Targeted Nutrients for the Brain

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Faculty/Presenter Disclosure

- **Faculty**: Hyla Cass M.D.

- **Relationships with commercial interests in the past year:**
  - **Speakers Bureau/Honoraria**: RLC Labs
  - **Medical Director**: Dr. Cass Better Balance Nutritional Supplements
Disclosure of Commercial Support

- None

Potential for conflict(s) of interest:
- None
Mitigating potential bias

- Information/recommendations in the program are evidence- and/or guidelines-based; opinions of the speaker will be identified as such.
- The program was developed and reviewed by a steering committee composed of independent third-party experts responsible for vetting the program’s needs assessment and content development to ensure accuracy and fair balance.
- The program was reviewed by selected CFPC reviewers and approved for submission for accreditation.
- The Speaker completed the CPFC Mainpro® Declaration.
BIO:

- Integrative medicine and psychiatry: clinical practice, writings, lectures, and media
- Diplomate American Board of Psychiatry & Neurology (ABPM); American Board of Integrative Holistic Medicine (ABIHM.org)
- Internship: LAC-USC Medical Center
- Residency in adult psychiatry, child and family: Cedars-Sinai/UCLA
- Former Assistant Clinical Professor of Psychiatry, UCLA School of Medicine
- Author of *Natural Highs*, *8 Weeks to Vibrant Health*, *Supplement Your Prescription*, *The Addicted Brain* and others
Overview

• How to discover brain imbalances
• How the brain works
• How to intervene with lifestyle, diet, and supplements
• How to not only overcome symptoms, but achieve potential brain power
The Brain is an Organ

- Weighs 3lbs, uses 20% of glucose, oxygen, nutrients
- Affected by body chemistry
- Comprised of neurons
- Neurons communicate via neurotransmitters
- Require specific nutrients
- Affected by dietary intake
Conventional Treatment

For depression, anxiety, PMS, menopausal symptoms, etc:

US doctors wrote more than 253.6 million prescriptions for antidepressants in 2010, making it the third-most-prescribed of any class of drugs

• Also: neuroleptics, anti-anxiety meds

• Does not take physiology/biochemistry into account
Is Psychiatry Evidenced Based?

- Does the current clinical practice of psychiatry follow evidence?
- The trend towards polypharmacy grows
- 13,079 psychiatric visits monitored: 1996-2006
- Visits with 2 or more psychiatric medications increased from 42% to 60%
- Very little evidence to support this
- 1.2 million children on 2 or more psych meds: even less evidence

Mojabai, R  *Arch Gen Psych* 2010; 67: 26-36
Evidence on Antidepressants

- Meta-analysis of RCTs from 1980 to 2009
- Effect size for mild to moderate depression: non-significant
- Separation increases as depression severity increases
- Reaches significance at HDRS of 25 (very severe = 13% of depressed patients)
- Reinforces Kirsch’s prior articles

Evidence on Antidepressants

• Meta-analysis of 6 PCDB studies (718 patients), minimum 6 wks on meds or placebo
• Most patients with severe symptoms had some drug benefit
• All others (mild, moderate and some severe depression patients) were same as placebo — but with side effects.

Publication Bias in Psychiatry

12,564 patients and 74 FDA registered studies reviewed
• 31% not published
• 94% of published trials positive (51% positive by FDA)
• 37 positive published, 1 positive not
• Vast majority of unpublished: negative
• Compared FDA effect size to published: increase ranged from 11 to 69%, **average distortion = 32%**

Turner, E  *NEJM* 2008, 17;358(3):252-60
Questions Long-Term Efficacy

Robert Whitaker

Robert Whitaker - How Safe & Effective are Psychiatric Medications?

- Books: *Mad in America* and *Anatomy of An Epidemic*
- Long term outcome for people with all psychiatric diagnoses & all types of medications: Patients do better with no medication or very limited medication.
- [www.madinamerica.com](http://www.madinamerica.com) blog
Safety, Efficacy and the Patient

- RCTs highlighted as gold standard, highly scrutinized
- Safety appears to be less well scrutinized
- Safety vs Efficacy: a paradigmatic split—CAM vs Conventional
- Patient preference should help to determine direction
- True informed consent rarely provided

Shannon, Weil, Kaplan Alternative and Complementary Therapies 2011,17 (2):84-91
Problems with Psychotropic Medications

- Inadequate response to antidepressants
- Weight gain, metabolic syndrome, type 2 diabetes
- Paxil may be associated with increased incidence of breast cancer in men as well as in women*
- Suicides, homicides
- Sexual side effects
- Deplete nutrients essential for mood: B vits, including folate; CoQ10 (Cass, H, Supplement Your Prescription, Basic Health Publications)

*Bahl S. Psychother Psychosom, 2003; Steingart A Int J Epi2003
Biochemical factors

- Nutrient and neurotransmitter deficiencies
- Specific laboratory testing
- Provide needed vitamins, minerals, and amino acids.
Primum Non Nocere

first, do no harm

Hippocrates
Medical Aspects

• Rule out medical conditions affecting brain function
• Food allergy
• Dysglycemia
• Thyroid
• Adrenal
• Sex hormone imbalances
• History, physical, labs as indicated
Laboratory Testing

- CBC
- Chem panel w fasting glucose
- If indicated:
  - Hbg A1C
  - CRP
  - Homocysteine
  - Amino acids (plasma, urine)
  - RBC vitamins & minerals
  - Essential fatty acids
  - Organic acids
- Neurotransmitters (urine, red cell)
- Hormones:
  - Thyroid (T3, T4, TSH)
  - Cortisol
  - DHEA-S
  - Estradiol
  - Progesterone
  - Testosterone
Basic Requirements

- Biochemical Individuality
- Synergy of nutrients
- Deficiencies: laboratory testing
- Specific supplementation with vitamins, minerals, amino acids, and herbs
  - mood, memory, cognition,
- Interrupts cravings for sugar/carbs, caffeine, alcohol
Nutrient Needs

- Carbohydrates as brain fuel
- Protein for amino acids -> neurotransmitters
- Vitamins and minerals as co-factors to catalyze their production
- “Good” fats
- Phospholipids
- Water
Blood Sugar Regulation

- Refined carbs, low glycemic index (more recently, “glycemic load”)
- Rapid rise of blood sugar—“sugar high”
- Insulin release sweeps it into the cells
- Drop in blood sugar
- Adrenalin release --> fight or flight, sympathetic nervous system response, anxiety symptoms

Case #1

36 yr old male, c/o anxiety, most pronounced when driving to work on freeway

DD: Psychological - work? freeway phobia?
Physical: environmental sensitivity?
Benzodiazepine deficiency?

Solution - dietary changes
✓ Breakfast: complex carbs, protein to maintain a steady release of glucose; small frequent meals
✓ Multivitamin high in B vitamins
✓ Chromium nicotinate 200 ugm bid
Mind- and Mood-Enhancing Neurotransmitters

Dopamine - energizing, motivating
Noradrenaline - mood enhancing
Adrenaline - stress response
Serotonin - mood enhancing, calming
Endorphins - euphoria, pain control
GABA - dampens, calms
Acetylcholine - memory and alertness
Interactive system with checks and balances
Source: amino acids from protein
How Neurotransmitters Work
TRYPTOPHAN

B vitamins, C + Zinc help these conversions

5-HTP

TMG + SAME helps make these

SEROTONIN

DOPAMINE NORADRENArin AL

OMEGA 3 fats improve neurotransmitter reception

Mood Enhancing Nutrients

PHENYLALANINE

TYROSINE

ADRENApin
Vitamin Study

Conclusions: Antisocial behaviors in prisons, including violence, are reduced by vitamins, minerals and essential fatty acids with similar implications for those eating poor diets in the community.

Vitamin C

• Antioxidant
• Neurotransmitter co-factor; increased need in smokers, stress, and with oral contraceptives; found in fruit, vegetables
• Dose: 2000-3000 mg daily with minimum 300 mg bioflavonoids per 1000 mg


Vitamin E

• Antioxidant; good for AD prevention
• Tardive dyskinesia 1600 IU daily (DB study)
• Use when taking fish oil to avoid free radical formation
• Mixed tocopherol
• Found in seeds/oils, fish, beans

Adler et al, Vitamin E treatment of tardive dyskinesia, Am J of Psychiatry 150, 1405-07, 1993
Vitamin E

• Alzheimers’ Study: **Conclusion:** Among patients with mild to moderate AD, 2000 IU/d of alpha tocopherol when compared with placebo, resulted in slower functional decline. There were no significant differences in the groups receiving memantine alone or memantine plus alpha tocopherol. These findings suggest benefit of alpha tocopherol in mild to moderate AD by slowing functional decline and decreasing caregiver burden.

B Vitamins

Essential co-factors for neurotransmitter production; depleted in stress
Deficiencies -> depression, irritability, cognitive
In whole grains, vegetables:
B1 (thiamine), B2 (riboflavin): poor concentration/attention
B3 (niacin): Hoffer & Osmond: depression, psychosis
B6 (pyridoxine): irritability, depression, poor memory
B Vitamins

**B12 (cobalamin):** (meat, fish, dairy, eggs); needs intrinsic factor - elderly are at-risk; RBC formation, O2 transport

**Folic acid** (leafy green vegetables): depression, “dementia”
- MTHFR issue – methylene-tetrahydro-folate reductase
- Look for high homocysteine; genetic testing; complex issue

Ref: Levitt AJ and Joffe RT. Folate, B12, and life course of depressive illness. Biol Psychiatry 1989;25:867-72
Minerals

Magnesium - deficiency--> anxiety, depression (125-300 mg tid and qhs), insomnia, muscle tension, osteoporosis, PMS
Average Dose: 200-600 mg/day

Depression: http://george-eby-research.com/html/magnesium-for-depression.pdf (125-300 mg tid and qhs)
Minerals

• 81 patients - 18-65 yrs with migraine (IHS) criteria (mean attack frequency 3.6 per month)
• Oral 600 mg (24 mmol) magnesium (trimagnesium dicitrate) daily for 12 weeks or placebo.
• In weeks 9-12 the attack frequency was reduced by 41.6% in the mg group, 15.8% in the placebo group.
• Decreased days with migraine & drug consumption decreased significantly in the mg group.
• Adverse events were diarrhea (18.6%) and gastric irritation (4.7%). **Conclusion: High-dose oral magnesium appears to be effective in migraine prophylaxis.**

Minerals

**Sodium (Na+)** - low in adrenal burnout; high in hypertension

**Iron** - deficiency -> anemia (male vs female dose) - depression, fatigue; chelated form is absorbed better (eg glycinate)

**Potassium (K+)** 99 mg - > electrolyte balance - > low K+ -> depression
Minerals

**Zinc** - 15-30 mg taste, smell, immunity, healing; anorexia, bulimia


**Selenium** - low levels in depression; Brazil nuts; Dose: 100 mcg per study below

DEPRESSION: Amino Acids

- **Catecholamines**: Phenylalanine and Tyrosine
- Precursors to stimulating neurotransmitters: dopamine, adrenaline, noradrenaline; thyroxine
- Associated with enhanced mood, energy and motivation
- DLPA produces phenethyamine PEA ("the love drug" in chocolate), endorphins
- Phenylalanine elevated mood in 31 of 40 depressives at 14 gm/day **Caution**: Hypertension in those susceptible; phenylketonurics.
- **Dosage**: 500-1000 mg on an empty stomach first thing in the morning; 1-3 times daily
  
DEPRESSION: Amino Acids

- L-Tryptophan and 5-Hydroxytryptophan (5-HTP)
- Precursors to serotonin (cf SSRIs - different mechanism)
- Promotes relaxation, mood elevation, deep sleep, healthy sleep-wake patterns, emotional stability
- For insomnia, take one hour before bedtime
- B vitamins, especially B6, as co-factor.
- Carbohydrate for transport into brain (insulin)
- **L-Tryptophan**: 500-1500 twice daily
- **5-HTP**: 50-150 mg twice daily

Omega-3 Fatty Acids and Mood

- Mood, mind and memory booster
- ADD, depression, bipolar
- EPA & DHA (DHA>EPA in brain)
- Building material for neuronal membranes and neurotransmitter receptor sites
- Precursors for prostaglandins/ eicosonoids, chemicals that influence mood and behavior
- Affect neurotransmitter balance: acetylcholine and serotonin

Omega-3 Fatty Acids and Mood

- Anti-inflammatory effect on brain tissue (including dementia, ADD, autism, MS, Parkinsonism, etc)
- RBC assay
- **Dose:** 250-3000 mg a day as a fish oil supplement or eat fatty fish three times a week


S-Adenosyl-methionine (SAMe)

- Found throughout body, especially liver, brain
- Synthesized from the combination of the amino acid L-Methionine, folic acid, vitamin B12, & trimethylglycine (TMG)
- **Methyl donor** -> enhances production of neurotransmitters, fatty acids, phospholipids, proteins, nucleic acids, glutathione
- Excellent antidepressant, rapid onset
- Caution in bipolar patients; MAOIs; serotonin syndrome with SSRIs (unlikely)
S-Adenosyl-methionine (SAMe)
Well researched - over 200 studies

Meta-analysis 1994 (Bressa): “The efficacy of SAMe in treating depressive syndromes and disorders is superior to that of a placebo and comparable to that of standard tricyclic antidepressants”

Acta Neurologica Scandinaiviqn, Vol 154, 1994, pp. 7-14

SAMe: Administration

- Use co-factors: Pyridoxal-5-phosphate (B6 metabolite), Folate/methylfolate, Vitamin B12
- High potency multi-vitamin is often adequate
- Short shelf life: easily degradable
- Use enteric coated tabs or refrigerated, stabilized capsules
- Dose: 200 mg in A.M., empty stomach, increase to 2 after 4 days if necessary
- Up to 4 daily (research - 1600 mg.)
SAMe: Cautions

• High doses may lead to irritability, anxiety, insomnia, nausea (take with food), or vomiting.
• In bipolar disorder, SAMe (like any antidepressant) may trigger a manic episode, so such individuals should be monitored carefully.
• Take SAMe with prescription antidepressants only under medical supervision, though unlikely to cause serotonin syndrome.
• SAMe can be used safely during pregnancy and breast feeding.
Anxiety: Natural Relaxants

- **GABA** - inhibitory neurotransmitter - brain's peacemaker, regulates the stress hormone adrenaline, dopamine, norepinephrine
- **Taurine and Glutamine** - precursors to GABA
- **L-Theanine** - from green tea
- **Herbs** – Kava, valerian
- **B vitamins**: co-factors in neurotransmitter production
GABA: “Modulator”

- Calming amino acid, enhances GABA neurotransmitter activity which counteracts stress hormones.
- Reduces anxiety, insomnia, tension, migraine, alcohol cravings
- **Cautions:** GABA can cause nausea and vomiting at very high doses.
- **Dose** 500 - 1000 mg twice daily between meals.

L-Glutamine

- Fuel for brain cells; helps build and balance neurotransmitters.
- Improves both mental energy and relaxation; reduces addiction; stabilizes blood sugar; promotes memory
- GI tract restoration
- Rare reports of headaches at high doses.
- **Dose:** 500–2500 mg twice daily between meals.

L. Young et al, Patients receiving glutamine-supplemented IV feedings report an improvement in mood, J Parenter Enteral Nutr, Vol 17, 1993, pp 422-7
L- Theanine  
(glutamic acid gamma-ethylamide)

- Amino acid found naturally in green tea (catechins)
- Antagonizes caffeine’s stimulatory effect
- Increases alpha wave activity
- Animal studies: modifies brain serotonin concentration by either reducing serotonin synthesis or degradation
- Dose: 100 – 200 mg twice daily
- Cautions: none known (little available research)

N-Acetyl-cysteine

- Antioxidant precursor to glutathione
- Modulates neuro-transmitter pathways, including glutamate and dopamine
- OCD, trichotillomania
- Addiction: Glutamatergic abnormalities
  - Marijuana, Nicotine
  - Pathological gambling
  - Schizophrenia

Memory and Cognitive Enhancement:

- Acetyl-L-Carnitine: fuel, precursor to acetyl choline, antioxidant; 500-1500 mg daily
- Vinpocetine: circulation; 10-40 mg daily
  - 12 normal subjects: memory ...significantly improved following treatment with vinpocetine 40 mg Huperzine A - Chinese club moss (huperzia serrata):
    Acetylcholinesterase inhibitor, like Aricept; 200 mcg/day
Ginkgo Biloba

- Improves circulation
- Antioxidant
- Mood, memory, concentration, and energy
- Blood thinner (acts on PAF)
- Over 200 studies regarding its efficacy

Cautions: Rare side effects of headaches, nausea, or nosebleeds have been reported at high doses. Use with caution if taking blood-thinning medications.

Dosage: 120–240 mg a day of a standardized extract providing 24 percent flavonoids, taken in two divided doses (60–120 mg twice daily).
Ginkgo Biloba

Conclusion: short-term administration of EGb 761 ginkgo extract appeared to improve mental health, quality of life, self-judged mood state, and motor reactions in healthy older people


Phospholipids

- **Phosphatidyl serine**: neuronal membranes, receptor sites
- Highest content is egg yolks
- Dose: 100 mg tid
- **Choline**, precursor to acetylcholine: as lecithin, phosphatidyl choline, citicholine, or alpha GPC
- Daily Dose: 5–10 g (approximately 1 tablespoon) of lecithin, or 2.5–5 g (a heaping tablespoon) of high-phosphatidylcholine lecithin, or 1–2 g of phosphatidyl choline, or 500 mg–2 g of choline chloride (fishy smelling);
- 500–1,000 mg of citicholine, alpha-GPC
Nutritional Psychiatry: Principles

- Address underlying medical conditions
- Look for common cause of multiple symptoms
- Determine underlying biochemical imbalance, using lab testing if necessary
- Use the most natural/physiological remedies
- Nutrients: Replacement + maintenance (vitamins, minerals, amino acids, herbs)
Lifestyle/Context

- Eliminate smoking, drug abuse; minimize sugar, caffeine and alcohol consumption
- Get sufficient sleep
- Exercise
- Address psychological and spiritual aspects
- Meditation, visualization, biofeedback, music, massage, yoga, movement and dance (see Natural Highs for details; research)
Resources

- Brogan, Kelly 2016: **A Mind of Your Own**
- Cass, H & Holford P: **Natural Highs** 2002
- Holford P: **Optimum Nutrition for the Mind**
- Greenblatt, J: **Breakthrough Depression Solution: Mastering Your Mood with Nutrition, Diet & Supplementation**
- Greenblatt, J; Brogan, K: **Integrative Therapies for Depression**
- Hyman, Mark: **The Ultramind Solution**