Malnourished Minds
A Functional Medicine Approach to Cognition, Memory and Mood*

Dietitians in Integrative and Functional Medicine
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James Greenblatt, M.D. † has dedicated his professional career to integrative psychiatry. He has worked with thousands of children, adolescents and adults, employing both medical and complementary therapies to support mental health and well-being. Dr. Greenblatt is dually board-certified in child and adult psychiatry. He received his M.D. and completed his adult psychiatry residency at George Washington University in Washington, D.C., and completed a fellowship in child and adolescent psychiatry at Johns Hopkins Medical School. In addition to serving as the chief medical officer and vice president of medical services at Walden Behavioral Care in Waltham, Massachusetts, Dr. Greenblatt is a clinical faculty member in the Department of Psychiatry at Tufts University School of Medicine.

†Dr. Greenblatt has been retained as a medical consultant in advising Pure Encapsulations. He is compensated for this service.
1. Describe how mineral cofactors are involved with brain function and contribute to the pathophysiology of depression.

2. Identify clinical symptoms associated with deficiencies in zinc, magnesium, copper, and lithium.

3. Determine safe therapeutic ranges for trace mineral supplementation.
Depression is NOT a Prozac deficiency.
Diagnosis and Treatment

General Medical Treatment:

- Symptoms
  - Measure Physiology
    - "Anti"-physiology treatment
  - Measure physiology and symptoms

Psychiatric Treatment:

- Symptoms
  - "Anti"-Symptom treatment given
  - Measure symptoms
Polypharmacy Highway

40% Relapsed within 15 weeks

20% Incapacitated or committed suicide

66% Residual symptoms
Have You Missed Your Dose Today?

*WARNING* Side Effects:
Anxiety, Weight Gain, Sedation
Psychosis, Paranoia, Violent
Thoughts Violent Actions, Suicidal Thoughts, Suicide
Criminal Behavior, Sexual Dysfunction...
ETC.

Effexor withdrawal
Advertise the truth!

Can bring you to your knees!
Toxic Psychiatry

Doesn’t Help Our Patients
A new model – Functional Psychiatry

Integrating nutritional biochemistry may enhance progress and maintain health.

**Urine Test**
- Opiate peptides
- HPHPA
- Yeast
- Organic Acids
- Amino Acids

**Hair Test**
- Copper
- Zinc
- Lead
- Magnesium
- Lithium

**Blood Test**
- Amino Acids
- Food Allergies
- Hormones
- Fatty Acids
- Vitamins
- Trace Minerals

**Saliva Test**
- Genetics
- Hormones
THE ZEEBRA Approach

T – Take Care of Yourself – stress, sugar, sleep
H – Hormones
E – Exclude – Celiac, allergies

Z – Zinc and Other Minerals
E – Essential Fatty Acids - cholesterol
E – Exercise and Energy
B – B Vitamins & Other Vitamins
R – Restore - Microbiome
A – Amino Acids and Protein
Trace Minerals and Depression

1. Magnesium
2. Zinc
3. Copper
4. Lithium
Serotonin and melatonin biosynthesis

L-tryptophan from diet → 5-HTP → Serotonin

Amino Acid Decarboxylase (AADC) with Zinc

Support the actions of existing serotonin

Magnesium, Chromium, Lithium

Zinc

Serotonin → Melatonin with Zinc
Zinc in the brain

- A positive and essential relationship between zinc status and mental health has been known since the 1920s.
- Practically all enzymatic reactions in the brain require zinc.
- Maintains protein structure.
- Involved in gene expression.
- Plays an important role in the hippocampus.
- Needed for the synthesis and function of neurotransmitters such as serotonin and dopamine.
All digestive enzymes, protein, fat and carbohydrate substrates, are Zinc dependent.

Zinc deficiency influences the activity of carbonic anhydrase (CA) a prequel for Hydrochloric Acid.
Zinc in Depression

- Seventeen studies, measuring peripheral blood zinc concentrations in 1643 depressed and 804 control subjects, were included.

Depression is associated with a lower concentration of zinc in peripheral blood.

Zinc Deficiency

Depression

Attention difficulties

Decreased appetite

Meat avoidance

Amenorrhea

Inhibition of EFA metabolism

Decreased taste

Changes in opioid receptors

Vulnerability to stress

Decreased pancreatic enzymes

Change in brain chemistry

Decreased melatonin

Nausea

Bloating GI discomfort

Malnourished Minds
“I started my vegetarianism for health reasons, then it became a moral choice, and now it’s just to annoy people.”
Depression

- Zinc
- Zinc Supplementation
- Zinc Augmentation

- Lab Testing not always Accurate
- ALKPHOS/ WBC
- Think Vegan – Bikram Yoga – Picky Eaters
- Copper Supplements
Copper assessment through hair analysis

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<th>NUTRITIONAL ELEMENTS</th>
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Ca: Calcium; Mg: Magnesium; Na: Sodium; K: Potassium; Cu: Copper; Zn: Zinc; P: Phosphorus; Fe: Iron; Mn: Manganese; Cr: Chromium; Se: Selenium; B: Boron; Co: Cobalt; Mo: Molybdenum; S: Sulfur; Sb: Antimony; U: Uranium; As: Arsenic; Be: Beryllium; Hg: Mercury; Cd: Cadmium; Pb: Lead; Al: Aluminum.
Copper

• Too much copper can deplete zinc
• Zinc depletion can increase copper levels
• Excess copper can result from:
  • Excess estrogen
  • Use of prescription medications containing copper
  • Smoking
  • Too much copper in drinking water
  • Manganese deficiency
• Broad Spectrum Multivitamin Mineral Supplementation

Symptoms
• Fatigue
• Hair Loss
• Celiac Disease

Copper Summary and Clinical Pearls

- Low or High?
- High Copper – Irritability and Depression
- Low Copper – Depression and Motivation
- Hair most reliable
- Ceruloplasmin/Copper Helpful
Magnesium: Mineral for the Mind

- **1921**: First study documented significant mood benefits in 220 out of 250 patients receiving a supplement.

- Studies over the last 50 years: Magnesium repletion is associated with:
  - Positive changes in mood
  - Healthy eating behavior
  - Healthy stress responses
  - Sleep quality
  - Better efficacy of other modalities
• Studies show inverse relationships between serum cortisol and magnesium

• The relationship between stress and magnesium is reciprocal
  – Magnesium maintains healthy responses to stress
  – Stress affects the body’s retention of magnesium
A cross-sectional, population-based data set (National Health and Nutrition Examination Survey) was used to explore the relationship of magnesium intake and depression in 8894 US adults (mean age, 46.1 years) from 2007 to 2011.

Researchers found significant association between very low magnesium intake and depression, especially in younger adults.

Dietary magnesium intake and the incidence of depression: A 20-year follow-up study

- 2320 Eastern Finnish men (42–61)

- Dietary magnesium intake had a statistically significantly decreased risk of getting a hospital discharge diagnosis of depression.

*Journal of Affective Disorders Volume 193, 15 March 2016, Pages 94–98*
Magnesium supports GABA receptor function*

- Magnesium supports the calming actions of GABA interacting with its receptor

- Patients with higher magnesium levels exhibit healthy amounts of serotonin in the cerebrospinal fluid
Ketamine and Depression

NMDA Receptor

Magnesium and Ketamine act as NMDA receptor Antagonists.
Selecting the ideal magnesium product

- 125-300 mg magnesium glycinate per meal and at bedtime provides clinically significant mood benefits

- 200-300 mg magnesium glycinate or citrate before bed supports sleep onset and duration through the night

Magnesium (citrate)
Magnesium (aspartate)
Magnesium (glycinate)
Magnesium (Threonate)
Magnesium (oxide)
Magnesium Clinical Pearls

- Hard to detect in laboratory testing
- RBC Magnesium helpful
- Hair Test Helpful – Ca/Mg ratios

Clinical Symptoms

- Constipation
- Anxiety
- Irritability
- Insomnia
The History of Lithium

• 1817: Lithium (from Greek “lithos” or stone) was first discovered as a mineral element
• 1929: Lithium citrate was used as an ingredient in soft drinks
• 1949: Australian psychiatrist John Cade discovered powerful effects on mood
• 1970: Lithium carbonate became available as a drug in the U.S.
• 2002: Review in the Journal of the American College of Nutrition suggested a daily dietary recommendation of 1,000 mcg

http://madgirlslament.com/2015/06/
Lithiated Lemon-Lime Soda

Lithiated products were common in the early part of the 20th century and were believed to be healthful and help with hangovers.

7 Up contained lithium citrate from 1929 until 1950.
‘I Don’t Believe in God, but I Believe in Lithium’
Side Effects of Lithium

**Lower Doses**
- Drowsiness
- Hand tremors
- Frequent urination
- Thirst
- Nausea
- Vomiting

**Higher Doses**
- Kidney damage
- Muscular weakness
- Interferes with thyroid function
- Poor coordination
- Ringing in the ears
- Blurred vision
Dosage

• “The dosage makes it either a poison or a remedy.”

  - Paracelsus

  Swiss-German physician, physician, botanist, alchemist, astrologer

  (1493-1541)
Two remarkable powers of lithium

1. Protecting neurons from damage

2. Alleviating existing damage by stimulating new neuronal growth
• Examined 27 Texas counties from 1978-1987
• Examined lithium levels in tap water in the 18 municipalities in Japan in relation to the suicide standardized mortality ratio
• Austrian study with nationwide sample of 6460 lithium measurements

Overall suicide rate and the suicide mortality ratio were inversely associated with lithium levels

Lithium and Suicide

- Study examined life-threatening or fatal suicidal acts in over 300 bipolar patients

- On lithium: rate of suicides and attempts decreased nearly 7-fold

- Off Lithium: suicidal acts increased 14-fold above rates found during treatment

First year off lithium: suicide rate rose 20-fold

Lithium for the Prevention of Suicide

Meta-analysis of evidence on effect of lithium on major depressive disorder (MDD)

Overall risk of suicides and attempts was 88.5% lower with lithium treatment than without

Low Dose Lithium in Practice

• Irritability
  - 4 year old
  - 17 year old
  - 43 year old

• Road rage
  - 43 year old

• Substance abuse
  - 14 year old
  - 28 year old
  - 54 year old

• Domestic violence
  - 32 year old

• OCD & Anxiety
  - 43 year old

• Anorexia Nervosa
  - 15 year old

• Lyme
  - 38 year old

• Autism
  - 6 year old

• ETC

Lithium Orotate
1-30 mg
Deficiency

- Infertility
- Aggressive behavior
- Diminished impulse control
- Depression
- Increased suicide risk

Courtesy of Laura Mischley
Pharmacological use

- Bipolar disorder
- Depression
- Seborrhea (topical)
- Dystonia?

Side Effects
- Weight gain
- Hypothyroidism
- Hyperparathyroidism

Courtesy of Laura Mischley
Toxicity

- Increase blood Ca
- Gastrointestinal complaints
- Tremor
- Confusion/ somnolence
- Seizure
- Death

Serum concentrations: 1.5-3 mEq/L
Courtesy of Laura Mischley
Maintenance

- Cell growth
- Electrolyte regulation across neuron membranes
- Neurorepair
- Regulate autophagy

Courtesy of Laura Mischley
• Comparison of 66 elderly patients with Bipolar Disorder who were on chronic lithium therapy and 48 similar patients without recent lithium therapy

• Alzheimer's disease was diagnosed in 3 patients (5%) on lithium and in 16 patients (33%) who were not on lithium (P<0.001)

Significant neurocognitive support at a very low dose

• Clinical study evaluated the effect of a microdose of 300 µg, administered once daily in aging patients requiring cognitive support, for **15 months**

• The lithium group maintained performance in a mental state examination test, compared to the control group whose scores declined

• Differences became statistically significant at 3 months and progressively increased throughout the study

Lithium and Alzheimer's Disease

**Inhibition of glycogen synthase kinase-3 (GSK-3)**

GSK-3 stimulates tau and beta amyloid production
Increased GSK-3 in Alzheimer's

**Inhibition of inositol monophosphatase-3 (IMP)**

IMP stimulates recycling and increases accumulation of beta amyloid and tau proteins
Lithium stimulates BDNF

- BDNF in the hippocampus, cortex, and other areas vital to learning, memory, and higher thinking
- High BDNF gene expression is associated with positive mood

BDNF

- Dendritic branching
- Robust cellular structure
BDNF activators and inhibitors

- Magnesium
- Zinc
- Lithium
- Probiotics

- Exercise
- Caloric Restriction

- Refined foods
- HPA activation
- Inflammation

Memory
Learning
Mood
LITHIUM—A SIMPLE METAL AND THE OLDEST DRUG IN PSYCHIATRY—MIGHT PROTECT THE BRAIN AGAINST MENTAL ILLNESS, ALZHEIMER’S, AND OTHER DISEASES.

ONE PROBLEM: THERE’S NO PROFIT IN IT.

BY PAUL RAEBURN; ADDITIONAL REPORTING BY MONICA HEGGER
“What if micro-dose lithium were again part of our standard nutritional fare? What if it were added back to soft drinks or popular vitamin brands or even put into the water supply? The research to date strongly suggests that suicide levels would be reduced, and even perhaps other violent acts. And maybe the dementia rate would decline. We don’t know because the research hasn’t been done.”
Clinical Symptoms
- Irritability

Psychiatric Diagnosis
- A-Z

*Family History
- Substance Abuse
- Mood Disorders
- Suicide Attempts
Depressogenic Complexity

Monoaminergic System:
- Zinc
- Magnesium
- Calcium
- Chromium
- Lithium

Glutamatergic System:
- Zinc
- Magnesium
- Iron

Depression:

GABAergic System:
- Zinc
- Magnesium

HPA axis:
- Zinc
- Magnesium

Marcia Angell, MD, a former editor of the New England Journal of Medicine reviewed three books that highlight the explosion of antidepressant use in our society and questions the effectiveness of antidepressants.

“If psychoactive drugs are useless...why are they so widely prescribed by psychiatrists and regarded by the public and the profession as something akin to wonder drugs?”
Mental Illness may be seen as a reflection of multiple errors in physiology. If we find the Causes, we may find the Cures.
THANK YOU