Learning objectives:

- Become aware of a new treatment for bipolar disorder.

- Identify possible mechanisms that could explain the efficacy of this treatment.

- Learn about the role of nutrient deficiency in mental function.

Disclaimer

- In April 2000 the supplement we are studying was assigned a name (E.M.Power) and is being manufactured and sold by Evince International in Salt Lake City, Utah.

- Contracts are in place to ensure that no investigator or co-investigator will personally benefit from the sale of this product.

Abstract

Recent research on various nutrients has suggested that some mental illness might be ameliorated by supplementation. Much work has focused on essential fatty acids (1), although various minerals are also being studied (especially zinc). We are evaluating a broad-based nutritional supplement that contains primarily trace minerals, plus vitamins and amino acids. Recent work has suggested that crops grown with western farming methods contain fewer of these essential nutrients than they did in years past (2). Although we have been examining the effects of the supplement on a variety of psychiatric symptoms in both children and adults, it appears to be particularly promising for bipolar disorder in adults. We will present an open case series of 10 male patients aged 20-46 years who thus far have taken the supplement for 1.5 - 6 months. Four were diagnosed with Bipolar I, four with Bipolar II, one with Bipolar Mixed, and one with Bipolar-NOS. In most cases, the supplement has

Abstract (continued)
entirely replaced psychoactive medications and the patients have remained well. Side effects (e.g., nausea) have been rare, minor, and transitory. In all cases, the patients have been evaluated periodically with the Hamilton-Depression Scale, the Brief Psychiatric Rating Scale, and the Young Mania Rating Scale. The change in mean scores for each scale from study entry to the time of the last visit are as follows: Ham-D (20.4 to 8.2), BPRS (37.3 to 9.9), YMRS (16.8 to 6.1), and OQ (75.2 to 48.2). A randomized, placebo-controlled trial of the supplement for Bipolar I has been funded and began in July 2000.

References:

1. Stoll AL, Severus E, Freeman MP, Rueter S, Zboyan HA, Diamond E, Cress KK, Marangell LB: Omega 3 fatty acids in bipolar disorder: A preliminary double-blind, placebo-controlled trial. Archives of General Psychiatry 1999; 56:407-412.
2. Mayer AB: Historical changes in the mineral content of fruits and vegetables. British Food Journal 1997; 99:207-211.

Introduction

- Recently, a nutritional intervention involving essential fatty acids was shown to ameliorate bipolar symptoms (Stoll et al., 1999). Other supplement research is being carried out around the world.

- In Alberta, two gentlemen successfully experimented with nutritional interventions to treat bipolar disorder in their own relatives and ultimately put together a broad-based supplement which is becoming quite popular amongst mental patients in our area.

- Our research team became involved in the evaluation of this supplement.

- As a first step, we have compiled data systematically on a case series of adults with bipolar disorder.

- A randomized placebo-controlled trial has also been started in July.

Methods

Patients

- 10 male patients aged 20-46 years: Bipolar I (n=4), Bipolar II (n=4), Bipolar Mixed (n=1), Bipolar NOS (n=1) (See Table 1 for description of sample.)

Measures

- Each patient was assessed periodically with the Hamilton-Depression Scale (Ham-D), Brief Psychiatric Rating Scale (BPRS), Young Mania Rating Scale (YMRS), and the Salt Lake City Outcome Questionnaire (OQ).

Intervention

- The nutritional supplement focuses mainly on minerals, but also contains a number of vitamins known to be important for brain function (Table 2).
- 34 of its 36 ingredients are normal, dietary constituents, although at higher-than-usual doses. The other two are antioxidants.
- Because of the bulkiness of many dietary minerals (e.g., calcium), the full dose required initially (and tested here) is 8 capsules q.i.d.

Results

- As of this time, the patients have been on the supplement anywhere from 15-68 weeks.

- The improvement on all outcome measures is statistically significant (refer to Figures):
  - Ham-D $t(7) = 5.29$, $p<.01$
  - BPRS $t(9)=2.89$, $p<.05$
  - YMRS $t(8)=4.90$, $p<.01$
  - OQ $t(5)=2.02$, $p=.10$

- The total number of psychotropic medications for the overall sample dropped from **28 to 10** (Table 3).

- Compliance has been a problem with two patients (#1008, #1011). They are both now returning to the supplement and will be monitored.

- Side effects were rare, minor (nausea), and transient.

Discussion

- The nutritional supplement was generally beneficial for this group of patients.

- These patients were not selected: they were the first 10 for whom we had systematic data.

- The patients themselves sometimes can distinguish medication-induced symptom reduction from the improved health they experience while on the supplement (which they preferred).

- A randomized, placebo-controlled trial has been funded by the Alberta Science and Research Authority, and began in July. Patients in the RCT are being restricted to the diagnostic category of Bipolar I.

Table 1. Description of Sample

Pt #	age	Time since Dx	Past Meds	ECT?/Hospitalizations?
1001	21 yrs	2 yrs	sertraline, imipramine, paroxetine, fluoxetine, bupropion, chlorpromazine, clonazepam, zolpidem, risperidone, nortriptyline, valproic acid, lithium, benztropine, buspirone, diazepam, trazodone, dextro-amphetamine, methylphenidate	No/No
1002	19 yrs	3 yrs	sertraline, carbamazepine, clonazepam, lamotrigine, quetiapine, clomipramine, paroxetine, valproic acid, lithium, risperidone, thioridazine, haldoperidol, nortriptyline, imipramine, fluoxetine, fluvoxamine, desipramine	Yes/Yes
1003	23 yrs	4 yrs	pemoline, dextro-amphetamine, fluoxetine, bupropion, sertraline, venlafaxine	No/No
1008	20 yrs	3 yrs	imipramine, desipramine, methylphenidate, sertraline, fluoxetine, valproic acid, paroxetine, lithium, venlafaxine	No/No
1011	21 yrs	3 yrs	paroxetine, fluoxetine, clonazepam, zolpidem	No/Yes
1014	45 yrs	3 yrs	methylphenidate, fluoxetine, lithium, valproic acid, thiozidazine, trifluoperazine, bupropion, dextro-amphetamine, venlafaxine	No/Yes
1015	34 yrs	16 yrs	lithium, zolpidem, desipramine, clonazepam, alprazolam, risperidone, trazodone, venlafaxine, sertraline, fluoxetine, valproic acid	No/No
2002	46 yrs	7 yrs	olanzapine, lithium, valproic acid, clozapine, gabapentin, fluoxetine, bupropion, rivotril, lamotrigine, quetiapine	Yes/Yes
2010	21 yrs	3 yrs	valproic acid, paroxetine	No/Yes
2011	31 years	2 yrs	valproic acid, lithium, lamotrigine, sertraline, olanzapine, serzone, gabapentin, venlafaxine, chlorpromazine, lorazepam, fluvoxamine, l-thyroxine, dextro-amphetamine, citalopram, methotrimeprazine	No/Yes

TABLE 2: E.M.Power Ingredients

Serving Size 8 Capsules, Servings per container = 56

	Amount Per serving	% Daily Value
Vitamin A (as retinyl palmitate)	**3,333 IU**	**67%**
Vitamin C (as ascorbid acid)	**250 mg**	**417%**
Vitamin D (as cholecalciferol	**400 IU**	**100%**
Vitamin E (as d-alpha tocopheryl succinate)	**100 IU**	**333%**
Vitamin B1 (as thiamine mononitrate)	**5 mg**	**333%**
Vitamin B2 (as riboflavin)	**5.5 mg**	**324%**
Vitamin B3 (as niacinamide)	**25 mg**	**125%**
Vitamin B6 (as pyridoxine hydrochloride)	**7 mg**	**350%**
Vitamin B9 (as folic acid)	**400 mcg**	**100%**
Vitamin B12 (as cyanocobalamin)	**250 mcg**	**4167%**
Biotin	**25 mcg**	**8%**
Pantothenic acid (as d-calcium pantothenate)	**6 mg**	**60%**
Calcium (as calcium complex*, calcium amino acid chelate)	**550 mg**	**55%**
Iron (as iron amino chelate, iron complex*)	**6 mg**	**33%**
Phosphorous (phosphorous complex)	**350 mg**	**35%**
Iodine (from kelp)	**75 mcg**	**50%**
Magnesium (as magnesium amino acid chelate, magnesium complex)	**250 mg**	**63%**
Zinc (as zinc amino acid chelate, zinc complex*)	**20 mg**	**133%**
Selenium (as selenium amino acid chelate, selenium complex*)	**100 mcg**	**143%**
Copper (as copper amino acid chelate, copper complex*)	**3 mg**	**150%**
Manganese (as manganese amino acid chelate, manganese complex)	**4 mg**	**200 %**
Chromium (as chromium amino acid chelate, chromium complex*)	**250 mcg**	**208%**
Molybdenum (as molybdenum amino acid chelate, molybdenum complex)	**66 mcg**	**88%**
Potassium (as potassium complex*)	**100 mg**	**3%**

dl-Phenylalanine	**300 mg**	****
Glutamine (as l-glutamine)	**150 mg**	****
Citrus Bioflavonoids (from peel)	**100 mg**	****
Grape Seed (*Vitis rinitera)*	**25 mg**	****
Choline (as choline bitartrate)	**100 mg**	****
Inositol	**33.3 mg**	****
***Ginkgo biloba* (from leaf)**	**20 mg**	****
Methionine (as l-methionine)	**16.6 mg**	****
Germanium (as *Germanium sesquioxide)*	**10 mg**	****
Boron (as boron amino acid chelate)	**1 mg**	****
Vanadium (as vanadium amino acid chelate, vanadium complex*)	**500 mcg**	****
Nickel (as nickel amino acid chelate, nickel complex*)	**67 mcg**	****

***Saccharide complex** ****Daily Value not established.**

TABLE 3: MEDICATIONS

Patient ID	Meds at Entry	Time on Supplement	Current Medications
1001	risperidone, zolpidem, nortriptyline, clonazepam, lithium	40 weeks	gabapentin, risperidone, clonidine
1002	clonazepam, carbamazepine, propanolol, sertraline, lamotrigine, quetiapine	45 weeks	lamotrigine
1003	None	41 weeks	none
1008	None*	32 weeks	nortriptyline
1011	paroxetine**	20 weeks	none
1014	lithium, fluoxetine, venlafaxine, methylphenidate	68 weeks	nortriptyline
1015	zolpidem, clonazepam	26 weeks	zolpidem for sleep
2002	lamotrigine, rivotril, lithium, quetiapine	34 weeks	quetiapine
2010	valproic acid, paroxetine	28 weeks	lorazepam for sleep
2011	lithium, sertraline, valproic acid, lorazepam	15 weeks	lithium

***Note from his psychiatrist: He was on many medications prior to entry with no success. He experienced a profound depression so he quit all meds 1 month prior to entry. His depression resolved only on the supplement. He stopped the supplement over the summer, regressed, and just began taking them again last month.**

****Note from his psychiatrist: He went off the supplement over the summer and regressed. He is just now restarting the supplement.**