common IgG sensitivities to wheat, dairy, corn and soy

IgG sensitivities are often the result of “leaky gut” where intact proteins are able to get into the blood stream and are responded to like foreign invaders, taxing the immune system

IGG FOOD SENSITIVITIES LINKED TO MENTAL HEALTH SYMPTOMS

High IgG antibodies to wheat found in 87% of patients with autism, and 86% with schizophrenia. High antibodies to casein (diary) found is 90% of patients with autism and 93% with schizophrenia. Gluten and casein free diet caused significant improvements in 81% of patients with autism and 81% with schizophrenia

R Cade et al. Autism and schizophrenia: Intestinal disorders. Nutritional Neuroscience 3: 57-72, 2003.

We can look into allergies using IgG Food Allergy Testing which looks at 93 most common allergens and eliminate those foods from the diet.

CANDIDA ALBICANS

-A yeast organism that resides in the GI tract. Can become overgrown with overuse of antibiotics, junk food diet, stress, birth control pill etc.

Neurological/psychiatric issues where yeast may be a factor:

Schizophrenia

Alzheimer's

Fibromyalgia

Chronic Fatigue

Depression

Seizures

CANDIDA RESEARCH

84% of patients with Chronic Fatigue Syndrome (CFS) had clearing of symptoms after antifungal treatment-only 12 of 685 on disability stayed on disability

Percentage of subjects experiencing common symptoms:

Depression 94%

Sleep issues 94%

Jessop C. Chronic Fatigue Syndrome Conference, April 15, 1989, San Francisco, CA.

Could Depression and Chronic Fatigue Syndrome be a candida infection in some people?

CLOSTRIDIA (C. DIF)

-A bacteria common in the GI tract that at abnormally high levels can cause psychiatric problems

Mechanism- Clostridia inhibits the enzyme dopamine-beta-hydroxylase which is responsible for converting dopamine into norepinephrine

-High levels of dopamine are linked to severe mental illness including autism and schizophrenia

-Clostrida can be measured with a simple urine test

CAN ANTIBIOTICS TREAT AUTISM?

-Small study of 11 autistic children given Vancomycin

-Significant improvements were noted in several children. The researchers stated, "These results indicate a possible gut flora-brain connection which warrants further investigation"

J. Child Neurol 2000 Jul; 15 (7): 429-35.

Antibiotics may be able to treat autism if the underlying biochemical "glitch" is Clostridia!!

TAKE AWAY

-Mood Disorders (and all mental health symptoms) can have numerous biochemical antecedents and often more than one.

-It is impossible to tell what the ROOT cause of any mental health diagnosis based on symptoms alone.

--Though some tests are specialized, many are easily obtained every MD---think Zinc, Folic Acid, B12, Vit D, Thyroid, CRP

-My challenge to you is to educate yourself so you can educate and advocate for your clients as they work to unravel their mental health challenge—IF YOU DON'T WHO WILL???

FOR MORE ABOUT FUNCTIONAL MEDICINE FOR DEPRESSION

The Ultra Mind Solution
Mark Hyman, MD

Depression Free Naturally
Joan Matthews Larson, Ph.D.

**The Breakthrough Depression
Solution** James Greenblatt, MD



Web Site: *AlternativeMentalHealth.com* (clearinghouse of info on integrative treatments for mental health)

Great Plains Laboratory (greatplainslaboratory.com)

INTEGRATIVE DEPRESSION SOLUTIONS

For more information on Dr. Friedman's work on uncovering the root causes of depression, follow him at:

IntegrativeDepressionSolutions.com and

Facebook: www.facebook.com/IntegrativeDepressionSolutions/