JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 14, Number 1, 2004

Pp. 115–122

Case Report

Improved Mood and Behavior During Treatment with a Mineral-Vitamin Supplement: An Open-Label Case Series of Children

Bonnie J. Kaplan, Ph.D.,[1,2] Jennifer E. Fisher, M.D.,[3] Susan G. Crawford, M.Sc.,[2] Catherine J. Field, Ph.D., R.D.,[4] and Bryan Kolb, Ph.D.[5]

ABSTRACT

Several studies have demonstrated that psychiatric symptoms such as depression, mood swings, and aggression may be ameliorated by supplementation with broad-based nutrient formulas containing vitamins, minerals, and sometimes essential fatty acids. These findings have been reported in young criminal offenders as well as in adults with mood disturbance and other psychiatric disorders. The purpose of the current case series was to explore the potential efficacy of a nutrient supplement in children. Children with mood and behavioral problems (N = 11; 7 boys, 4 girls; 8–15 years old) participated; 9 completed this open-label trial. Parents completed the Child Behavior Checklist (CBCL), Youth Outcome Questionnaire (YOQ), and Young Mania Rating Scale (YMRS) at entry and following at least 8 weeks of treatment. Intent-to-treat analyses revealed decreases on the YOQ ($p < 0.001$) and the YMRS ($p < 0.01$) from baseline to final visit. For the 9 completers, improvement was significant on seven of the eight CBCL scales, the YOQ, and the YMRS (p values from 0.05–0.001). Effect sizes for all outcome measures were relatively large. The findings suggest that formal clinical trials of broad nutritional supplementation are warranted in children with these psychiatric symptoms.

INTRODUCTION

Most would agree that good nutrition is fundamental for good physical health. In contrast, the role of nutrition in maintaining good mental health is still a matter of considerable debate in spite of the fact that the importance of micronutrients (i.e., vitamins and minerals) for normal brain function is well established by decades of scientific research. For example, low levels of minerals such as zinc, calcium, and iron have been found in association with psychiatric symptoms (Benton and Donohoe 1999; Dubovsky et al. 1994; Maes et

[1]Departments of Paediatrics and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada.
[2]Behavioural Research Unit, Alberta Children's Hospital, Calgary, Alberta, Canada.
[3]Department of Psychiatry, University of Calgary, Calgary, Alberta, Canada.
[4]Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada.
[5]Department of Psychology, University of Lethbridge, Lethbridge, Alberta, Canada.

al. 1997). Supplementation studies have demonstrated improved mental function and mood following treatment with selenium, iron, and B vitamins, amongst others (Benton and Cook 1991; Benton et al. 1997; Hoffer 1999; Sandstead et al. 1998). Although less commonly investigated, multi-ingredient interventions have also positively affected mood and aggressive behavior (Benton et al. 1995; Carroll et al. 2000; Gesch et al. 2002; Schoenthaler and Bier 2000). A growing body of research has focused on the role of essential fatty acids in brain function, and intervention studies have demonstrated benefit from essential fatty acid supplementation for patients with various psychiatric symptoms (Nemets et al. 2002; Peet and Horrobin 2002; Richardson and Puri 2002).

Recently, research has been published on a broad micronutrient supplement consisting of chelated minerals and vitamins called E.M.Power+. In two children studied in ABAB reversal designs, on-off control of mood lability and explosive rage was reported with this micronutrient formula (Kaplan et al. 2002). The same formula used in adults with bipolar disorder resulted in a large treatment effect size using standard measures of depression and mania (Kaplan et al. 2001). Replications have been published by two psychiatrists who tracked approximately 20 clinical patients each (Popper 2001; Simmons 2002). In a preliminary evaluation of the potential benefit of this supplement for children with unstable mood, an open-label case series in children with mood and behavior problems was carried out.

METHODS

Participants

To enter this study, children with unstable mood and behavioral problems (e.g., 2-hour tantrums, explosive rage) had to be clinically diagnosed with an anxiety, mood, or behavioral disorder by the referring clinician and had to be on a stable psychiatric medication regimen as judged by their physician. A well-established clinical history of such symptomatology was chosen rather than a specific diagnostic category because (a) the prior literature on micronutrient supplementation has focused on symptom amelioration rather than diagnostic categories (e.g., the work of Gesch et al. 2002), and (b) children with these types of problems often receive various diagnoses depending on their age and the clinician responsible for diagnosis. Exclusion criteria included current use of antibiotics, presence of any unstable medical condition, or known abnormality of metabolism. Eleven children (7 boys, 4 girls; mean age = 11.4 years, SD = 2.6 years) participated; 6 had been diagnosed and referred by their psychiatrists, 4 by developmental pediatricians, and 1 by a clinical psychologist. Physical examinations over the years revealed no abnormalities; these were all healthy children, other than their mood and behavioral difficulties. Each family was knowledgeable about standard pharmacological treatments for their children, and in 9 of the 11 cases the children had already tried several such medications. There were no exclusions. The 11 patients described here were the first 11 referred. The only concurrent intervention was the psychiatric medication intake by 5 of the patients (Table 1).

The available safety and toxicity information was provided to each family, and the rationale for this research was presented. The research protocol was reviewed and approved by the local Faculty of Medicine ethics committee. Written informed consent was obtained from parents, and written assent was obtained from children.

Intervention

The supplement was manufactured and distributed under the name E.M.Power+ at the time of this trial. It consisted of 36 minerals, vitamins, amino acids, and antioxidants, in quantities that are higher than a person's usual level of daily dietary intake (Kaplan et al. 2001). Improved technology has now reduced the dosage to 18 capsules per day and has also resulted in a powder form mixed in juice, but the data reported herein were collected with the previous version that required 32 capsules per day: 8 capsules taken four times daily with food. The precise formulation employed in this case series can be found in the Appendix. The newly available formulation, employing

TABLE 1. CLINICAL DATA BY SUBJECT

Patient no.	Sex/age	Disorder	Medications at entry	No. weeks on supplement	Medications at final visit
1	Female/10 years	Bipolar, ADHD, ODD	None	11	None
2	Female/15 years	Asperger, GAD[a]	Fluoxetine 40 mg, risperidone 0.25 mg bid	17	Fluoxetine 20 mg every 2nd day, risperidone 0.25 mg bid
3	Female/10 years	Bipolar	None	13	None
4	Male/9 years	ADHD + mood lability	None	14	None
5	Male/14 years	ADHD, ODD, GAD, depression	Dextroamphetamine 40 mg, desipramine 50 mg qhs	12	Dextroamphetamine 25 mg
6	Male/14 years	Prader-Willi syndrome, ODD, anxiety[a]	Paroxetine 15 mg/day Risperidone 0.5 mg/day	16	Paroxetine 10 mg/day Risperidone 0.5 mg/day
7	Male/8 years	ADHD, rage	None	17	None
8	Male/10 years	Bipolar, anxiety	None	15	None
9	Male/10 years	ADHD, ODD, anxiety[a]	None	8	None
10	Female/15 years	Asperger, OCD, GAD	Risperidone 1 mg tid	5	Risperidone 1 mg tid
11	Male/10 years	ADHD + mood lability	Methylphenidate SR 40 mg/day	1	Methylphenidate SR 40 mg/day

ADHD = attention deficit hyperactivity disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder.

[a]Several children with anxiety had some degree of anxiety-related obsessional thoughts but did not reach the level of severity for clinical diagnoses of OCD.

the lower dose, is now called Empowerplus and can be found on the manufacturer's Website: www.truehope.com.

Safety issues

In unpublished pilot work, 12 children were monitored repeatedly while taking the supplement for 16 weeks: heart rates, blood pressures, and blood and urine samples remained normal. In addition, the help line that monitors patients for the company manufacturing this supplement has kept track of over 4,000 individuals taking this supplement, with few difficulties reported other than the known interactions with psychiatric medications (Popper 2001).

Measurement of outcome

At study entry and completion, the Child Behavior Checklist (CBCL; Achenbach 1991) was completed by parents. Principal components analyses of the CBCL have revealed eight syndromes across ages, sexes, and informants (i.e., parents vs. teachers): Withdrawn Behavior, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. The Anxious/Depressed scale, of greatest importance to the current investigation, has high internal consistency (above 0.85) as well as test-retest reliability (above 0.74) (Mash and Terdal 1997).

Each follow-up visit involved completing the Young Mania Rating Scale (YMRS; Young et al. 1978), an 11-item scale that covers symptoms such as irritability and disruptive aggressive behaviors, and the Youth Outcome Questionnaire (YOQ; Burlingame et al. 1998), a 64-item checklist measuring mood and behavior for children ages 4–17 years.

Design and procedures

At the first appointment, the experimental nature of the treatment was described to each

family; the inclusion/exclusion criteria were reviewed; and the CBCL, YOQ, and YMRS were completed. The YMRS was problematic; some parents found it too difficult to apply the adult-oriented items to their children and asked to exclude it.

Although designed as an eight-visit, 8-week trial, summer vacations, illnesses, and other events intervened so that the actual number of weeks required to obtain eight follow-up visits ranged from 8–17 (mean trial duration = 13.6 weeks, SD = 2.9 weeks).

Physicians were free to adjust medications during the trial but were informed of the medication interactions observed in adult trials (Popper 2001). Hence, they generally chose a cautious approach of minimizing medications during the trial.

RESULTS

Withdrawals

Two children withdrew prematurely. A 15-year-old girl (see Table 1, subject 10) with severe pervasive developmental disorder and generalized anxiety began the supplement at one quarter the recommended dose because of uncertainty regarding medication interactions. Subsequent attempts to increase the dose were associated with increased anxiety, and the patient withdrew from the study. The other noncompleter was a 10-year-old boy (see Table 1, subject 11) with attention deficit hyperactivity disorder and mood swings, who was taking 40 mg/day of methylphenidate concurrently. After 1 week on the combination, the family reported extreme anger and mood lability. In spite of the physician's recommendation to decrease the methylphenidate, the boy refused to do so and instead withdrew from the study.

Intent-to-treat analyses

Paired t tests revealed significant decreases in scores between baseline and final visit for the YOQ, $t(10) = 5.66$, $p < 0.001$, and the YMRS, $t(5) = 5.89$, $p < 0.01$. The CBCL could not be analyzed on an intent-to-treat basis, because the two children who withdrew had CBCL data only at study entry.

Completer analyses

For the nine children who completed the study (defined as taking the supplement for a minimum of 8 weeks), paired t tests revealed significantly lower scores after treatment for the following CBCL scales (Fig. 1): Withdrawn Behavior, $t(8) = 3.79$, $p < 0.01$; Anxious/Depressed, $t(8) = 2.97$, $p < 0.05$; Social Problems, $t(8) = 2.89$, $p < 0.05$; Thought Problems, $t(8) = 3.67$, $p < 0.01$; Attention Problems, $t(8) = 3.85$, $p < 0.01$; Delinquent Behavior, $t(8) = 3.71$, $p < 0.01$; and Aggressive Behavior, $t(8) = 3.46$, $p < 0.01$. Only the Somatic Complaints scale did not change.

At study entry, at least two thirds of the children scored in the clinical range (70 or higher, reflecting 2 SD above normative means) on the Anxious/Depressed, Social Problems, Attention Problems, and Aggressive Behavior scales on the CBCL. By the end of the trial, none of the children had elevated scores on the Withdrawn Behavior or Anxious/Depressed scales. Only one child had elevated scores on each of the following scales: Somatic Complaints, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. On the other hand, three of the six children high on Social Problems at baseline were still elevated at the end of the trial.

The YOQ also showed significant improvement posttreatment; $t(8) = 5.97$, $p < 0.001$. The manual for the YOQ suggests that a decrease of at least 13 points is clinically significant (Burlingame et al. 1998) and that a cutoff for normal functioning should be at 46. At study entry, all children had scores greater than 46. Scores for eight of the nine children decreased at least 13 points, and four fell below the cutoff of 46 points. The limited data (four children) on the YMRS also showed significant improvement posttreatment; $t(3) = 4.54$, $p < 0.05$. The three completers who had been taking psychiatric medications at entry were still taking medications at the final visit, but all three were on lower doses (Table 1).

The effect sizes for each CBCL scale that changed, for the YOQ, and for the YMRS were

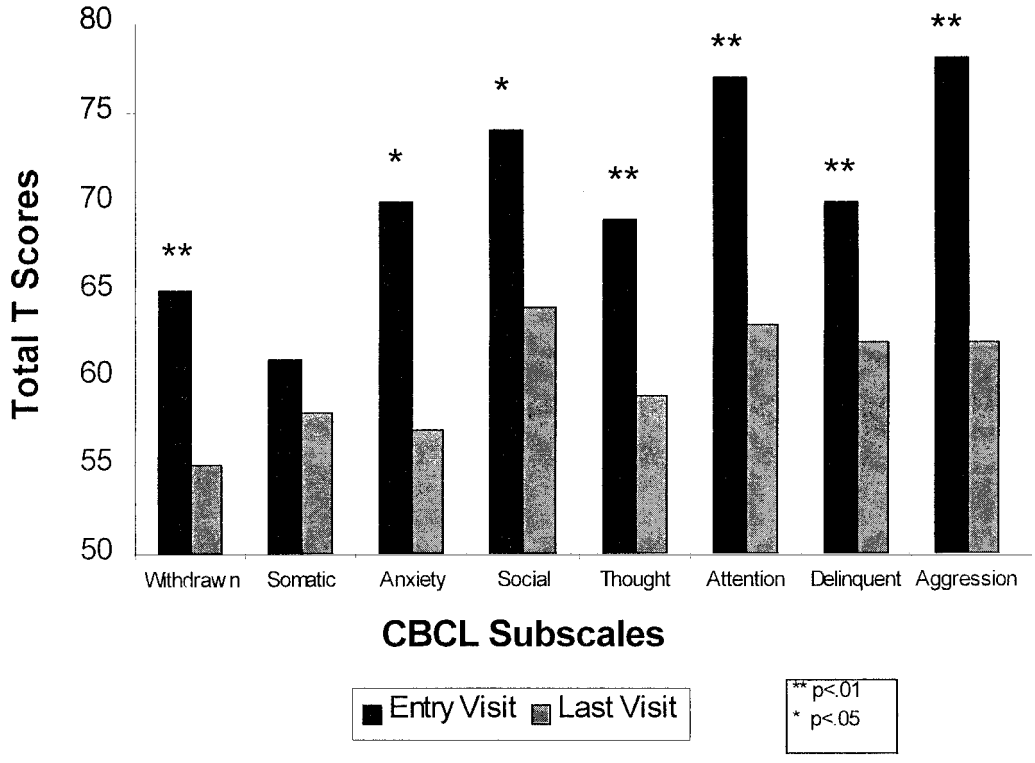

FIG. 1. Improvement on the Child Behavior Checklist.

calculated by taking the mean difference divided by the standard deviation of the difference scores, as suggested by Cohen (1988). Using Cohen's formula, all effect sizes were large (more than 0.80). Dunlop et al. (1996) argued for a more stringent approach, using the between-groups *t*-test value to compute effect sizes for correlated designs. Even with Dunlop et al.'s approach, effect sizes were still in the medium range (0.40–0.68).

Adverse effects

Adverse effects were minimal, and compliance was high, despite the fact that children were taking 32 capsules daily. Two children reported episodes of nausea and vomiting; one vomited both before and after a noontime dose (and may have had the flu that day), and the other vomited once after taking the supplement. Two others, both of whom were taking psychiatric medication, experienced moderate agitation and excitability. No agitation was reported from any of the children who were not taking psychiatric medication concomitantly.

DISCUSSION

In this open-label study of a broad-based nutrient treatment, the results demonstrated statistically significant improvements in mood and anxiety in the nine children who completed the trial. All effect sizes were relatively large (more than 0.8), consistent with the findings in adults studied previously (Kaplan et al. 2001). Two patients did not complete the protocol; both were on concurrent psychiatric medications, and both withdrew because of symptom exacerbation. Seven of the eight CBCL scales revealed statistically significant improvements, as did the other measures, the YMRS and YOQ. Nausea was noted by two children, one occurrence of which was likely associated with a flu, but no one discontinued because of adverse effects.

Limitations

Observer bias is inherent in any case series. The outcome data relied heavily on the observations of parents who had specifically chosen

an experimental nutritional supplement rather than traditional psychiatric medications. In this open-label study, they knew that their children were taking this supplement. Furthermore, in the current health environment, there could be a large expectancy effect associated with the use of any natural health product. On the other hand, most of these children had been through multiple treatment programs, including medications, and expectancy effects in those situations did not appear to reach the magnitude of the treatment effect documented in this study. In addition, in other research involving this supplement (Kaplan et al. 2002), expectancy effects tended to habituate in 2–3 weeks; following the children in the current cases series for at least 2 months (range from 2 months to over 4 months) may have reduced the likelihood that the documented treatment benefit was due to expectancy. Also, in previous work in which the children were followed for over 2 years of follow-up, the beneficial impact of this supplement did not habituate (Kaplan et al. 2002).

An additional limitation to this study was the absence of an independent confirmation of diagnosis for the participants; however, each one had a long history of mental health service involvement and parental concerns. Thus, although there might be disagreement as to the specific diagnostic category to which each child could be assigned, there was consistent agreement that the children evidenced a history of mood and behavioral symptoms.

Adverse effects

Transient nausea was reported in two subjects. Adults taking this supplement have reported headache, gastrointestinal complaints, and increased psychiatric symptoms (e.g., racing thoughts, agitation, irritability) (Kaplan et al. 2001; Popper 2001). The increased psychiatric symptoms have been documented only in patients taking concurrent medication, making it impossible to know whether to attribute these effects to the supplement or to possible medication–supplement interactions.

A far greater challenge than adverse effects was the interaction of the nutrients with psychiatric medications. Although interactions of minerals and vitamins with psychiatric medications are not well described, we have noted that many adult and child patients who have taken this nutrient supplement in combination with psychiatric medications have experienced what appear to be significant problems with interactions. This observation has been reported by many clinicians who have observed the use of this supplement, both in research protocols and in clinical practice (Popper 2001). The manufacturers of the supplement recommend decreasing the dose of the psychiatric medications in this situation, and despite significant concerns about safety and clinical stability, this has appeared to us to be a reasonable approach. The nature of the interaction is difficult to specify, but it appears that the supplement amplifies the effect of psychiatric medications, consistent with the observations that the problems are ameliorated by dosage reductions or discontinuation of the psychiatric medications (Popper 2001). All three medicated patients who completed this trial were able to decrease their medications and still benefit from the adjunctive effect of the supplement. This result is consistent with observations in the adults previously studied, where as a group they were able to be managed on about 50% less psychiatric medication (Kaplan et al. 2001).

Clinical implications

As discussed elsewhere (Kaplan et al. 2001, 2002), given the many studies that have shown the effect of individual nutrients on mood, it seems logical to speculate that a broader intervention such as that with the micronutrient supplement in the present study could in fact have a larger effect size than individual nutrients. The mechanism responsible for such an effect cannot yet be defined, but a reasonable hypothesis is that mood lability and its behavioral manifestations (e.g., rage) are manifestations of metabolic deficiencies in key neurobiological pathways.

Obtaining patient compliance with a treatment regimen that requires many large capsules would be a challenge in any clinical setting. As mentioned, the current version of the supplement has permitted reducing pill

number by roughly one half, and also there is a powder form available for mixing in juice. Even so, this type of approach probably requires greater patient motivation than the ingestion of one or two small pills per day, as is typically required for traditional pharmaceutical interventions.

This convenience sample of children was heterogeneous in terms of psychiatric diagnoses. Based on these data and previous research, it appears that nutritional supplementation may exert a stabilizing effect on mood, temper, and anxiety in a manner that is relatively independent of diagnostic category. Even though the effect is nonspecific, it appears to be strong (as supported by the relatively large effect size on all outcome measures) and clinically useful. The findings are consistent with those reported from the randomized, placebo-controlled trial by Gesch and colleagues, who found a significant decrease in rule infractions and violent acts in young adult criminal offenders taking a broad-based nutrient supplement (Gesch et al. 2002).

On the other hand, some of the children in this series still had residual problems post-treatment. Four continued to have at least one CBCL subscale score that remained at 70 or higher. For instance, the child with Prader-Willi syndrome remained elevated on both Social Problems and Thought Problems. Three boys with significant social-skills deficits remained elevated on the Social Problems scale.

In this open-label case series, the pervasiveness of improvement on multiple outcome instruments along with the magnitude of the effect sizes provides preliminary encouragement for more systematic research. Randomized placebo-controlled trials are planned.

ACKNOWLEDGMENTS

This study was supported in part by the Alberta Children's Hospital Foundation and the Wacker Foundation. The Synergy Group provided the nutritional supplement at no cost. For consultation we thank Mr. David Hardy, Mr. Anthony Stephan, and Dr. Charles W. Popper; for research assistance we thank Dr. Stan Whitsett.

APPENDIX

Ingredients of E.M.Power+ as Employed in the Current Study

	Amount per serving
Vitamin A (as retinyl palmitate)	2,400 IU
Vitamin C (as ascorbic acid)	250 mg
Vitamin D (as cholecalciferol)	400 IU
Vitamin E (as d-alpha tocopheryl succinate)	100 IU
Vitamin B1 (as thiamine mononitrate)	5 mg
Vitamin B2 (as riboflavin)	5.5 mg
Vitamin B3 (as niacinamide)	25 mg
Vitamin B6 (as pyridoxine hydrochloride)	7 mg
Vitamin B9 (as folic acid)	400 μg
Vitamin B12 (as cyanocobalamin)	250 μg
Biotin	25 μg
Pantothenic acid (as d-calcium pantothenate)	6 mg
Calcium (as calcium complex[a], calcium amino acid chelate)	550 mg
Iron (as iron amino chelate, iron complex[a])	6 mg
Phosphorous (phosphorous complex)	350 mg
Iodine (from kelp)	75 μg
Magnesium (as magnesium amino acid chelate, magnesium complex)	250 mg
Zinc (as zinc amino acid chelate, zinc complex[a])	20 mg
Selenium (as selenium amino acid chelate, selenium complex[a])	100 μg
Copper (as copper amino acid chelate, copper complex[a])	3 mg
Manganese (as manganese amino acid chelate, manganese complex)	4 mg
Chromium (as chromium amino acid chelate, chromium complex[a])	250 μg
Molybdenum (as molybdenum amino acid chelate, molybdenum complex)	66 μg
Potassium (as potassium complex[a])	100 mg

Note. Serving size is eight capsules taken four times per day for the study protocol. The product also includes a proprietary blend consisting of dl-phenylalanine, l-glutamine, citrus bioflavonoids, grape seed, choline, inositol, ginkgo biloba, methionine, germanium sesquioxide, boron, vanadium, and nickel. It is manufactured for Truehope/The Synergy Group of Canada.

[a]Other ingredients include gelatin, magnesium stearate, microcrystalline cellulose, and silicon dioxide.

REFERENCES

Achenbach TM: Manual for the Child Behavior Checklist/4–18 and 1991 Profile. Burlington (Vermont), University of Vermont, 1991.

Benton D, Cook R: The impact of selenium supplementation on mood. Biol Psychiatry 29:1092–1098, 1991.

Benton D, Donohoe RT: The effects of nutrients on mood. Public Health Nutr 2:403–409, 1999.

Benton D, Griffiths R, Haller J: Thiamine supplementation mood and cognitive functioning. Psychopharmacology (Berl) 129:66–71, 1997.

Benton D, Haller J, Fordy J: Vitamin supplementation for 1 year improves mood. Neuropsychobiology 32:98–105, 1995.

Burlingame GM, Wells MG, Hoag MJ, Hope CA, Nebeker RS, Konkel K, McCollam P, Peterson G, Lambert MJ, Latkowski M, Ferre R, Reisinger CW: Administration and Scoring Manual for the YOQ 2.0. Stevenson (Maryland), American Professional Credentialing Services, 1998.

Carroll D, Ring C, Suter M, Willemsen G: The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: A double-blind placebo-controlled trial. Psychopharmacology (Berl) 150:220–225, 2000.

Cohen J: Statistical Power Analysis for the Behavioral Sciences, 2nd ed. Hillsdale (New Jersey), Lawrence Erlbaum, 1988.

Dubovsky S, Thomas M, Hijazi A, Murphy J: Intracellular calcium signalling in peripheral cells of patients with bipolar affective disorder. Eur Arch Psychiatry Clin Neurosci 243:229–234, 1994.

Dunlop WP, Cortina JM, Vaslow JB, Burke MJ: Meta-analysis of experiments with matched groups or repeated measures designs. Psychol Methods 1:170–177, 1996.

Gesch CB, Hammon SM, Hampson SE, Eves A, Crowder MJ: Influence of supplementary vitamins, minerals and essential fatty acids on the antisocial behaviour of young adult prisoners. Randomised, placebo-controlled trial. Br J Psychiatry 181:22–28, 2002.

Hoffer A: Vitamin B-3 and Schizophrenia. Kingston (Ontario), Quarry Press, 1999.

Kaplan BJ, Crawford SG, Gardner B, Farrelly G: Treatment of mood lability and explosive rage with minerals and vitamins: Two case studies in children. J Child Adolesc Psychopharmacol 12:203–218, 2002.

Kaplan BJ, Simpson JS, Ferre RC, Gorman CP, McMullen DM, Crawford SG: Effective mood stabilization with a chelated mineral supplement: An open-label trial in bipolar disorder. J Clin Psychiatry 62:936–944, 2001.

Maes M, Vandoolaeghe E, Neels H, Demedts P, Wauters A, Meltzer HY, Altamura C, Desnyder R: Lower serum zinc in major depression is a sensitive marker of treatment resistance and of the immune/inflammatory response in that illness. Biol Psychiatry 42:349–358, 1997.

Mash EJ, Terdal LG: Assessment of child and family disturbances: A behavioral-systems approach. In: Assessment of Childhood Disorders. Edited by Mash EJ, Terdal LG. New York, Guilford Press, 1997, pp 3–68.

Nemets B, Stahl Z, Belmaker RH: Addition of omega-3 fatty acid to maintenance of medication treatment for recurrent unipolar depressive disorder. Am J Psychiatry 159:477–479, 2002.

Peet M, Horrobin DF: A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. Arch Gen Psychiatry 59:913–919, 2002.

Popper CW: Do vitamins or minerals (apart from lithium) have mood-stabilizing effects? [commentary]. J Clin Psychiatry 62:933–935, 2001.

Richardson AJ, Puri BK: A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. Prog Neuropsychopharmacol Biol Psychiatry 26:233–239, 2002.

Sandstead HH, Penland JG, Alcock NW, Dayal HH, Chen XC, Li JS, Zhao F, Yang JJ: Effects of zinc and other micronutrients on neuropsychologic performance and growth of Chinese children. Am J Clin Nutr 68:470S–475S, 1998.

Schoenthaler SJ, Bier ID: The effect of vitamin-mineral supplementation on juvenile delinquency among American schoolchildren: A randomized, double-blind placebo-controlled trial. J Altern Complement Med 6:7–17, 2000.

Simmons M: Letter to the editor. J Clin Psychiatry 64:338, 2002.

Young RC, Biggs JT, Ziegler VE, Meyer DA: A rating scale for mania: Reliability, validity and sensitivity. Br J Psychiatry 133:429–435, 1978.

Address reprint requests to:
Bonnie J. Kaplan, Ph.D.
Alberta Children's Hospital
1820 Richmond Road, SW
Calgary, AB T2T 5C7, Canada

E-mail: kaplan@ucalgary.ca