Nutritional Management of Bipolar Disorder in Adults and Youth

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Sponsored by

Charles Popper, M.D.

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None of the agents discussed in this talk
have been approved
for the treatment of mood disorders
by the U.S. Food and Drug Administration.

Managing Bipolar Disorder:

Nutritional “Good Health” Measures

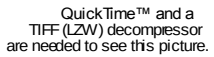
Wholesome foods, good cooking practices, sensible meal times.

Minimize junk food - Excess fats and sugars, salt loads, corn syrup.

Ample fluids.

Avoid alcohol, caffeine, nicotine/smoking, and recreational drugs.

Add nutritional support - Multivitamins, omega fatty acids.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TIFF (LZW) decompressor
are needed to see this picture.

Traditional Diet is Associated with Reduced Depression and Anxiety Disorder

Jacka et al., Am J Psychiatry March 2010

Traditional Diet	Vegetables, fruit, beef, lamb/meat, fish, whole grains.
Junk Food Diet	Processed meats, refined grains, sugary products, fried foods, beer.
Health Food Diet	Fruits, salads, fish, tofu, beans, nuts, yogurt, red wine.

After accounting for energy intake, BMI, age, SES, education, alcohol consumption, or smoking:

Traditional Diet	Lower risk of DSM major depression or dysthymia.
	Lower risk of DSM anxiety disorders.
☐ Junk Food Diet	More psychological symptoms.
Health Food Diet	Trend: *Higher* risk of major depression or dysthymia.
	Better than Junk Food Diet, but not much better (why?).

Cross-sectional study: Direction of causality?

Unhealthy Diet is Risk Factor for Later Depression

Two Large-Scale Prospective Studies

Sáchez-Villegas et al., Arch Gen Psychiatry 2009

Risk factors for new-onset depression:

Adherence to a Mediterranean dietary pattern.

More intake of fruits, nuts, and legumes.

Higher intake ratio of mono-unsaturated to saturated fatty acids.

Akbaraly et al., Br J Psychiatry 2009

Whole foods were associated with reduced risk of depression (OR 0.74)

Processed foods were associated with increased risk of depression (OR 1.58)

Managing Bipolar Disorder:

General “Good Health” Measures

Healthful nutrition, hydration, avoid alcohol/caffeine/etc., multivitamins.

Sleep regularity - Regular wake-up times, adequate duration, comfortable bed.

Exercise.

Rest.

Relaxation.

Social connection - conversation, companionship, closeness, moral caring.

General hygiene - Personal cleanliness, contagion prevention.

Air management - Clean indoor environment.

Time management.

Stress management.

Disease management.

Prevention measures, including weight management and medical checkups.

Managing Bipolar Disorder:

Specific Treatments

Psychosocial

Psychopharmacological

Neurostimulation - ECT, TMS, VNS, DBS; neurofeedback; light therapy. .

Nutrient alternatives to pharmaceutical approaches

- Essential fatty acids.
- SAMe, 5HTP, choline, inositol, L-theanine.
- Vitamins and minerals

Micronutrients = Vitamins and Minerals

Broad-Spectrum Micronutrient Treatments

Vs.

Single Vitamins and Single Minerals

Single Vitamin Deficiencies Can Cause Psychiatric Symptoms

Thiamine	B1	Wernicke's encephalopathy (short-term memory loss, disorientation/confabulation, hallucinations) Beriberi (irritability, emotional lability)
Niacin	B3	Pellagra (mental confusion, dementia, depression, anxiety, agitation, aggression, hallucinations, paranoia)
Pyridoxine	B6	Depression, irritability
Biotin	B7	Anxiety
Folate	B9	Depression
Cobalamin	B12	Pernicious anemia (depression, mania, hallucinations, paranoia) ?OCD
Ascorbate	C	Scurvy (depression, irritability)

Single Mineral Deficiencies Can Cause Psychiatric Symptoms

Iodine	“Myxedema madness”
Zinc	ADHD?
Iron	Depression, irritability; ADHD?
Magnesium	Attention deficits?
Boron	Attention deficits

Single Micronutrient Deficiencies or Interventions Can Affect Mood

B Vitamins	
B1	Thiamine
B3	Niacin
B6	Pyridoxine
B7	Biotin
B9	Folate
B12	Cobalamin
Vitamin C	Ascorbic acid
Vitamin D	Cholecalciferol
Vitamin E	D-alpha tocopheryl
Iron	
Copper	
Zinc	
Chromium	

Kaplan et al., Psychol Bulletin 2007

Single Micronutrients on Mood: Randomized Double-Blind Placebo-Controlled Trials

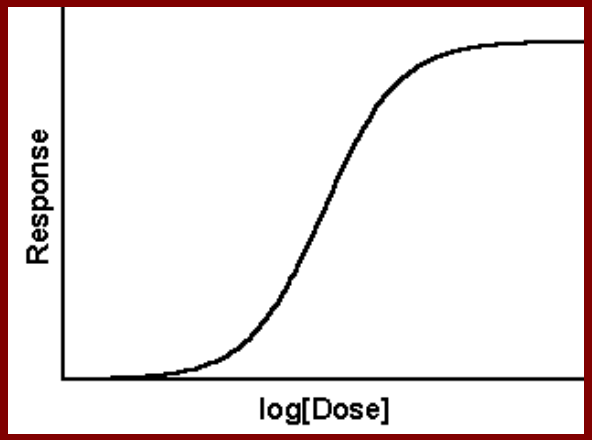
Citation	Sample	Diagnosis	Outcome	Intervention
Cohen 1982	6 Adults	Manic episode	Improved mood	Lecithin
Godfrey 1990	41 Adults	Depression-24 Schizophr-17	Improved mood	Folic acid
Benton 1991	50 Adults	Normal volunteers	Improved mood	Selenium
Benton 1997	120 Adults	Normal volunteers	Improved mood	Thiamine
Thys-Jacobs 1998	466 Adults	Premenstrual syndrome	Improved mood	Calcium
Wyatt 1999 Metaanalysis	940 9 RTCs	Premenstrual syndrome	Improved overall, esp. depression	Pyridoxine
Giannini 2000	20 Adults	Mania	Improved mania	Magnesium
Davidson 2003	15 Adults	Atypical depression	Improved symptom scores	Chromium

Assembled by Taron Fletcher and Jared Hardy

The Medical Model of Pharmacology

1 Drug : 1 Disease : 1 Effect

One Dose-Response Curve



Insulin : Diabetes : Reduce Blood Sugar

Rationale for Broad-Spectrum Micronutrient Treatment - 1

Many vitamins and minerals, each with multiple physiological functions.

Most micronutrients operate in concert with other micronutrients.

The balance among micronutrients optimizes their functioning and minimizes their adverse effects.

Rationale for Broad-Spectrum Micronutrient Treatment - 2

Biochemical individuality.

Nutrient requirements change over time in individuals.

Numerous and varied absolute nutritional deficiencies in the general population.

Relative (functional) deficiencies are more difficult to identify clinically than absolute deficiencies.

Physicians do not usually know what nutrients are (absolutely or relatively) deficient in an individual at a particular time.

Rationale for Broad-Spectrum Micronutrient Treatment - 3

Broad-spectrum micronutrient treatments can promote balanced chemical microenvironments in populations of individuals with varying physiological needs and nutritional resources.

Medical Model of Pharmacology

vs.

Nutritional Model of Pharmacology

A Nutritional Model of Pharmacology

Ask not “What are the effects of
one or two nutrients at a time?”

But “What are the effects of a
broad spectrum of nutrients at once?”

What is Good Nutrition?

Recommended Daily Allowance (RDA) =

The amount of an individual micronutrient required to prevent frank deficiency diseases.

Recommended Daily Intake (RDI)

The amount meeting the nutritional needs of 97-98 % of 14 to 70 year old males and females.

Dietary Reference Intake (DRI) =

A newer set of recommended amounts for optimal physical health.

What is Good Nutrition?

Optimal nutrient intake depends on the targeted health goal:

Cardiovascular vs. immunological vs. mental vs. longevity

Research on Broad-Spectrum Micronutrient Interventions in Mental Health

Research on:

- Cognitive Functioning in Normal Volunteers
- Mood and Anxiety in Normal Volunteers
- Violent and Antisocial Behavior in Schools and Prisons
- Bipolar Disorder in Adults and Youth

Broad-Spectrum Micronutrients on Cognitive Functioning

Attention in Young Adults

Benton et al., Psychopharmacol 1995

127 young healthy adult volunteers.

Double-blind placebo-controlled trial.

Treatment Multivitamins at 10 times RDA level for 12 months.

Outcome Females showed improved attentional measures.

Nonverbal Intelligence In Children

Benton, Neurosci Biobehav Rev 2001

In a review of double-blind placebo-controlled studies of multi-micronutrient use on intelligence in children, 10 of 13 studies showed improved measures of non-verbal intelligence, with benefits observed in a minority of subjects.

Broad-Spectrum Micronutrient Effects on Mood and Anxiety in Normal Volunteers

Mood

Benton et al., Neuropsychobiol 1995

129 young healthy adult volunteers.
Double-blind placebo-controlled trial for 12 months.
Treatment Multi-vitamins at 10 x RDA level.
Outcomes Females and males felt more "agreeable."
Females reported better mood.

Anxiety

Carroll et al., Psychopharmacology (Berlin) 1995

80 young healthy adult volunteers.
Randomized double-blind placebo-controlled for 1 month.
Treatment 12 vitamins and minerals.
Outcome Reduced anxiety and perceived stress.
Fewer somatic complaints.

Schlebusch et al., South Afr Med J (2000)

300 healthy adult volunteers.
Randomized double-blind placebo-controlled trial for 1 month.
Treatment 10 vitamins and minerals.
Outcome Reduced anxiety and perceived stress.

Broad-Spectrum Micronutrient Effects on Violent and Antisocial Behavior

Schoenthaler and Bier, J Altern Complement Med 2000

80 children (6-12 yo) in public schools with conduct disorder with aggressivity.

Randomized double-blind placebo-controlled trial.

Treatment Vitamin-mineral formula at 50% of RDA levels for 4 months.

Outcome 47% reduction in disciplined violent and nonviolent misconduct (including threats and fights, vandalism, defiance, disrespect, obscenities).

Gesch et al., Brit J Psychiatry 2002

231 young antisocial adults in prison.

Randomized, double-blind, placebo-controlled.

Treatment 26 micronutrients (at RDA levels) and essential fatty acids for a mean of 5 months.

Outcome 26% fewer disciplinary offenses and 35% fewer violent acts if treated for more than 2 weeks.

Clinical Implication: Perhaps consider broad-spectrum micronutrient treatment at RDA levels for conduct-disordered/juvenile delinquent youths and adult offenders with antisocial or aggressive behavior.

Broad-Spectrum Micronutrient Research and Treatment in Psychiatry

No published rigorously controlled studies document the safety or efficacy of broad-spectrum micronutrient treatment in treating any psychiatric disorder.

Broad-Spectrum Micronutrient Treatment of Bipolar Disorder

An Unexpected Origin:

Derived from knowledge
developed by agribusiness
for reducing destructive aggression
among farm animals.

Original Observers of the Broad-Spectrum Micronutrient Treatment Effects on Bipolar Disorder

David Hardy

Tony Stephan

Bonnie Kaplan

Broad-Spectrum Micronutrient Treatment Research on Bipolar Disorder

Hardy and Stephen developed a 36-ingredient product, derived from a formula that reduced aggression among farm animals, which helped children and then relatives with bipolar disorder.

Other commercial broad-spectrum micronutrient formulations have been proposed to treat bipolar disorder.

However, all of the research to date has been conducted on a single set of formulations (brand name EMPowerPlus®), developed by Hardy and Stephan, which we will call MCN36.

MCN36 Research on Bipolar Disorder

	Dx	N	
Letter/Comment			
Youth	Bipolar	1	Popper J Clin Psychiatr 2001
Adult	Bipolar	19	Simmons J Clin Psychiatr 2001
Mixed	Bipolar	22	Popper J Clin Psychiatr 2001
Case Reports			
Youth	Bipolar	2	Kaplan JCAP 2002
Child	Bipolar+psychosis	1	Frazier JCAP 2010
Adult	OCD+Dep+Anx	1	Rucklidge J Anx Disorders 2009
Adult	Bipolar+ADHD+Anx	1	Rucklidge CNS Spectrums
Case Series			
Adult	Bipolar	11	Kaplan J Clin Psychiatr 2001
Child	Bipolar	11	Kaplan JCAP 2004
Adult	Bipolar+ADHD	14	Rucklidge J Atten Disord 2010
Mixed	Autism+Comorbidity	88	Mehl-Madrona JCAP 2010
Database Analyses			
Adult	Bipolar	358	Gately Clin Med: Psychiatr 2009
Child	Bipolar	120	Rucklidge (Submitted)
Controlled Trials		0	
Number of Subjects		649	
Number of Investigative Groups		6	

JCAP = J Child Adolesc Psychopharmacol

Case Series: Adults with Bipolar Disorder

Kaplan et al., J Clin Psychiatr 2001

11 adults with DSM bipolar disorder.

Open-label clinical trials. No drug reversals.

Treatment MCN36 x 6 months.

Outcome Marked symptom improvement.

(HAM-D 19→5, YMRS 15→6, BPSR 35→7).

50% reduction in medication dose.

5 of 11 discontinued all psychiatric meds.

3 of 14 drop-outs.

Informally Reported Single Case Report: Child

Popper, J Clin Psychiatr 2001 (Commentary)

10 yo with medication-naïve bipolar disorder and severe temper tantrums.

Open-label naturalistic treatment with multiple reversals: ABAB[+ABAB].

Treatment MCN36 for 6 months [+ 10 yr follow-up].

Outcome Complete symptom remission in 5 days.

No psychiatric medications.

Subsequently verified with multiple off-on reversals over years.

Informally Reported Case Series: Mixed Ages

Popper, J Clin Psychiatr 2001 (commentary)

22 patients (adults and youth) with DSM bipolar disorder.

Open-label naturalistic treatment. No drug reversals.

Treatment MCN36 for 2-6 months.

Outcome 19 of 22 (86%) showed clinical improvement
(2 mild, 7 moderate, 10 marked).

11 of 15 off all medications.

Two Case Reports: Child

Kaplan et al., J Child Adolesc Psychopharmacol 2002

2 medication-naïve children (8 and 12 yo) with mood lability, explosive rage; 1 had OC.

Open-label clinical trial with naturalistic ABAB design.

Treatment MCN36 over 2 years.

Outcome Improved scores on irritability, temper, and obsessionality (CPRS, CBCL, YBOCS) in 3 weeks during active treatment phases.

Informally Reported Case Series: Adults

Simmons, J Clin Psychiatr 2003 (letter)

19 adults with DSM bipolar disorder.

Open-label naturalistic treatment. No drug reversals.

Treatment MCN36 for 5-11 months.

Outcome 16 of 19 (84%) showed clinical improvement (1 mild, 3 moderate, 12 marked).

13 off psychiatric medication.

Case Series: Child

Kaplan et al., J Child Adolesc Psychopharmacol 2004

11 children (8-15 yo) with mood and behavioral problems.

Open-label naturalistic treatment. No drug reversals.

Treatment MCN36 for 8 weeks.

Outcome Among 9 of 11 (82%), improvement in YMRS and all CBCL subscales (withdrawn, anxious/depressed, social probs, thought probs, inattention, delinquent, aggressive) except somatic.

Six discontinued all psychiatric medications.

Database Analysis: Adults with Bipolar Disorder

Gately and Kaplan, Clinical Medicine: Psychiatry 2009

Database analysis of self-reports of open clinical trials in 358 adults with "bipolar disorder" (81% initially taking psychiatric medications); major comorbidity was excluded.

Treatment MCN36 > 6 months, trials conducted by numerous clinicians.

Outcome Response rate: 53% reported ≥ 50% improvement at 6 months.

Mean symptom severity was 41% lower than baseline at 3 months and 45% lower than baseline at 6 months.

Medication use reduced from 78% to 55% at 3 mos and 44% at 6 mos.

Case Report – Child with OCD plus Mood/Anxiety Dx

Rucklidge, J Anx Disorders 2009

18 yo with OCD with partial response (severe→moderate) to CBT for 1 year, plus major depression and anxiety.

Open-label in naturalistic ABAB reversal design.

Treatment MCN36 for 8 weeks (in first B).

Outcome Symptom improvement of about 50% in ratings of OCD, anxiety, and mood during active treatment (BDI, BAI, GAF, CBCL).

Case Report – Child with Bipolar Disorder, Psychosis

Frazier et al., J Child Adolesc Psychopharmacol 2009

12 yo with bipolar disorder with psychotic features, partially responding to conventional meds x 6 yrs.

Open-label naturalistic treatment. No drug reversals.

Treatment Transitioned from conventional medications to MCN36.

Outcome Over 3 weeks-2 months, mood and psychotic symptoms were virtually resolved, with better global functioning, sleep, sociability, and cognition.

All medications were discontinued, with better functioning than on conventional meds.

Case Series - Autism

Mehl-Madrona et al., J Child Adolesc Psychopharmacol, 2010

88 patients (age 2-28 yrs) with autism with mixed comorbidity in clinical practice.

Treatment	Open-label naturalistic treatments.
	Half chose MCN36, half chose conventional meds, for mean 15 months (3 months - 10 years).
Outcome	Both groups improved similarly on CARS (autism) and CPRS.
	MCN36 group did better on CGI (global improvement) and ABC (autism): anger and irritability, social withdrawal, activity level, interpersonal spontaneity and self-injurious behavior.

Case Report - Child

Rucklidge and Harrison, CNS Spectrums, at press

21 yo with bipolar disorder, ADHD, social anxiety, and panic disorder poorly responsive to conventional meds.

Open-label naturalistic ABAB clinical treatment.

Treatment MCN36 for 8 weeks, with 12-month follow-up.

Outcome Improved mood, anxiety, and ADHD during active treatment at 8 weeks (YMRS, MADRS, CAARS, CGI).

Full remission persisting at 12 months.

Hyperactivity/impulsivity improved faster than inattention. Also improved processing speed and verbal memory.

Case Series - Adult

Rucklidge et al. J Attention Disorders, at press

14 adults with ADHD + comorbid mood/anxiety disorders.

Open-label naturalistic ABA clinical treatments.

Treatment MCN36 for > 8 weeks

Outcome 10 of 12 (83%) showed >50% reduction in depression symptoms -- 67% in remission MADRS < 10 -- at 8 weeks.

Improved on anxiety and anger scores.

ADHD: More effect on hyperactivity/ impulsivity than inattention (CAARS).

Further improvement at 4 months.
Symptom return when treatment stopped.

Database Analysis: Child

Rucklidge et al., manuscript submitted

Database analysis of self-reports of open clinical trials by 120 children (7-18 yo) with "bipolar disorder." Major comorbidity was excluded. 79% initially taking psychiatric medications). 24 % had "ADHD."

Trials conducted by numerous clinicians.

Treatment MCN36 > 6 months.

Outcome Response rate: 46% reported ≥ 50% improvement at 6 months.

Mean symptom severity was 46% lower than baseline at 3-6 months.

Medication use reduced from 79% to 38%. Mean doses reduced by 74%.

Summary of MCN36 Research

No randomized double-blind placebo-controlled studies.

12 published (or at press) open-label reports, 649 subjects, 6 clinicians/teams, with two database analyses of 358 adults and 120 youths. 19 cases included drug reversal design (ABA, ABAB, or more).

In database cases managed by unselected clinicians, 46-53% of patients with mood disorders responded (>50% decrease in symptom severity), and mean symptom severity was reduced by 41-46%.

In cases reported by experienced clinicians, about 80% of patients improved, and symptom reduction was 50-80% on both mania and depression rating scales.

Summary of MCN36 Research - 2

These open-label data suggest the effects in patients with bipolar disorder and probably major depressive symptoms are comparable to the responses to conventional psychiatric medications. Typically, open-label responses are higher than responses in controlled trials.

Also, apparent improvements in symptoms of anxiety, OCD, ADHD, and possibly autism *when associated with mood disorders*: Unclear whether effective in absence of comorbid mood disorder.

Medication use declined from 78% to 41%. That is, 47% of patients treated with psychiatric medication at baseline were treatable on MCN36 without any medication at 6 months. Other patients managed with lower doses.

Summary of MCN36 Research - 3

Generally minimal adverse effects.

No changes in laboratory measures.

Summary of MCN36 Research - 4

Tentatively, broad-spectrum micronutrients appear to have mood-stabilizing and antidepressant properties, seemingly comparable to psychiatric medications, but with fewer adverse effects than psychiatric medications.

Controlled trials evaluating safety and efficacy are needed.

MCN36 Formulation

Consists of 36 ingredients, including:

- A broad range of minerals.
- All the standard vitamins except for K.
- A variety of antioxidants, including 3 botanicals:
  - Ginkgo Biloba (leaf), Grape Seed, and Citrus Bioflavonoids.
- Three amino acids:
  - L-Glutamine, DL-Phenylalanine, L-Methionine
- Choline and inositol.

<u>Contains neither omega fatty acids nor lithium</u>.

Chemical Description of MCN36 Vitamins

Standard daily dose 15 capsules (Five capsules three times daily) with food

	15 Capsules	RDA/AI	UL/TUIL	> UL
Vitamin A (retinyl palmitate)	1,920 µg	700-900	2,800-3,000*	
Vitamin C (ascorbic acid)	600 mg	65-90	1,800-2,000	
Vitamin D (cholecalciferol)	36 µg	200-400	2000	
Vitamin E (d-alpha tocopheryl succinate)	240 mg	15	800-1,000	
Vitamin B1 (thiamine mononitrate)	18 mg	1.0-1.2	NE, NA	
Vitamin B2 (riboflavin)	13.5 mg	1.0-1.3	NE, NA	
Vitamin B3 (niacinamide)	90 mg	14-16	30-35 mg (niacin)	#
Vitamin B5 (d-calcium pantothenate)	21.75 mg	5	NE, NA	
Vitamin B6 (pyridoxine HCl)	36 mg	1.2-1.7	80-100	
Vitamin B9 (folic acid)	1,440 µg	400	800-1,000	#
Vitamin B12 (cyancobalamin)	900 µg	2.4	NE, NA	
Vitamin H (biotin)	1,080 µg	25-30	NE	

Chemical Description of MCN36 Minerals

Standard daily dose 15 capsules (Five capsules three times daily) with food

	15 Capsules	RDA/AI	UL/TUIL	> UL
Calcium	1,320 mg	1,000-1,300	2500	
Iron	13.9 mg	8-15	45	
Phosphorous	840 mg	700-1,250	4000	
Iodine	204 µg	150	900-1,100	
Magnesium	600 mg	310-420	350	#
Zinc	48 mg	8-11	34-40	#
Selenium	204 µg	55	400	
Copper	7.1 mg	0.9	8-10	
Manganese	9.75 mg	1.6-2.3	9-11	
Chromium	624 µg	20-35	NE	
Molybdenum	144 µg	43-45	1,700-2,000	
Potassium	240 mg	4700	No UL	

Chemical Description of MCN36 Proprietary Ingredients

[Quantities Not Published]

- Minerals
  - Vanadium (as chelate)
  - Nickel (as chelate)
  - Boron (as chelate)
  - Germanium (sesquioxide)
- Small organic molecules
  - Inositol
  - Choline (bitartrate)
- Amino acids
  - L-Glutamine
  - DL-Phenylalanine
  - L-Methionine
- Phytochemicals
  - Ginkgo Biloba (leaf)
  - Grape Seed (Vitis rinitera)
  - Citrus Bioflavonoids

Chemical Description of MCN36

Some ingredients are a□□□t high dose, but generally below Tolerable Upper Intake Limits. Four that exceed the TUL do so for logical reasons.

The ratios among ingredients are critical for maintaining a proper balance among components; for example, calcium/magnesium/phosphorus and zinc/copper ratios are particularly critical.

Chelates, which are largely vegetable-based, improve gastrointestinal absorption of certain ingredients.

A unique "micro-grinding" process is used to obtain small-particulate powder, which improves absorption.

These technological advances enhance bioavailability and effectiveness.

Routine over-the-counter multivitamin-multimineral products would require an enormous number of pills to match the delivery of MCN36. As is, the usual daily dose of MCN36 is 15 pills daily, largely because of the bulk contributed by the chelates.

MCN36 Pharmacology

Some unusual pharmacological properties of this broad-spectrum micronutrient formula have been observed.

It it is unclear whether these pharmacological properties are specifically characteristic of MCN36 or, more generally, of broad-spectrum micronutrient formulas.

Other commercial broad-spectrum micronutrient formulas may or may not have similar pharmacological or clinical properties.

Pharmacological Characteristics of MCN36

Unexpected pharmacokinetics and pharmacodynamics

1) Amplification of the effects of CNS-active drugs by micronutrients, including therapeutic, adverse, and withdrawal effects of psychiatric medications.

2) Potent mineral-mineral interactions.

Unexpected Pharmacologic Phenomenon #1

Nutrient-Drug Interactions

Nutrient-Drug Interactions

MCN36 potentiates (amplifies) the effects of most CNS-active substances:

- Psychiatric medications.
- Prescription and OTC drugs that have CNS therapeutic effects or CNS side effects.
- Certain hormones.
- All recreational drugs, including caffeine, alcohol, nicotine, marijuana.

MCN36 potentiates most CNS-active drugs by a factor of 3-5 fold.

Nutrient-Drug Interactions

Potentiation of CNS drugs' therapeutic effects.

Potentiation of CNS drugs' side effects.

Potentiation of CNS drugs' withdrawal effects.

Reduced therapeutic effectiveness of MCN36.

These effects may operate concurrently.

Nutrient-Drug Interactions: CNS Drugs

Patients starting MCN36 should expect potentiation of nutrient-drug interactions, so may need to stop or reduce:

- Psychiatric medications
- Medical medications
- Alcohol
- Caffeine (coffee, tea, chocolate)
- Nicotine (smoking)
- Recreational drugs

Without such dose reductions, expect increased side effects of these agents -- and less effectiveness of MCN36.

Nutrient-Drug Interactions: Medical Drugs

CNS-active medical drugs to be avoided (or used at lower dose) in combination with MCN36:

- Cold medications, including dextromethorphan and pseudoephedrine.
- Some antihistamines, especially ceterizine.
- Theophylline.
- Narcotic analgesics.

Also, expect potentiations when adding these medications to an ongoing MCN36 regimen.

Nutrient-Drug Interactions

In transitioning from conventional treatment to MCN36, the doses of psychiatric medications must be lowered – and preferably discontinued – in order to:

Avoid increased medication side effects

AND

Avoid decreased MCN36 effectiveness.

Nutrient-Drug Interactions

Do prior psychiatric drugs absolutely need to be discontinued?

No, MCN36 can be used with lowered doses of psychiatric medications.

But continued low doses of conventional medications will undercut the full effectiveness of micronutrients.

Unexpected Pharmacologic Phenomenon #2

Potentiated and Protracted Drug Withdrawal

Potentiated and Protracted Drug Withdrawal

MCN36 potentiates drug withdrawal syndromes in both

intensity (*potentiated withdrawal*)

and

duration (*protracted withdrawal*).

Potentiated and Protracted Drug Withdrawal

MCN36 potentiates withdrawal syndromes of:

All serotonin reuptake inhibitors, esp. venlafaxine, paroxetine.

Benzodiazepines

Pseudobenzodiazepines (zaleplon, zolpidem, eszopiclone).

Tramadol (opiate mu receptor agonist, venlafaxine analog).

Trazodone

Certain antipsychotics, esp. quetiapine, aripiprazole, pimozide.

Drug Discontinuation Syndromes

Serotonergic:

- Odd head feeling ("headache without the headache”), mental fog.
- Odd gastrointestinal feeling ("nausea without the nausea"), GI upset.
- Flu-like symptoms, lightheadedness, dizziness, headache, anorexia, nausea/vomiting, fatigue, malaise, myalgia.
- Anxiety, irritability, insomnia, agitation, confusion, vertigo, hot and cold flashes, tremors, parathesias, “buzzing all over,” generalized pruritis, “electric shock-like sensations”, visual “jolts.”

Cholinergic:

- Anxiety, agitation, sweating, pupil dilation, tremors, anorexia, hot and cold flashes.

Serotonergic plus anticholinergic:

- Visual trailing, similar to LSD (treatable with donepezil).

Unexpected Pharmacologic Phenomenon #3

Delayed Drug Discontinuation Syndromes

Delayed Drug Discontinuation Syndromes

MCN36-potentiated symptoms can appear with a delay of weeks, months (and at times years) after stopping a conventional medication, especially for drugs with long half-lives.

Symptoms are triggered by physiological stressors, including exercise, pregnancy, dieting, temperature and climate change, body work (including massage, acupuncture, rolfing), saunas.

These symptoms can mimic psychiatric symptoms (e.g., anxiety, agitation, insomnia) and appear long after clinicians no longer suspect drug discontinuation to be relevant.

Delayed Drug Discontinuation Syndromes

Mechanism is unclear:

Are small residues of medication still being cleared from the body, mobilized by stress into circulation from fat or protein bound sites, months or years after last administration?

Are activated neuronal network firings, sensitized by multiple prior MCN36-potentiated discontinuation reactions, persistently triggered by stressors?

Unexpected Pharmacologic Phenomenon #4

Mineral-Mineral Interactions

Mineral-Mineral Interactions

MCN36 potentiates lithium by about 100-fold.

Compare to the 3-5 fold potentiation of most CNS drugs.

When using lithium in a patient receiving MCN36,

the usual dose range is 20 mg (1-5 mg four times) daily.

Usual range without MCN36: 600-2000 mg.

Beyond 20 mg daily, classical lithium toxic symptoms appear.

Mineral-Mineral Interactions

Plasma lithium levels are undetectable, so mineral-mineral potentiation is pharmacodynamic (not pharmacokinetic).

Other aspects of routine lithium monitoring (thyroid, renal, etc.) remain necessary with **lithium "micro-dosing."**

Similarly potent mineral-mineral interactions are described at receptor sites, G proteins, and ATP.

Clinical Implications of Micronutrient Pharmacology

A patient's clinical transition from conventional to micronutrient treatment can be difficult to navigate:

- Discontinuing psychiatric drugs, so risk of relapse.
- Increase in psychiatric drug side effects.
- Potential psychiatric drug discontinuation effects potentiated by MCN36.

All happening concurrently.

Clinical Implications of Micronutrient Pharmacology

Transitioning from conventional to MCN36 treatment is tricky:

Do not try this on your own without training and available consultation.

When Learning to Use MCN36

Start with a “simple” patient with bipolar disorder.

Select a patient who has NOT received psychiatric or CNS drugs for at least several weeks or months.

And preferably a medication-naïve patient.

Learning Broad-Spectrum Micronutrient Treatment

Once you get a sense of the dynamics of this treatment, then work with a patient who is on a simple pharmacological regimen. For such patients, cross-tapering is typically conducted over a 2-4 week period.

Do not attempt to transition a patient recently treated with SSRIs or benzodiazepines until you have a good feel of the transition process in several simpler cases.

You will need a consultant to advise on patient suitability, to guide you through developing a cross-tapering schedule, how quickly to increase MCN36, when and how to lower the psychiatric drug doses, what to do if withdrawal effects appear, how to manage side effects, how to interpret adverse changes in behavior, and managing concurrent medical factors, selecting alternatives to CNS-active medications.

Initial Micronutrient Regimen for Patients with Current or Recent Use of CNS Agents

Prepare patients AND families for regression and include in consent documentation.

Expect benefits to be delayed by the transition complications (return of psychiatric symptoms, potentiated drug side effects, and potentiated withdrawal).

During the transition, most patients experience significant anxiety, due to symptom relapse, potentiated drug overstimulation, potentiated discontinuation, and related situational anxiety. {The anxiety can be managed by natural agents, especially balanced amino acid mixtures.}

Initial Micronutrient Regimen for Patients with Current or Recent Use of CNS Agents

Transition process may take days, sometimes weeks.

Rarely, a patient can be dysfunctional for some months before discontinuation effects of prior drug treatment resolve.

Most people do not miss any work or school.

Transitional complications may cease gradually or suddenly.

As transitional complications are residing, it becomes easier to evaluate treatment effects.

MCN36 Starting Regimen for Patients with **NO** Recent CNS Drug Use

Day 1	One pill three times daily.
Day 2	Two pills three times daily.
Day 3	Three pills three times daily.
Day 4	Four pills three times daily.
Day 5	Five pills three times daily.

Manage adverse effects, go slower if needed.

Basic Dosing Guidelines for MCN36

Modal dose 15 pills daily Taken as 5 pills three times daily.

Typical range 12-18 pills daily Same across weights and ages > age 8

Take with food, best in the *middle* of a meal. Aids absorption.

Administer no more than 6 pills at a time (calcium absorption is limited).

Best if doses are spread through day, but keep at least 2 hours between.

4 daily doses might be needed to sustain effect; 2 is rarely adequate.

Missed doses can be made up the next day.

Available in capsules, pills, or flavored powders for liquid consumption.

Starting MCN36 for Patients with Current or Recent CNS Drug Use

Rate of increase in dose of MCN36 is more gradual.

Speed of tapering medication dose depends on drug, duration of drug treatment, other concurrent medications, and the unfolding clinical course.

The cross-tapering procedure is especially complex for patients with current/recent use of benzodiazepines, SRIs, and psychiatric drugs with difficult withdrawal syndromes.

Get training and ongoing consultation.

Clinical Response

For Patients with **NO** Recent CNS Drug Use

Might see benefits beginning:

Mania	Within 5 days at full dose.
Depression	Within 4-8 weeks at full dose (longer if chronic or psychotic).

Approximately 80% responders in open-label trials to unmodified MCN36 by 2 months without conventional psychiatric medication.

For Patients **WITH** Recent CNS Drug Use

Benefits may be difficult to perceive until transition is complete.

Approximately 50% responders in open-label trials.

Database (Gately and Kaplan 2009):

53% responders (>50% symptom reduction) at 3 months.
Mean symptom reduction 41% at 3 months (45% at 6 mos).
Medication use reduced from 78% to 55% at 3 mos (44% at 6)
Probably more responders if MCN-experienced clinician.

Clinical Outcome: Opinion

Better response to MCN36 if no recent prior use of psychiatric medications.
Slower response and fewer responders than if recent CNS drug use.

Fewer adverse effects, especially cognitive.

Fewer residual symptoms.

No or lower doses of psychiatric medications.

Over time, increasing benefits for at least several months (as psychiatric medications wash out?)

More stable and even course than with conventional psychiatric medications

- Fewer dose adjustments
- Fewer doctor's visits
- Fewer relapses
- Fewer hospitalizations

Terminating MCN36 Treatment

Typical reasons

- Cannot tolerate the transition process, usually due to drug withdrawal problems.
- Lack of benefit.
- Cannot manage the number of pills involved.
- Cannot manage the uninsured cost.

Dose management

- If MCN36 treatment was brief, discontinue MCN36 without tapering and restore medication doses as tolerated.
- If stopped after longer use (> 2 weeks), medication doses may need to be gradually increased over days or weeks, as the micronutrient effects gradually subside.

Treating Residual Psychiatric Symptoms in Combination with MCN36

If mania, depression, or anxiety remain despite MCN36 treatment, residual symptoms are best treated by additional agents.

Unlike conventional psychiatric medications, certain agents can be combined with MCN36 without nutrient-drug interactions and untoward complications.

Note: The dose ranges for these agents are somewhat lower than usual *when* used with broad-spectrum micronutrients.

Treating Residual Mania in Combination with MCN36

Lithium in *micro-doses*

In combination with MCN36, typical dose range is 1 mg to 5 mg four times daily.

Choline bitartrate

In combination with MCN36, typical dose range is 50-100 mg four times daily.

Treating Residual Depression: SAMe in Combination with MCN36

SAMe (S-adenosyl methionine)

In combination with MCN36,
typical SAMe dose range is
200-400 mg each morning.

Without MCN36, usual SAMe dose is 400-800 mg.

Treating Residual Depression: 5HTP in Combination with MCN36

5HTP (5-Hydroxytryptophan)

In combination with MCN36

and decarboxylase inhibitor carbidopa

25 -50 mg each morning,

the typical 5HTP dose range is

0.01 to 1 mg each morning.

Without MCN36, usual 5HTP dose is 50-100 mg.

Treating Residual Anxiety in Combination with MCN36

Inositol

Typical dose range with MCN36 is

1,000-5,000 mg four times daily.

L-theanine

Typical dose range with MCN36 is

200-600 mg four times daily.

Amino acids

Balanced mixtures as tolerated.

Adverse Effects of MCN36

Vitamin and mineral toxicities are well-established in medicine.

Micronutrient Toxicities

Vitamin A (Retinoic acid)
- Dry mucous membranes
- Headache
- Insomnia
- Fatigue
- Hair loss
- Bone abnormalities - bone and joint pain
- Anorexia
- Vomiting
- Anemia
- Liver damage, hepatomegaly
- Hypercalcemia
- Hyperlipidemia
- Menstrual irregularities
- Spontaneous abortions, birth defects
- Dizziness
- Blurred vision / diplopia
- Muscular incoordination
- Birth defects

Vitamin B1 (Thiamine)
- Gastric upset

Vitamin B3 (Niacin)
- Vascular dilation, flushing
- Hyperuricemia
- Liver changes
- Nausea
- Heartburn
- Fatigue
- Dry hair
- Sore throat
- Inability to focus eyes
- GI irritation
- Increased muscle glycogen utilization
- Decreased serum lipids

Vitamin B5 (Pantothenic acid)
- Diarrhea
- Edema

Vitamin B6 (Pyridoxine)
- Dizziness
- Nausea
- Peripheral neuropathy
- Ataxia

Vitamin C (Ascorbic acid)
- Nausea, abdominal cramps, diarrhea
- Renal stones
- Mobilization of bone minerals
- Abortion
- Hemochromatosis

Vitamin D (Cholecalciferol)
- Nausea, vomiting
- Anorexia, weight loss
- Constipation
- Muscular weakness
- Joint pain
- Excessive thirst and urination
- Hypercalcemia

Vitamin E (Tocopherol)
- Gastric upset

Potassium
- Cardiac arrest

Calcium
- Anorexia
- Muscle weakness
- Lethargy, apathy
- Confusion, clouded consciosness
- Nausea, vomiting
- Constipation
- Shortened ST segments, arrythymias
- Hypertension
- Muscle weakness
- Myopathy
- Renal stones
- Calcification of heart, lungs, kidneys

Magnesium
- Diarrhea
- Nausea
- Anorexia
- Mental status changes
- Muscle weakness
- Difficulty in breathing
- Extremely low blood pressure
- Arrhythmias, bradycardia, vasodilation

Iron
- Constipation, diarrhea, bloody diarrhea
- Vomiting
- Hemosiderosis, hemochromatosis
- Cirrhosis
- Increased incidence of hepatoma
- Diabetes
- Cardiac failure

Zinc
- Copper deficiency
- Reduced HDL
- Reduced immune function
- Stomach cramps, nausea, and vomiting
- Pancreas damage
- Gastrointestinal irritation, vomiting,
- Microcytic anemia

Iodine
- Goiter, hypothyroidism

Selenium
- Nausea, abdominal pain, diarrhea
- Fatigue, irritability
- Hair loss
- White blotchy nails
- Peripheral neuropathy

Copper
- Liver damage
- Weakness
- Nausea, diarrhea, gastric pain

Manganese
- Psychosis
- Parkinsonian syndrome

Molybdenum
- Gout
- Copper deficiency

Vanadium
- GI symptoms
- Depressed growth
- Green tongue

Nickel
- GI symptoms

No Known Micronutrient Toxicity at Any Dose:

- Riboflavin (Vitamin B2)
- Folate (Vitamin B9)
- Cyanocobalamin (Vitamin B12)
- Biotin (Vitamin H)

Micronutrient Toxicity is Not Strictly Dose-Dependent

Certain forms of micronutrient toxicity can be increased OR decreased by the balance of other micronutrients.

That is, toxicity can be adequately countered by an appropriate balance of other micronutrients, or aggravated by an inappropriate balance.

Safe levels of intake for various single vitamins and minerals are well studied and are continually updated by governmental standards.

However, given potentiating interactions among micronutrients, the safety of a combination of micronutrients cannot be inferred from the safety data on individual ingredients.

Micronutrient Toxicity

Although “multivitamins” are generally presumed safe,
nutrient-nutrient interactions are significant,
so controlled studies of any micronutrient formulation
will be required before safety claims can be made.

Despite such uncertainties about micronutrient formulations,
they appear safer than psychiatric drugs,
even at relatively high doses,
at least in balanced broad-spectrum formulations.

Adverse Effects of MCN36

Common	
Loose stools, semi-formed diarrhea	Usually transient.
Nausea	Take with more food and water.
Insomnia	Move last dose earlier.
Headache	Temporarily lower dose.
Anxiety, agitation, impulsivity, mania	Increase ***or decrease*** dose.
Candida (yeast) infection	MCN36 can induce or aggravate.
“Neon” yellow urine	Not a problem (B2 excretion).
Uncommon	
Vomiting	Take with more food and water.
Flatulence	Simethacone.
Watery diarrhea	Green bananas, or briefly reduce MCN dose.

Other Potential Risks

Suicide

One report of suicidal overdose of multivitamins in the medical literature.

Overdose

Accidental multivitamin ingestion is the most frequent inquiry to pediatric poison control centers, mostly pre-school children; 1/3 require treatment, 0.3% life-threatening due to iron overload.

Physical Dependence and Withdrawal

No known cases of physical dependence or discontinuation syndrome with MCN36 or micronutrients generally.

Contraindications

Strict contraindications

Wilson's disease	re copper
Hemochromatosis	re iron
Phenylketonuria	re phenylalanine
Trimethylaminuria	re choline
Prostate cancer	
? Other cancers	

Micronutrients May Increase the Spread of Prostate Cancer

Prospective study of 295,000 men Lawson et al. 2007

Three of the most commonly used commercial vitamin brands were examined.

Increase in prostate cancer:

- 32% increase in metastatic prostate cancer.
- 98% increase fatal prostate cancer.
- No increase in new-onset or localized (non-metastatic) cancer.

So no evidence of causing (new) cancer, but may increase the spread of metastases and death in prostate cancer, especially if PC family history.

Observed when multivitamins were used *more than once* daily, not when taken once daily.

Contraindications

Prostate cancer

Consider broad-spectrum micronutrient treatment as

- contraindicated in men with prostate cancer,
- probably in men with elevated PSA's, and
- possibly in all older men with a family history of prostate cancer.

Other cancers, too ??

Contraindications

Relative contraindications

- Recreational drug dependence.
- Recent use of medical drugs with withdrawal syndromes.
- Necessary medical treatment with CNS-active agents.
- Treatment-resistant Candida.
- Infections requiring chronic or repeated antibiotic (or antifungal) treatment.
- Autoimmune thyroid disease or nodular goiter (iodine).
- Liver or renal disease.
- High alcohol intake, hyperlipidemia, or severe protein malnutrition (increased susceptibility to Vit. A toxicity).
- ?Pregnancy

Pregnancy

Relative contraindication?

No large-scale systematic studies.

But broad-spectrum micronutrients are healthy for the fetus, and are routinely recommended to pregnant mothers.

Vitamin A toxicity to the fetus

In pregnancy, Upper Limit (UL) for Vitamin A is 3,000 µg/d (or 2,800 µg/d if mother < 18 yo).

MCN36 contains 1,920 µg in a daily dose of 15 pills.

Contraindication? or Potential Indication?

Medical Monitoring

Baseline medical evaluation

Baseline physical examination, esp. re vitamin or mineral toxicity.

Baseline laboratory tests are not required:

- CBC with differential
- Fasting blood glucose
- AST, ALT, Bili-T
- Creatinine and BUN
- Thyroid stimulating hormone
- Albumin, Uric acid
- PT, PTT, INR
- Iron, ferritin
- Potassium, Sodium, Calcium, Magnesium, Copper
- Lipid panel
- Vitamins A and D
- Urinalysis
- EKG

Periodic follow-up is optional: PE and lab tests every 6-12 months.

Course of Treatment

Course of Treatment:
If symptoms return during treatment…

First, examine for presence of interfering factors:

- Start/change CNS-active medications (psychiatric, medical, OTC).
- Use of caffeine, smoking, alcohol, marijuana, abusable drugs.
- Oral antibiotics.
- Systematic infection, such as Candida.
- Gastrointestinal symptoms affecting nutrient absorption; use of laxatives, antacids, and proton pump inhibitors.
- Recurrent or chronic medical conditions.
- Treatment noncompliance.

Consider possibility of delayed drug withdrawal.

Re-optimize micronutrient intake by trying both higher and lower doses (A return of previously stable psychiatric symptoms might require an increase OR decrease in micronutrient dose).

MCN36 Appears to have Fewer Cognitive and Emotional Adverse Effects Compared to Conventional Psychopharmacological Treatment

Virtually every adult who successfully transitions from conventional to MCN36 treatment reports a striking difference in mental clarity.

Almost to a person, patients describe less “brain fog” and mental slowness than MCN36 compared to traditional medications.

Many say that they had not been aware of their long-term drug-induced cognitive slowness and emotional “sludge” until after transitioning to micronutrients.

Catastrophic Psychological Reactions

On completing the transition from conventional to micronutrient treatment, about 5-10% of patients experience the “shock” of realizing that they had spent many years in mental disease or drug-induced dysfunction, which they can now examine from a psychological distance.

This perspective can be harshly distressing for some individuals, who may need considerable support in mourning the past and accepting the increased expectations by self and others.

This is clinically very distinct from a depressive reaction.

Clinical opinion: I have never observed this with a psychopharmacological treatment.

“Superbabies”

Some mothers who used MCN36 during pregnancy have given birth to children who are reported to appear unusually healthy.

Anecdotes of babies who, compared to siblings, appear calmer, more attentive, less fussy, less crying, fewer heatlh problems, and show more rapid developmental attainments.

Unpublished:

107 women on MCN36 during pregnancy:

Low miscarriage rate: < 5% (vs. 8-25% in general population).

Virtually no birth defects (vs. 3% in general population).

Large-scale systematic data are lacking.

First-line Use?

Not recommended for general use:

Lack of controlled trials regarding safety or efficacy.

Perhaps defensible in some cases if presentation is mild and non-acute.

“Low clinical risk to delaying established treatment” must be clearly supported in chart documentation.

Caution: Clinician’s responsibility to manage a patient’s potentially excessive enthusiasm for a treatment.

Clinical Opinion: Summary

Unproven but probable mood-stabilizing and antidepressant effects.

Compared to standard psychopharmacological treatment:

- *Fewer adverse effects*
- *Fewer residual symptoms*
- *Fewer relapses*
- *Fewer hospitalizations*
- *Fewer dose adjustments*
- *Fewer doctor's visits*

But…

Clinical Opinion: Summary

But:

- *Lack of controlled safety data.*
- *Lack of controlled efficacy data.*
- *Worsening of certain infections and possibly certain cancers.*
- *Difficulty of transitioning from conventional medications.*
- *Not for certain patients, such as drug abusers.*
- *No insurance reimbursement.*
- *More out-of-pocket expense: $150 monthly.*

Clinical Recommendations: Opinion

With safety and efficacy are not established, this treatment is not ready for general use by the public. Established conventional psychiatric drug treatments remain the standard of care.

In selected cases, some clinicians may want to offer the treatment, with carefully informed consent (lack of controlled safety and efficacy data, risk of relapse, drug interactions, cancer question, Candida, availability of established treatments).

Start with an unmedicated patient with bipolar or major depressive disorder in a mild, non-acute, low-risk presentation. Training and consultation are advisable for management of adverse effects and intercurrent medical complications.

Clinicians without specialized training and supervisory consultation should not attempt to transition patients from conventional to micronutrient treatment.

Nutrients with Mood-Stabilizing Properties

Lithium

Omega-3 fatty acids

MCN36

Clinical Indications

Established indications

- **None**

Probable (future) indications

- Bipolar disorder
- Major depressive disorder

Speculative Uses

- Dysthymic disorder
- Postpartum depression
- Depressive anxiety
- Obsessive compulsive disorder
- (ADHD)
- Aggression and antisocial behavior in incarcerated criminals

Potential Applications for Broad-Spectrum Micronutrients

Other psychiatric disorders

E.g., anxiety disorders, OCD, ADHD, eating disorders, autism.

In investigating other psychiatric indications, researchers will need to deal with the possibility that observed symptom improvements may be due to indirect effects mediated by MCN36 effects through the comorbid mood disorder (or even just concurrent mood!) and related functional gains.

For some psychiatric conditions, studies on subjects without comorbid mood disorders may be preferred.

Imaginable Applications for Broad-Spectrum Micronutrients

Cognition and mood in normal subjects.
Neurological conditions; e.g., seizures, migraine.
General medical disorders; e.g., vascular, immunological.
Neurorecovery; e.g., nerve injury.
Neuroprotection; e.g., Alzheimer's, neurodegenerative disorders
Neurodevelopmental disorders; e.g., learning disorders, autism.
Prevention
Pregnancy
Enhancement of general health
- **Sleep architectural improvement**
- **Anti-aging**
- **"Normal" development:**
  - **Stronger bodies, better brains, "superbabies"**
  - **"Everyone above average"**

Super-Pooch

Development aided by Broad-Spectrum Micronutrients

The Future of Nutritional Psychopharmacology: Over-the-Counter Self-Treatment of Bipolar Disorder?

Even if nutritional treatments become trivially easy, psychiatric patients will still need help with:

- Lack of awareness of symptoms or severity.
- Identification of medical causes and mimics of psychiatric symptoms.
- Diagnosis and management of comorbidity.
- Education about illness.
- Psychological support and psychodevelopmental treatment.
- Diagnosis and treatment of psychiatric disorders in family members (a child's parents, a parent's children).
- Education, support, and management counseling for family.

Commercial Implications

Micronutrients are potential low-cost alternatives to expensive pharmaceuticals.

Vitamins and minerals are not patentable.

Multinutrient formulas are patentable, but patent protection is weak.

Brand names are patentable, with added value if attached to scientific research.

Research Needs

Clinical studies on safety and efficacy of micronutrient combinations in psychiatric, neurological (seizures, migraine, nerve injury, etc.), and medical disorders and other applications, such as pregnancy, prevention, developmental enhancement, and anti-aging.

Individualization of micronutrient formulations aimed at specific health goals.

Investigations into mechanisms involved in different applications.

- Nutrient interaction with enzymes, genes, receptors, membranes, etc.
- Nutrient-nutrient interactions at these sites.
- Drug-nutrient interactions at these sites.
- Alterations in physiology and systems characteristics in different micronutrient environments.

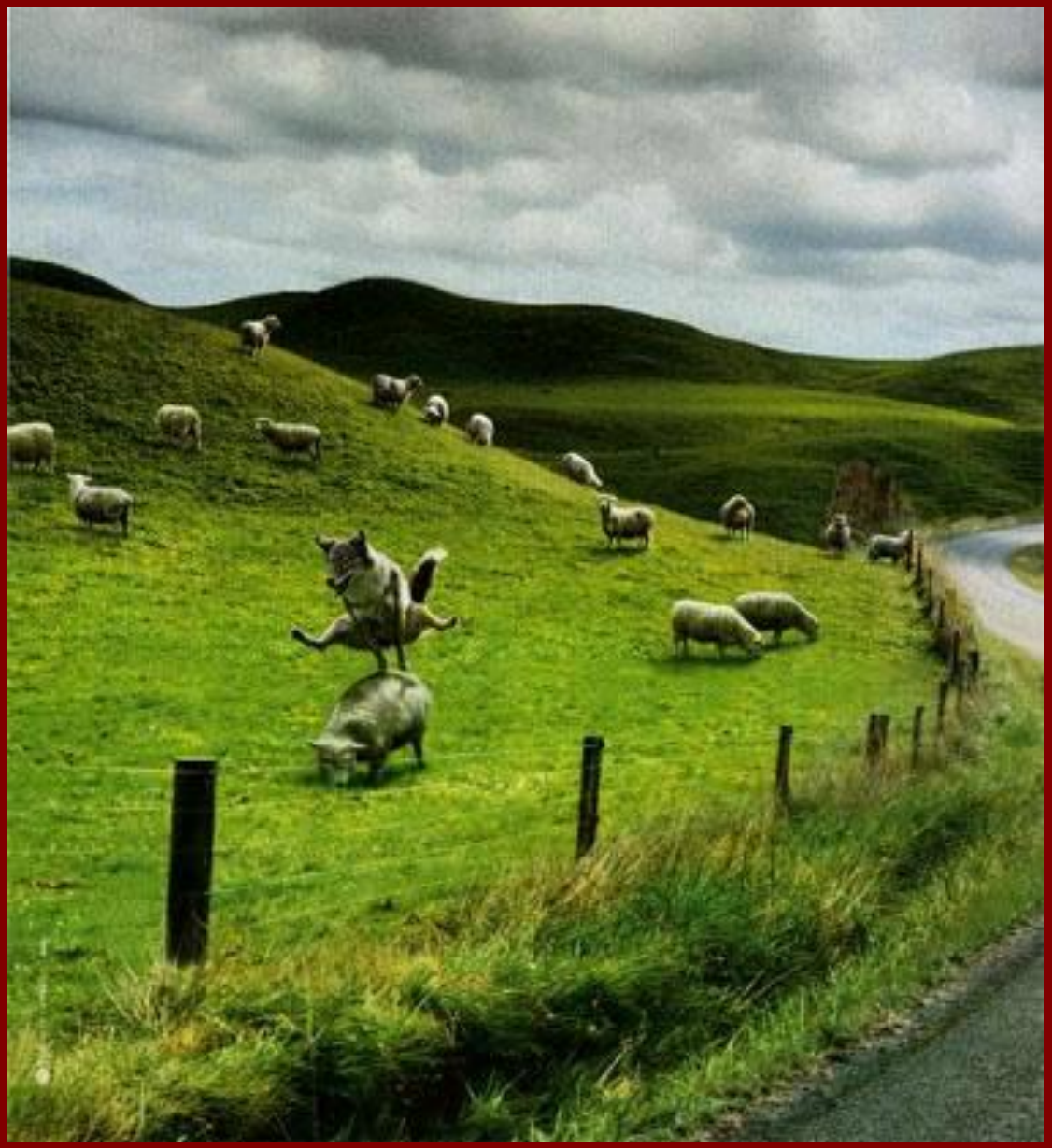
Policy Needs

Legal and regulatory changes to foster research (INDs for multi-ingredient products), commercial development of micronutrient products, FDA marketing approval (nutraceuticals for specific disease indications, not just general health claims) and quality control, and insurance coverage for specific nutritional treatments once controlled studies of safety and efficacy are available.

Governmental, university, and private programs to promote improved nutrition in institutions (schools, corporations, prisons) and for the general public.

Policies aimed at improving agricultural methods (e.g., soil management, nutrient repletion).

Yooki before Micronutrients



Yooki on Micronutrients

Micronutrients for Mental Health Association

presents a workshop on

Micronutrient Treatment and Research for Mental Health

May 14-16, 2010

Truckee, CA (near Reno)

Registration: 1-866-397-2209

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Mechanisms of Micronutrient Action

EVERY biological function, including (briefly):

- Modulate gene expression.
- Modulate enzyme activity as cofactors.
- Alter neurotransmitter metabolism.
- Change drug biotransformation.
- Transform receptors or ion channels.
- Modify membrane fluidity.
- Influence second or third messenger systems.
- Alter the action of other nutrients and other molecules, including medications; e.g., interactions at receptors, channels, etc.
- Vary the absorption of other nutrients.