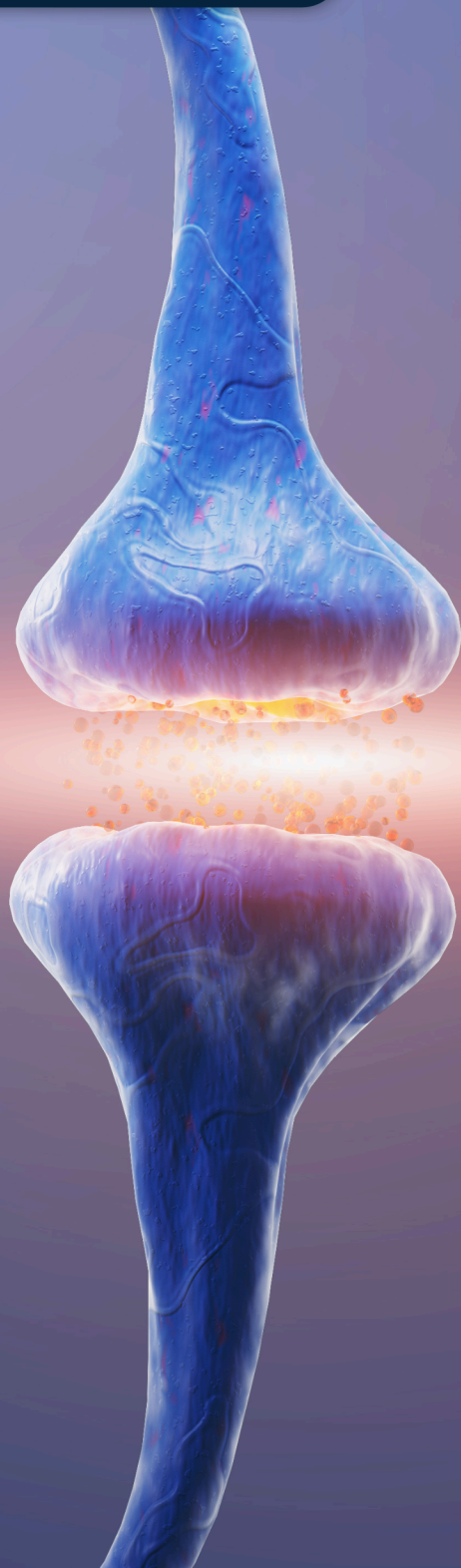


# RESEARCH SUMMARY

The latest research behind  
EMPowerplus Advanced™,  
also known as **NeuroC3™**,  
the groundbreaking  
micronutrient formula  
behind our flagship  
product, **Lightning™**



35 Publications as of Spring 2020

# CONDITION

# STUDY#

ADHD.....	9, 10, 12, 13, 14, 16, 21, 24, 26
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Anxiety.....	2, 7, 16, 17, 18, 22, 29
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Explosive Rage.....	5, 32
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Premenstrual Syndrome.....	1
Psychosis.....	3, 4, 17
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Stress.....	2, 8, 11, 18, 22
Traumatic Brain Injury.....	5

# 1. Hana Retallick-Brown, PhD, Neville Blampied, MSc, and Julia J. Rucklidge, PhD

A Pilot Randomized Treatment-Controlled Trial Comparing Vitamin B6 with Broad-Spectrum Micronutrients for Premenstrual Syndrome  
The Journal of Alternative and Complementary Medicine/published 2020

## ABSTRACT

**Objective:** Premenstrual syndrome (PMS) affects 20%–30% of women but current medical treatments are limited in their efficacy. The objective of this study was to compare efficacy of a broad-spectrum micronutrient formula (consisting mainly of minerals and vitamins) to a single vitamin (B6) for treatment of PMS, for which B6 has already been shown to be efficacious.

**Methods:** This double-blind, randomized, treatment-controlled trial allocated 78 (72 completed) regularly menstruating women with PMS to consume micronutrients or vitamin B6 (80 mg/day) daily following a two-cycle baseline period, for three menstrual cycles. The primary outcome measure, Daily Record of Severity of Problems (DRSP), established PMS as well as tracked change in five PMS symptoms: psychological, somatic, total symptoms, impact ratings, and worst day ratings.

**Results:** Linear-mixed model analyses indicated both treatments produced comparable reduction in PMS symptoms with medium effect sizes (ES) across all PMS variables as measured by the DRSP (micronutrient ES = 0.50–0.56; B6 ES = 0.43–0.56), with 72% of the micronutrient and 60% of the vitamin B6 group identified as in full remission in PMS symptoms after three cycles. The micronutrient-treated participants showed greater improvement than the B6 group (between group  $d = 0.51$ ,  $p < 0.05$ ) in health-related quality of life. For those women ( $n = 28$ ) who met criteria for premenstrual dysphoric disorder (PMDD), the DRSP ES were larger for those who had been in the micronutrient condition (ES = 1.28–1.67) as compared with those on B6 (ES = 0.50–0.75), although the group differences were not statistically reliable. There were no group differences in side effects, nor any serious adverse effects reported.

**Conclusions:** Both treatments provided similar benefit for reducing PMS symptoms, with greater effect of micronutrients on quality of life as well as potential clinical benefit of micronutrients for PMDD. This study provides further efficacy data on B6 and also identifies the nutritionally broader spectrum intervention as possibly having specific advantages for those whose symptoms are more severe. As this is the first study to investigate these treatments for PMDD, systematic replication is required.

# 2. Ellen J. Sole, Julia J. Rucklidge, Neville M. Blampied

Anxiety and Stress in Children Following an Earthquake: Clinically Beneficial Effects of Treatment with Micronutrients  
J Child Family Study/published online February 24, 2017

## ABSTRACT

This study examined the effects of micronutrients on children with clinically elevated stress and anxiety 23–36 months after experiencing a natural disaster (a major earthquake). A single-case multiple-baseline design allocated 14 children (7 males, 7 females; aged 8–11 years; 10 with formal anxiety-disorder diagnoses) randomly to 1, 2 or 3 week baselines. Participants then took eight capsules/day of a micronutrient formula (EMPowerplus) during an 8-week open-label trial. Assessment instruments were the Children's Global Assessment Scale (CGAS), the Screen for Child Anxiety-Related Emotional Disorders (SCARED), the Pediatric Emotional Distress Scale (PEDS), and the Revised Children's Manifest Anxiety Scale (RCMAS). Symptom severity declined slightly in baseline for some children and declined much more during intervention for all children. Effect sizes at end of treatment were  $-1.40$  (RCMAS),  $-1.92$  (SCARED),  $+1.96$  (CGAS), and  $-2.13$  (PEDS). Modified Brinley plots revealed decreases in anxiety and improvements in overall functioning for 10 out of 11 completing participants. Side effects were mild and transient. The study provided evidence that treatment with a dietary supplement containing micronutrients reduced children's post-disaster anxiety to a clinically significant degree. Future placebo-controlled randomized-controlled trials and treatment-comparison research is recommended to determine if this is true of anxiety in general.

# 3. Bonnie J. Kaplan, Wanrudee Isaranuwachai, and Jeffrey S. Hoch

Hospitalization cost of conventional psychiatric care compared to broad-spectrum micronutrient treatment  
International Journal of Mental Health Systems/published online January 31, 2017

## ABSTRACT

**Background:** Healthcare costs are skyrocketing, with mental health treatment amongst the most expensive, especially when hospitalization is involved. According to the Mental Health Commission of Canada, one in five Canadians is living with a mental disorder in any given year, at an annual cost of \$50 billion. In light of this societal burden, alternative approaches are being evaluated, such as brief psychotherapy by phone, peer support, and, as part of the emerging field of nutritional mental health, treatment with micronutrients (minerals and vitamins). Effectiveness of micronutrients has been demonstrated for many types of psychiatric symptoms, in about 45 studies of formulas that are either multinutrient (e.g., several B vitamins) or broad-spectrum (usually over 20 minerals and vitamins). Although this literature demonstrates therapeutic benefits, the potential economic impact of micronutrient treatment has been evaluated in only one case study of childhood psychosis.

**Methods:** The current case study was initiated to evaluate mental health-related hospitalization costs from 1997 to 2003 for a female adult diagnosed with various mood and psychotic symptoms. She was treated for the first 5 years with conventional methods and then subsequently with a broad-spectrum micronutrient formula.

**Results:** The patient's annual mental health hospitalization costs during conventional treatment averaged \$59,864 across 5 years (1997–2001), with a peak annual cost of about \$140,000. Since transitioning to broad-spectrum micronutrients, she has incurred no provincial hospitalization costs for mental health care, though her self-funded costs are currently \$720/year for the micronutrients.

**Conclusion:** Further exploration of the treatment of mental health problems with broad-spectrum micronutrient formulas has the potential to make two significant contributions: improved mental health, and decreased costs for governments.

## 4. Lewis Mehl-Madrona and Barbara Mainguy

Adjunctive Treatment of Psychotic Disorders with Micronutrients

The Journal of Alternative and Complementary Medicine/published 2017

### ABSTRACT

**Objective:** To evaluate the effect of micronutrients (minerals and vitamins) on adult psychosis when added to conventional medications by using a placebo-controlled randomized design with a 1-month open-label run-in.

**Design:** Longitudinal comparison study following a randomized, controlled trial that had failed because participants declined to undergo randomization.

**Setting/Locations:** Rural primary care and psychiatry clinic in northern New England (town of 16,000 people).

**Participants:** People older than age 18 years diagnosed with a psychotic disorder who were receiving medications.

**Intervention:** Fifty consecutive clients seen in 1 month's time were invited to participate; 19 completed a 1-month open-label phase of the addition of a micronutrient to their medication regimen; all 19 then withdrew rather than risk randomization to a placebo. This finding itself was important, so the study was restructured to compare the response of those 19 patients during 24 months of micronutrients + medication to the response of the 31 people who declined participation, enriched by an additional 28 consecutive patients recruited over the second month of the study. This yielded a total of 59 patients who received medication without micronutrients.

**Outcome measures:** All clients were evaluated with the Positive and Negative Symptom Scale and the Clinical Global Impression scale at study baseline and after 3, 6, 9, 12, 15, 18, and 24 months. Psychosis was confirmed with clinical interview by using Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision, criteria. All participants had normal physical examinations and laboratory studies.

**Results:** Outcomes were similar for both groups until 15 months, although the micronutrient group used significantly less antipsychotic medication throughout that time ( $p < 0.001$ ). At 15 months, the micronutrients + medication group exhibited significantly fewer symptoms than the medication-only group, a difference that was even stronger at 24 months.

**Conclusions:** Micronutrients may appear to be a beneficial long-term, adjunctive strategy for people with psychotic disorders, allowing for smaller doses of medication to achieve the same effectiveness with fewer side effects.

## 5. Bonnie J. Kaplan, Caroline Leaney, and Ekaterina Tsatsko

Micronutrient Treatment of Emotional Dyscontrol Following Traumatic Brain Injury

Annals of Psychiatry and Mental Health/published August 29, 2016

### ABSTRACT

**Introduction:** Emotional dyscontrol following traumatic brain injury (TBI) impairs social relationships and employability. Micronutrients (minerals, vitamins) stabilize emotional lability in psychiatric patients, and various individual nutrients have been used to treat experimental brain injury in laboratory animals in the acute phase. However, the current case report appears to be the first documentation of micronutrients resulting in normalization of emotion regulation in a long-standing brain injury in a human.

**Case presentation:** A broad-spectrum formula of micronutrients was evaluated in a 35-year-old male who had incurred a severe TBI eight years previously. Resolution of most post-TBI symptoms was achieved during those eight years, but not his episodic loss of emotional control, which psychiatrists evaluated as being permanent. The trial of micronutrients began after five weeks of baseline symptom monitoring with a mood stability scale. By three months mood stability had improved markedly according to data submitted by two raters (the patient and his clinician) who were blind to each other's evaluations. Data collection continued for one year, showing significant improvement ( $p < .0001$ ),

at which time the patient reported that his emotional control had returned to his pre-TBI level. The improvements led to his establishing his own business and improving his family relationships.

**Conclusions:** Micronutrient treatment resulted in resolution of this patient's longstanding post-TBI emotional dyscontrol. Broad-spectrum micronutrient formulas are showing benefit for the treatment of mood lability in various types of psychiatric patients; this report indicates there is also potential value in using them for the emotional dyscontrol found in post-TBI patients.

## 6. Michael I. Gurevich, MD and Cassandra L. Robinson, MS, LPN

An Individualized Approach to Treatment-resistant Bipolar Disorder: A Case Series  
EXPLORE/volume 4, number 2, March 2015/www.gahmj.com

### ABSTRACT

**Objective:** Determine retrospectively if individualized, integrative treatment strategies applied while withdrawing pharmaceuticals were beneficial and safe among a TRBD clinic population.

**Method:** A chart review was performed for six adult patients, treated in a private psychiatric practice. Data were collected regarding psychiatric diagnosis, hospitalizations, medications, side effects, substance abuse, and applied treatments.

**Results:** Using individualized, integrative psychiatric treatment methods, the majority of medications were eliminated. Long-term remission was attained in all cases, defined as clinical stability with no discernable symptoms of bipolar disorder for at least one year.

**Conclusions:** Applying an integrative treatment approach, and eliminating most medications, provided lasting resolution of symptoms and side-effects in a selected sample of TRBD outpatients. These data may provide the basis for future randomized, controlled trials.

## 7. Kaplan BJ, Hilbert P, Tsatsko E

Micronutrient treatment for children with emotional and behavioral dysregulation: A Case Series  
Journal of Medical Case Reports 2015, 9:240 doi:10.1186/s13256-015-0735-0

### ABSTRACT

**Introduction:** In clinical studies of adults and children, broad-spectrum micronutrients (minerals and vitamins) have proven beneficial for improving mood regulation and attention. We report here pilot work whose primary objective was to evaluate the feasibility of studying micronutrient treatment in school-aged children with emotional and behavioral problems. Issues examined included feasibility of participant recruitment from a culturally diverse population, probability of sample retention for a 12-week trial, acceptability of the outcome measures, supplement adherence, as well as trends in treatment benefit.

**Case Presentation:** The families of two boys (ages 5 and 6) and one girl (age 14) were invited to participate in a 12-week pilot trial of micronutrients carried out during the summer months. All children were enrolled in the private school at which future research was being considered. During the previous school year, all three had been extremely difficult to educate due to their inability to pay attention and learn, as well as their behavior problems. Although the two younger children had not been formally diagnosed, parents and teachers provided reports of hyperactivity and inability to focus on education in the classroom. The oldest child was often aggressive, and had been diagnosed with bipolar disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder. All three children were Hispanic and spoke both Spanish and English. For 12 weeks, after signing consent forms, the children's parents provided weekly ratings on the parent-report Child Mania Rating Scale; the children consumed the micronutrient formula daily and provided a daily rating of how they felt. The parent ratings revealed significantly improved behavior,  $p = .002$ . Children's ratings approached the ideal level of 7, indicating "happy" self-reports. Parent interviews confirmed the weekly scores. Several feasibility questions were answered: all three children completed the 12-week trial, all scores were completed by parents and children, adherence to the protocol was excellent, and no adverse reactions emerged.

**Conclusions:** Family physicians and pediatricians are often confronted with the challenge of improving the lives of families whose children experience school crises due to emotional and behavioral dysregulation. Three children, who participated in pilot work to determine the feasibility of further investigations, experienced impressive changes that clearly warrant both research and clinical exploration.

## 8. Kaplan BJ, Rucklidge JJ, Romijn AR

A randomized trial of nutrient supplements to minimize psychological stress after a natural disaster  
Psychiatry Research, August 30, 2015, Volume 228, Issue 3, Pages 373–379

### ABSTRACT

After devastating flooding in southern Alberta in June 2013, we attempted to replicate a New Zealand randomised trial that showed that micronutrient (minerals, vitamins) consumption after the earthquakes of 2010–11 resulted in improved mental health. Residents of southern Alberta were invited to participate in a study on the potential benefit of nutrient supplements following a natural disaster. Fifty-six adults aged 23–66 were randomised to receive a single nutrient (vitamin D,  $n=17$ ), a few-nutrients formula (B-Complex,  $n=21$ ), or a broad-spectrum mineral/vitamin formula (BSMV,  $n=18$ ). Self-reported changes in depression, anxiety and stress were monitored for six weeks. Although all groups showed substantial decreases on all measures, those consuming the B-Complex and the BSMV formulas showed significantly greater improvement in stress and anxiety compared with those consuming the single nutrient, with large effect sizes (Cohen's  $d$  range 0.76–1.08). There were no group differences between those consuming the B-Complex and BSMV. The use of nutrient formulas with multiple minerals and/or vitamins to minimise stress associated with natural disasters is now supported by three studies. Further research should be carried out to evaluate the potential population benefit that might accrue if such formulas were distributed as a post-disaster public health measure.

## 9. Gordon HA, Rucklidge JJ, Blampied NM, Johnstone JM

Clinically Significant Symptom Reduction in Children with Attention-Deficit/Hyperactivity Disorder Treated with Micronutrients: An Open-Label Reversal Design Study  
J Child Adolesc Psychopharmacol. 2015 Dec;25(10):783-98. doi: 10.1089/cap.2015.0105

### ABSTRACT

**Objective:** The purpose of this study was to investigate the clinical effect and safety of a broad spectrum, 36 ingredient micronutrient (vitamins and minerals) in treating children with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** This open-label, on-off-on-off (reversal design) study followed 14 participants (8–12 years of age) with ADHD, diagnosed using standardized instruments, for 6 months with no dropouts. Following baseline assessment, including hematology and biochemistry screening, participants began an 8 week treatment phase with micronutrients titrated up to maximum dose (15 capsules/day). Treatment was withdrawn for 4 weeks, reinstated for a further 8 weeks, and then withdrawn for 4 weeks. Primary outcomes included the Conners' Parent Rating Scale, the Clinical Global Impressions Scale (CGI), and the Strengths and Difficulties Questionnaire – Parent version (SDQ). Secondary outcomes were mood and global functioning.

**Results:** Modified Brinley plots revealed a reduction in ADHD symptoms, improved mood, and improved overall functioning during intervention phases, and deterioration in ADHD symptoms, mood, and overall functioning during the withdrawal phases. Reliable change analyses, Cohen's d and percent superiority effect sizes, 95% confidence intervals and t tests confirmed clinically and statistically significant change between the intervention and withdrawal phases, with large effect sizes observed pre- to post-exposure of micronutrients (d = 1.2–2.2) on ADHD symptoms during intervention phases. Seventy-one percent of participants showed at least a 30% decrease in ADHD symptoms by the end of the second treatment phase, and 79% were identified as "much improved" or "very much improved" at the end of the second phase (5 months) based on the clinician-rated CGI when considering functioning generally. The SDQ showed that these benefits occurred across other areas of functioning including emotional symptoms, conduct problems, and prosocial behaviours. The children's self-reports confirmed the improvements. Excellent adherence to treatment occurred throughout, side effects were mild and transitory, and no safety issues were identified through blood analyses.

**Conclusions:** This study demonstrates the clinical benefit, feasibility, and safety of broad-spectrum micronutrients in the treatment of childhood ADHD. Replications utilizing double-blind placebo-controlled studies are warranted. Trial is registered with the Australia and New Zealand Clinical Trial Registry: ACTRN12612000645853

## 10. Rucklidge JJ, Frampton C, Gorman B, Boggis A

Vitamin-mineral treatment of ADHD in adults: A one-year follow-up of a randomized controlled trial  
Journal of Attention Disorders, ePub/published online 2017

### ABSTRACT

**Objective:** Despite widespread use, there is little data investigating the long-term impact of micronutrients on psychiatric disorders. This study investigated the naturalistic outcome 1-year post-baseline of a randomized controlled trials (RCT) that compared micronutrients with placebo in 80 adults with ADHD.

**Method:** All participants were contacted and clinician-rated questionnaires completed.

**Result:** A total of 72 (90%) of the sample participated; although there was significant regression in psychiatric functioning from the end-of-trial on all measures, outcomes remained significantly improved from baseline. Dominant treatment from the end-of-treatment to follow-up was investigated as a mediator of outcome; those staying on the micronutrients performed better than those who switched to medications or discontinued micronutrients. Cost was the most substantial reason why people stopped micronutrient treatment.

**Conclusion:** For the small number of participants who stayed on micronutrients, the benefits conferred through the controlled trial were maintained. The results are limited by small sample, lack of blinding, expectation, and reliance on self-report of symptoms.

## 11. Rucklidge JJ\*, Blampied N, Gorman B, Gordon H, Sole E

Psychological functioning 1 year after a brief intervention using micronutrients to treat stress and anxiety related to the 2011 Christchurch earthquakes: A Naturalistic Follow-up  
Hum. Psychopharmacol Clin Exp (2014). doi: 10.1002/hup.2392

### ABSTRACT

**Objective:** We investigated whether micronutrients given acutely following the Christchurch earthquakes continued to confer benefit 1 year following the treatment.

**Method:** Sixty-four adults from the original 91 participants experiencing heightened anxiety or stress 2.3 months following the 22nd February 2011 earthquake and who had been randomized to receive three different doses of micronutrients completed on-line questionnaires assessing mood, anxiety, stress, and symptoms associated with post-traumatic stress disorder 1 year after completing the initial study. Twenty-one out of 29 nonrandomized controls who did not receive the treatment also completed the questionnaires.

**Result:** Both the treated and control groups experienced significant improvement in psychological functioning compared with end-of-trial. However, treated participants had better long-term outcomes on most measures compared with controls (ES = 0.69.1.31). Those who stayed on micronutrients through to follow-up or stopped all treatment reported better psychological functioning than those who switched to other treatments including medications.

**Conclusion:** Disaster survivors improve psychologically over time regardless of receiving intervention; however, those taking micronutrients during the acute phase following a disaster show better outcomes, identifying micronutrients as a viable treatment for acute stress following a natural disaster with maintenance of benefits 1 year later.

## 12. Rucklidge JJ, Frampton CA, Gorman B, Boggis A

Vitamin-mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomized placebo-controlled trial

The British Journal of Psychiatry, January 30, 2014

### ABSTRACT

**Background:** The role of nutrition in the treatment of attention-deficit hyperactivity disorder (ADHD) is gaining international attention; however, treatments have generally focused only on diet restriction or supplementing with one nutrient at a time.

**Aim:** To investigate the efficacy and safety of a broad-based micronutrient formula consisting mainly of vitamins and minerals, without omega fatty acids, in the treatment of ADHD in adults.

**Method:** Intent-to-treat analyses showed significant between-group differences favoring active treatment on self- and observer- but not clinician-ADHD rating scales. However, clinicians rated those receiving micronutrients as more improved than those on placebo both globally and on ADHD symptoms. Post hoc analyses showed that for those with moderate/severe depression at baseline, there was a greater change in mood favoring active treatment over placebo. There were no group differences in adverse events.

**Conclusion:** This study provides preliminary evidence of efficacy for micronutrients in the treatment of ADHD symptoms in adults, with a reassuring safety profile.

## 13. Rucklidge JJ, Johnstone J, Gorman B, Boggis A, Frampton CA

Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement

Prog Neuro-Psychopharmacol Biol Psychiatry (2013); <http://dx.doi.org/10.1016/j.pnpbp.2013.12.014>

### ABSTRACT

**Background:** To date there has been no research investigating moderators of response to micronutrient treatment of mental illness, specifically baseline nutrient levels.

**Method:** We conducted analyses of data from a randomized placebo-controlled trial (RCT) of 80 adults (.16 years) with Attention-Deficit Hyperactivity Disorder (ADHD), whereby participants were treated acutely (8 weeks) with micronutrients or placebo followed by an open-label (OL) phase of 8 weeks whereby all participants received micronutrients. To ensure that all participants had been exposed to the micronutrients for 8 weeks, only those who had adhered to the treatment protocol and completed 8 weeks on nutrients were included in the data analysis: from the group micronutrient arm, and from the group that had been randomized to the placebo group and hence had only received nutrients in the OL phase. Six outcomes were examined: change in ADHD symptoms (self/clinician), ADHD responder, Clinical Global Impression-Improvement (CGI-I), change in mood, and change in Global Assessment of Functioning (GAF). Demographic, developmental and psychiatric history, current clinical characteristics, and baseline nutrient levels were all considered as putative predictors.

**Result:** There were significant changes in all outcome variables after 8 weeks' exposure to the micronutrients. Among the nutrients recorded at baseline, substantial deficiencies (27%) were only observed for vitamin D.

## 14. Rucklidge JJ

Could Yeast Infections Impair Recovery From Mental Illness? A case study Using Micronutrients and Olive Leaf Extract for the Treatment of ADHD and Depression

Advances, Summer 2013. Vol. 27, No. 3

### ABSTRACT

Micronutrients are increasingly used to treat psychiatric disorders including attention-deficit/hyperactivity disorder (ADHD), mood disorders, stress, and anxiety. However, a number of factors influence optimal response and absorption of nutrients, including the health of the gut, particularly the presence of yeast infections, such as Candida. As part of a wider investigation into the impact of micronutrients on psychiatric symptoms, many participants who experienced a yeast infection during their treatment showed a diminished response to the micronutrients. One case was followed systematically over a period of 3 years with documentation of deterioration in psychiatric symptoms (ADHD and mood) when infected with Candida and then symptom improvement following successful treatment of the infection with olive leaf extract (OLE) and probiotics. This case outlines that micronutrient treatment might be severely compromised by infections such as Candida and may highlight the importance of gut health when treating psychiatric disorders with nutrients. Given the role that inflammation can play in absorption of nutrients, it was hypothesized that the infection was impairing absorption of the micronutrients.

## 15. Frazier EA, Gracious B, Arnold LE, Failla M, Chitchumroonchokchai C, Habash D, Fristad MA

Nutritional and Safety Outcomes from an Open-Label Micronutrient Intervention for Pediatric Bipolar Spectrum Disorders

Journal of Child and Adolescent Psychopharmacology / published October 2013

### ABSTRACT

**Objective:** Report safety, tolerability, serum micronutrient concentrations and their correlations with mood changes from an 8-week pilot feasibility study of a 36-ingredient multinutrient supplement, Truehope® EMPowerplus, for pediatric bipolar spectrum disorders (BPSD).

**Method:** Ten children aged 6-12 received Truehope® EMPowerplus escalating from 1 to 4 capsules t.i.d., with four children increased to the maximum suggested dose, 5 capsules t.i.d. Outcome measures were micronutrient concentrations in serum and red blood cells, vital signs, body mass index (BMI), dietary intake (Food Frequency Questionnaire and 24-hour dietary recall interview) and mood and global functioning ratings.

**Result:** Seven children (70%) completed the study. Three (30%) terminated early due to tolerability and compliance issues. Adverse effects were mild and transient, and chiefly initial insomnia or GI upset. No differences occurred in BMI ( $p = 0.310$ ) or waist-hip ratio (WHR;  $p = 0.674$ ) pre- to post-supplementation. Four of the tested serum vitamin concentrations increased from pre- to post-supplementation: vitamin A- retinol; vitamin B6; vitamin E- $\alpha$ -tocopherol; and folate (all  $p < 0.05$ ). The increase in serum 25-OH vitamin D approached significance ( $p = 0.063$ ). No differences were found in dietary intake pre- to post- supplementation, suggesting blood nutrient level increases were due to Truehope® EMPowerplus.

**Conclusion:** In this open prospective study, short-term use of Truehope® EMPowerplus in children with BPSD appeared safe and well-tolerated, with a side effect profile preferable to first-line psychotropic drugs for pediatric bipolar spectrum disorders. A double-blind, randomized clinical trial is feasible, appears safe, and is warranted by open-label clinical outcomes and plausible mechanisms of action combined with documentation of increased serum concentrations of specific micronutrients.

## 16. Harrison R, Rucklidge JJ, Blampied N

Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal Design: A case study

Journal of Psychoactive Drugs / published online June 4, 2013

### ABSTRACT

Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol, and cocaine. As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes, and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol. This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programs and encourage more rigorous trials.

## 17. Rodway M, Vance A, Watters A, Lee H, Bos E, Kaplan BJ

Efficacy and cost of micronutrient treatment of childhood psychosis

BMJ Case Reports. doi: 10.1136/bcr-2012-007213 / published 2012

### ABSTRACT

Psychosis is difficult to treat effectively with conventional pharmaceuticals, many of which have adverse long-term health consequences. In contrast, there are promising reports from several research groups of micronutrient treatment (vitamins, minerals, amino acids, and essential fatty acids) of mood, anxiety, and psychosis symptoms using a complex formula that appears to be safe and tolerable. We review previous studies using this formula to treat mental symptoms, and present an 11-year-old boy with a 3-year history of mental illness whose parents chose to transition him from medication to micronutrients. Symptom severity was monitored in three clusters: anxiety, obsessive compulsive disorder, and psychosis. Complete remission of psychosis occurred, and severity of anxiety and obsessional symptoms decreased significantly ( $p < .001$ ); the improvements are sustained at 4-year follow-up. A cost comparison revealed that micronutrient treatment was <1% of his inpatient mental health care. Additional research on broad spectrum micronutrient treatment is warranted.



## 18. Rucklidge JJ, Andridge R, Gorman B, Blampied N, Gordon H, Boggis A

Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses

Hum Psychopharmacol Clin Exp. doi:10.1002/hup.2246/published June 8, 2012

### ABSTRACT

**Objective:** To compare two micronutrient (vitamins and minerals) formulas (Berocca™ and CNETM) and assess their impact on emotions and stress related to the 6.3 earthquake on February 22nd 2011 in Christchurch, NZ.

**Method:** 91 adults experiencing heightened anxiety or stress 2-3 months following the earthquake were randomized to Berocca™, CNETM low dose (CNE4), or CNETM high dose (CNE8), for 28 days and monitored weekly via on-line questionnaires and followed one month post-trial. A non-randomized control group (n=25) completed questionnaires at baseline and 4 weeks.

**Result:** All treatment groups experienced significant declines in psychological symptoms ( $p < .001$ ). CNETM groups experienced greater reduction in intrusive thoughts as compared with Berocca™ ( $p = 0.05$ ), with no group differences on other measures of psychological symptoms. However, CNE8 group reported greater improvement in mood, anxiety, and energy ( $p < .05$ ) with twice as many reporting being “much” to “very much” improved and five times more likely to continue taking CNETM post-trial than Berocca™ group. Treated participants had better outcomes on most measures over 4 weeks as compared to controls.

**Conclusion:** This study supports micronutrients as an inexpensive and practical treatment for acute stress following a natural disaster with a slight advantage to higher doses. ACTRN 12611000460909

## 19. Frazier EA, Fristad MA, Arnold LE

Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders

Journal of Alternative and Complementary Medicine, 18(7):678-685/published 2012

### ABSTRACT

**Objective:** Current psychotropic medications for childhood bipolar spectrum disorders (BPSD) are associated with significant adverse events. As nutrients play an important role in physical and mental health, they may be useful in treating mood disorders with few side effects. This open-label study explored the feasibility of testing therapeutic effects of a multinutrient supplement, Truehope® EMPowerplus, for pediatric BPSD.

**Design:** Truehope® EMPowerplus started at 1 capsule t.i.d. and escalated to a goal of 4 capsules t.i.d., which eight children attained. Four of these increased to the maximum dose, 5 capsules t.i.d. Mood symptoms were assessed seven times over eight weeks.

**Subjects:** Ten children, age 6-12 with BPSD were enrolled in 6.5 months. Seven participants completed the full trial. Three dropped out due to palatability and/or adherence issues.

**Result:** Mean medication adherence was 91%. With one-tailed nonparametric Fisher's Randomization Tests, intent-to-treat analyses demonstrated a 37% decrease in depression scores ( $p < 0.06$ ) and a 45% decrease in mania scores ( $p < 0.01$ ) from the start of treatment through final visit, suggesting improvement and possible treatment response. Study completers demonstrated significant decreasing trends in both depression and mania scores from baseline to final visit ( $p < 0.05$ ). Side effects were minor and transient, mostly temporary gastric discomfort. Conclusion: Future randomized, placebo-controlled trials of Truehope® EMPowerplus are warranted and feasible.

## 20. Rucklidge JJ, Johnstone J, Harrison R

Effect of micronutrients on neurocognitive functioning in adults with ADHD and Severe Mood Dysregulation: A Pilot study

Journal of Alternative and Complementary Medicine/published 2011

### ABSTRACT

**Objective:** Little research has investigated how micronutrients (minerals and vitamins) affect cognitive functioning despite preliminary studies showing they may improve psychiatric functioning. Intervention: This pilot study investigated the impact of a 36 ingredient micronutrient formula consisting mainly of vitamins and minerals on neurocognitive functioning in 14 adults with Attention-Deficit/Hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD).

**Design:** The formula was consumed in an open-label trial over an 8-week period.

**Outcome Measures:** The participants completed tests of memory (Wide Range Assessment of Memory and Learning) and executive functioning (Delis-Kaplan Executive Functioning System and Conners Continuous Performance Test) at baseline and at the end of the trial. A gender and age matched control group of 14 non-ADHD adults not taking the formula were assessed on the same tests 8 weeks apart in order to investigate the impact of practice on the results.

**Result:** There were no group differences in ethnicity, socio-economic status and estimated IQ. Significant improvement was observed in the ADHD group, but not the control group, across a range of verbal abilities including verbal learning, verbal cognitive flexibility and fluency, and verbal inhibition. These neurocognitive improvements were large and consistent with improved psychiatric functioning. No changes were noted above a practice effect in visual-spatial memory and there were no improvements noted in reaction time, working memory or rapid naming for either groups.

**Conclusion:** Although the pilot and open label design of the study limits the generalizability of the results, it supports a growing body of literature recognizing the importance of nutrients for mental health and cognition. The results also provide evidence supporting the need for randomized clinical trials of micronutrients as well as other experimental studies in order to better assess whether improved neurocognitive functioning may contribute to improved psychiatric symptoms.

## 21. Rucklidge JJ, Blampied NM

**Post-earthquake psychological functioning in adults with Attention-Deficit/Hyperactivity Disorder: Positive effects of micronutrients on resilience**  
**New Zealand Journal of Psychology, 40(4):51-57/published 2011**

### ABSTRACT

The September, 2010, 7.1 magnitude earthquake in Christchurch, New Zealand, provided an opportunity to study the after-effects of a major earthquake where death and injury were absent. It created a natural experiment into the protective effects on well-being of taking Truehope® EMPowerplus, a micronutrient supplement, in a group of 33 adults diagnosed with ADHD who had been assessed prior to the earthquake. Fortuitously, 16 were currently taking the supplement as part of on-going research at the time of the quake, while 17 were not (they had completed their trial of Truehope® EMPowerplus or were waiting to begin consumption). The Depression Anxiety and Stress Scale (DASS-42) which had been administered at varying times before the earthquake on recruitment into the micronutrient study was re-administered by telephone 7-10 and again 14-18 days post-earthquake to volunteer, earthquake-exposed participants. A modified Brinley plot analysis of the individual DASS-42 scores showed that the 16 participants on the nutritional supplement were more resilient to the effects of the earthquake than the 17 individuals not taking the supplement. This effect was particularly marked for Depression scores.

## 22. Rucklidge JJ, Johnstone J, Harrison R, Boggis A

**Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/Hyperactivity Disorder**  
**Psychiatry Research, 189:281-87. doi:10.1016/j.psychres.2011.06.016/published June 20, 2011**

### ABSTRACT

The role of good nutrition for resilience in the face of stress is a topic of interest, but difficult to study. A 7.1 earthquake took place in the midst of research on a micronutrient treatment for Attention-Deficit/Hyperactivity Disorder (ADHD), providing a unique opportunity to examine whether individuals with ADHD taking micronutrients demonstrated more emotional resilience post-earthquake than individuals with ADHD not taking micronutrients. Thirty-three adults with ADHD were assessed twice following the earthquake using a measure of depression, anxiety and stress also completed at some point pre-earthquake (baseline). Seventeen were not taking micronutrients at the time of the earthquake (control group), 16 were (micronutrient group). While there were no between-group differences one week post-quake (Time 1), at two weeks post-quake (Time 2), the micronutrient group reported significantly less anxiety and stress than the controls (effect size 0.69). These between group differences could not be explained by other variables, such as pre-earthquake measures of emotions, demographics, psychiatric status, and personal loss or damage following the earthquake. The results suggest micronutrients may increase resilience to ongoing stress and anxiety associated with a highly stressful event in individuals with ADHD and are consistent with controlled studies showing benefit of micronutrients for mental health.

## 23. Simpson JSA, Crawford SG, Goldstein ET, Field C, Burgess E, Kaplan BJ

**Safety and tolerability of a complex micronutrient formula used in mental health: A compilation of eight datasets**  
**BMC Psychiatry/published April 18, 2011; 11:62; <http://www.biomedcentral.com/1471-244X/11/62>**

### ABSTRACT

**Background:** Theoretically, consumption of complex, multinutrient formulations of vitamins and minerals should be safe, as most preparations contain primarily the nutrients that have been in the human diet for millennia, and at safe levels as defined by the Dietary Reference Intakes. However, the safety profile of commercial formulae may differ from foods because of the amounts and combinations of nutrients they contain. As these complex formulae are being studied and used clinically with increasing frequency, there is a need for direct evaluation of safety and tolerability.

**Objective:** The aim of this project was to compile all known safety and tolerability data collected on one complex nutrient formula.

**Data Sources and Results:** Data were assembled from all the known published and unpublished studies for the complex formula with the largest amount of published research in mental health. Biological safety data from 144 children and adults were available from six sources: there were no occurrences of clinically meaningful negative outcomes/effects or abnormal blood tests that could be attributed to toxicity. Adverse event (AE) information from 157 children and adults was available from six studies employing the current version of this formula, and only minor, transitory reports of headache and nausea emerged.

Only one of the studies permitted a direct comparison between micronutrient treatment and medication: none of the 88 pediatric and adult participants had any clinically meaningful abnormal laboratory values, but tolerability data in the group treated with micronutrients revealed significantly fewer AEs and less weight gain.

**Conclusions:** This compilation of safety and tolerability data is reassuring with respect to the broad spectrum approach that employs complex nutrient formula as a primary treatment.

## 24. Rucklidge JJ, Taylor MR, Whitehead KA

Impact of a micronutrient formula on ADHD and mood dysregulation in adults with ADHD: Evidence from an 8-week open label trial with natural follow-up  
*Journal of Attention Disorders*, 2011;15(1):79-91

### ABSTRACT

**Objective:** To investigate the impact of a 36-ingredient micronutrient formula consisting mainly of minerals and vitamins in the treatment of adults with both Attention-deficit/hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD).

**Method:** 14 medication-free adults (9 men, 5 women; 18-55 years) with ADHD and SMD completed an 8-week open-label trial.

**Result:** A minority reported transitory mild side effects. Significant improvements were noted across informants (self, observer, clinician) on measures of inattention and hyperactivity/impulsivity, mood, quality of life, anxiety, and stress all with medium to very large effect sizes (all  $p$ s < .01); however, the mean of inattention remained in a clinical range whereas the means on measures of mood and hyperactivity/impulsivity were normalized. Follow-up data showed maintenance of changes or further improvement for those who stayed on the micronutrients.

**Conclusion:** Although this study, as an open trial, does not in itself prove efficacy, it provides preliminary evidence supporting the need for a randomized clinical trial of micronutrients as treatment for the more complex presentations of ADHD.

## 25. Rucklidge JJ, Gately D, Kaplan BJ

Database analysis of children and adolescents with Bipolar Disorder consuming a micronutrient formula  
*BMC Psychiatry*/published September 28, 2010; 10:74. doi:10.1186/1471-244X-10-74 ; <http://www.biomedcentral.com/content/pdf/1471-244X-10-74.pdf>

### ABSTRACT

**Background:** Eleven previous reports have shown potential benefit of micronutrient treatment for psychiatric symptoms. The current study asked whether children (7-18 years) with pediatric bipolar disorder (PBD) benefited from the same micronutrient formula; the impact of Attention-Deficit/Hyperactivity Disorder (ADHD) on their response was also evaluated.

**Method:** Data were available from 120 children whose parents reported a diagnosis of PBD; 79% were taking psychiatric medications that are used to treat mood disorders; 24% were also reported as ADHD. Using Last Observation Carried Forward (LOCF), data were analyzed from 3 to 6 months of micronutrient use.

**Result:** At LOCF, mean symptom severity of bipolar symptoms was 46% lower than baseline (effect size (ES) = 0.78) ( $p$  < 0.001). In terms of responder status, 46% experienced >50% improvement at LOCF, with 38% still taking psychiatric medication (52% drop from baseline) but at much lower levels (74% reduction in number of medications being used from baseline). The results were similar for those with both ADHD and PBD: a 43% decline in PBD symptoms (ES = 0.72) and 40% in ADHD symptoms (ES = 0.62). An alternative sample of children with just ADHD symptoms ( $n$  = 41) showed a 47% reduction in symptoms from baseline to LOCF (ES = 1.04). The duration of reductions in symptom severity suggests that benefits were not attributable to placebo/expectancy effects. Similar findings were found for younger and older children and for both sexes.

**Conclusion:** The data are limited by the open label design, the lack of a control group, and the inherent self-selection bias. While these data cannot establish efficacy, the results are consistent with a growing body of research suggesting that micronutrients appear to have therapeutic benefit for children with PBD with or without ADHD in the absence of significant side effects and may allow for a reduction in psychiatric medications while improving symptoms. The consistent reporting of positive changes across multiple sites and countries are substantial enough to warrant a call for randomized clinical trials using micronutrients.

## 26. Rucklidge JJ, Harrison R

Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A Case Study  
CNS Spectrums/published January 13, 2010; 15(5):231-237

### ABSTRACT

Bipolar disorder with co-occurring attention-deficit/hyperactivity disorder (ADHD) is a challenge to treat. Ten previous reports have shown potential benefit of a micronutrient treatment (consisting mainly of vitamins and minerals) for various psychiatric symptoms, including mood and ADHD. This case study aimed to investigate the longer term impact of the micronutrients on both psychiatric and neurocognitive functioning in an off-on-off-on (ABAB) design with 1-year follow-up. A 21-year-old female with bipolar II disorder, ADHD, social anxiety, and panic disorder entered an open-label trial using a nutritional treatment following a documented 8 year history of on-going psychiatric symptoms not well managed by medications. After 8 weeks on the formula she showed significant improvements in mood, anxiety, and hyperactivity/impulsivity. Blood test results remained normal after 8 weeks on the formula. She did not report any adverse side effects associated with the treatment. She then chose to come off the formula; after 8 weeks her depression scores returned to baseline, and anxiety and ADHD symptoms worsened. The formula was reintroduced, showing gradual improvement in all psychiatric symptoms. This case represents a naturalistic ABAB design showing on-off control of symptoms. After 1 year, the patient is now in remission from all mental illness. Neurocognitive changes mirrored behavioral changes, showing improved processing speed, consistency in response speed, and verbal memory. A placebo response and expectancy effects cannot be ruled out although previous poor response to treatment and the duration of the current positive response decrease the likelihood that other factors better explain change. These consistently positive outcomes alongside an absence of side effects indicate that further research, particularly larger and more controlled trials, is warranted using this multinutrient approach.

## 27. Mehl-Madrona L, Leung B, Kennedy C, Paul S, Kaplan BJ

Micronutrients versus standard medication management in autism: A Naturalistic Case-Control Study  
Journal of Child and Adolescent Psychopharmacology/published 2010; 20(2):95-103;  
<http://www.liebertonline.com/doi/pdfplus/10.1089/cap.2009.0011>

### ABSTRACT

Autism spectrum disorder (ASD) is often accompanied by self-injurious behavior (SIB), aggression, and tantrums, symptoms that have reportedly improved with micronutrient (vitamins and minerals) treatment. The current study took advantage of naturally occurring differences in parental preferences for treatment approaches. The micronutrient group asked for treatment without pharmaceuticals (n=44, aged 2.28 years at entry [M=8.39+5.58]). Their records were matched with those of 44 similar children whose families requested conventional treatment (medication group). Both groups improved on both the Childhood Autism Rating Scale and the Childhood Psychiatric Rating Scale (all p values <0.0001). Both groups also exhibited significant decreases in total Aberrant Behavior Checklist scores, but the micronutrient group's improvement was significantly greater (p<0.0001). SIB Intensity was lower in the micronutrient group at the end of the study (p=0.005), and improvement on the Clinical Global Impressions scale was greater for the micronutrient group (p=0.0029). It is difficult to determine whether the observed changes were exerted through improvement in mood disorder or through an independent effect on autistic disorder. There were some advantages to treatment with micronutrients: lower activity level, less social withdrawal, less anger, better spontaneity with the examiner, less irritability, lower intensity SIB, markedly fewer adverse events, and less weight gain. Advantages of medication management were insurance coverage, fewer pills, and less frequent dosing.

## 28. Gately D, Kaplan BJ

Database analysis of adults with bipolar disorder consuming a micronutrient formula

Clinical Medicine: Psychiatry/published 2009; 4: 3-16; [http://la-press.com/article.php?article\\_id=1384](http://la-press.com/article.php?article_id=1384)

### ABSTRACT

**Background:** Bipolar disorder is a lifelong problem with imperfect available treatments. Recent research has shown potential benefit of nutritional treatment for mood symptoms. The goal of the current study was to determine whether adults with bipolar disorder reported treatment benefit from consuming a micronutrient formula.

**Method:** Self-report data were available from 682 adults who reported a diagnosis of bipolar disorder; 81% were taking psychiatric medications. Those reporting additional diagnoses were excluded, as well as those who provided data <60 times during 180 days of using the micronutrients, leaving 358 for analysis.

**Result:** Mean symptom severity was 41% lower than baseline after 3 months (effect size = 0.78), and 45% lower after 6 months (effect size = 0.76) (both paired t-tests significant, p < 0.001). In terms of responder status, 53% experienced >50% improvement at 6 months. Half the sample were taking medications approved for bipolar disorder (lithium, anticonvulsants, atypical antipsychotics), and half were either medication-free or taking other medications: the magnitude of treatment benefit did not differ between these two groups. Regression analyses indicated that decreased symptom severity over the 6 months was associated with increasing micronutrient dosage and with reducing medication. Symptom improvements were significant and sustained at 6 months, suggesting that benefits were not attributable to placebo/expectancy effects.

**Conclusion:** Further research on this micronutrient formula is warranted.

## 29. Rucklidge JJ

Successful treatment of OCD with a micronutrient formula following partial response to CBT: A Case Study  
*Journal of Anxiety Disorders*/published February 26, 2009; 23:836-840

### ABSTRACT

Obsessive Compulsive Disorder (OCD) affects 0.5-2% of young people many of whom are resistant to conventional treatments. This case study describes an 18-year-old male with OCD who first underwent cognitive behavioral therapy (CBT) for a 1-year period with a modest response (his OCD had shifted from severe to moderate). Within a year, his anxiety had deteriorated back to the severe range and he now had major depression. He then entered an ABAB design trial using a nutritional formula consisting mainly of minerals and vitamins (together, known as micronutrients). After 8 weeks on the formula, his mood was stabilized, his anxiety reduced, and his obsessions were in remission. The treatment was then discontinued for 8 weeks, during which time his obsessions and anxiety worsened and his mood dropped. Reintroduction of the formula again improved the symptoms. This case illustrates the importance of considering the effect micronutrients have on mental illness.

## 30. Frazier EA, Fristad M, Arnold LE

Multinutrient Supplement as Treatment: Literature Review and Case Report of a 12-year-old Boy with Bipolar Disorder  
*Journal of Child and Adolescent Psychopharmacology*/published 2009; 19:453-460

### ABSTRACT

Early-onset bipolar disorder has significant morbidity and mortality. Development of safe, effective treatments to which patients will adhere is critical. Pharmacologic interventions for childhood bipolar spectrum disorders are limited and are associated with significant risk for adverse events (Kowatch et al 2005). Diet and nutrition research suggests vitamins, minerals, and other nutrients are important underpinnings of general physical and mental health; further, they may even be useful in treating mood dysregulation by providing a more favorable risk-benefit ratio than contemporary psychotropic agents (Kaplan, Crawford, Field, & Simpson 2007). This article reviews the literature on multinutrient supplementation and mental health, and examines a case study of a 12-year-old boy with bipolar disorder and comorbid diagnoses treated for 6 years with conventional medication and finally a multinutrient supplement. The multinutrient supplement in this case study is Truehope® EMPowerplus, a 36-ingredient supplement containing sixteen minerals, fourteen vitamins, three amino acids and three antioxidants. It was used to treat a 12-year-old boy initially diagnosed with bipolar disorder-not otherwise specified (BP-NOS) at age 6, whose diagnosis evolved by age 10 to bipolar I (BP-I), mixed, with psychotic features. He also met criteria for generalized anxiety disorder by age 8 and obsessive-compulsive disorder by age 10. After six years of conventional treatment (ages 6-12), he received fourteen months of Truehope® EMPowerplus. Symptom manifestation over seven years is described in conjunction with treatment history. Truehope® EMPowerplus resulted in superior outcome over conventional treatment. This report adds to accumulating preliminary evidence that further basic science and clinical studies of multinutrient supplements are warranted.

## 31. Kaplan BJ, Fisher JE, Crawford SG, Field CJ, Kolb B

Improved mood and behavior during treatment with a mineral-vitamin supplement: An Open-Label Case Series of Children  
*Journal of Child and Adolescent Psychopharmacology*/published 2004; 14(1), 115-122

### 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.

## 32. Kaplan BJ, Crawford SG, Gardner B, Farrelly G

Treatment of mood lability and explosive rage with minerals and vitamins: Two Case Studies in Children  
*Journal of Child and Adolescent Psychopharmacology*/published 2002; 12(3), 203-218

### ABSTRACT

A micronutrient supplement containing a broad range of dietary minerals and vitamins is being examined for the treatment of mood lability in both adults and children (Kaplan et al. 2001; Popper 2001). During pilot work, two medication-free boys with mood lability and explosive rage were studied in an open-label treatment followed by reversal and retreatment. One child was an 8-year-old with atypical obsessive-compulsive disorder, and the other was a 12-year-old with pervasive developmental delay. Both boys were monitored using the mood and temper items from the Conners Parent Rating Scale, as well as the Child Behavior Checklist. In addition, the boy with atypical obsessive-compulsive disorder was monitored with the child version of the Yale-Brown Obsessive Compulsive Scale. Both boys benefited from the micronutrient supplement when examined in ABAB designs: mood, angry outbursts, and obsessional symptoms improved when initially treated, returned when not taking the supplement, and remitted when the micronutrient supplement was reintroduced. Both boys have been followed and are stable on the nutritional supplement for over 2 years. These cases suggest that mood lability and explosive rage can, in some cases, be managed with a mixture of biologically active minerals and vitamins, without using lithium or other traditional psychopharmacologic agents.

## 33. Simmons M

Letter to the Editor

*Journal of Clinical Psychiatry*/published March 2003; 64(3):338

### ABSTRACT

In a letter to the editor of the *Journal of Clinical Psychiatry*, Dr. Miles Simmons, a psychiatrist in private practice in Brunswick, Maine, reported his clinical experience with Truehope® EMPowerplus. Impressed by the striking response of one of his patients to Truehope® EMPowerplus, Dr. Simmons carefully monitored treatment-resistant patients from his private practice who were willing to try this nutritional approach.

**Result:** Of 19 patients that met the DSM-IV criteria for bipolar disorder (14 bipolar I and 5 bipolar II), Dr. Simmons observed that "12 of the 19 patients showed marked clinical improvement, 3 showed moderate improvement, and 1 showed mild improvement" (84% positive response rate). Of 16 medicated patients (who were taking 2.7 psychiatric medications on average) 13 were able to completely discontinue their psychiatric medications (over an average of 5.2 weeks) had remained stable on Truehope® EMPowerplus alone for an average of 13 months.

## 34. Kaplan BJ, Simpson JSA, Ferre RC, Gorman C, McMullen D, Crawford SG

Effective mood stabilization in bipolar disorder with a chelated mineral supplement  
*Journal of Clinical Psychiatry*/published December 2001; 62(12): 936-944

### ABSTRACT

**Background:** To determine in open trials the therapeutic benefit of a nutritional supplement for bipolar disorder.

**Method:** The sample consisted of 11 patients with DSM-IV-diagnosed bipolar disorder aged 19 to 46 years, who were taking a mean of 2.7 psychotropic medications each at a study entry. Three additional patients dropped out prematurely. The intervention is a broad-based nutritional supplement of dietary nutrients, primarily chelated trace minerals and vitamins, administered in high doses. At study entry and periodically thereafter, patients were assessed with the Hamilton Rating Scale for Depression (HAM-D), the Brief Psychiatric Rating Scale (BPRS), and the Young Mania Rating Scale (YMRS).

**Result:** For those who completed the minimum 6-month open trial, symptom reduction ranged from 55% to 66% on the outcome measures; need for psychotropic medications decreased by more than 50%. Paired t tests revealed treatment benefit on all measures for patients completing the trial: HAM-D mean score at entry = 19.0, mean score at last visit = 5.4,  $t = 5.59$ ,  $df = 9$ ,  $p < .01$ ; BPRS mean score at entry = 35.3, mean score at last visit = 7.4,  $t = 2.57$ ,  $df = 9$ ,  $p < .05$ ; YMRS mean score at entry = 15.1, mean score at last visit = 6.0,  $t = 4.11$ ,  $df = 9$ ,  $p < .01$ . The effect size for the intervention was large ( $> .80$ ) for each measure. The number of psychotropic medications decreased significantly to a mean  $\pm$  SD of  $1.0 \pm 1.1$  ( $t = 3.54$ ,  $df = 10$ ,  $p < .01$ ). In some cases, the supplement replaced psychotropic medications and the patients remained well. The only reported side effect (i.e. nausea) was infrequent, minor, and transitory.

**Conclusion:** Some cases of bipolar illness may be ameliorated by nutritional supplementation. A randomized, placebo-controlled trial in adults with bipolar I disorder is currently underway, as well as open trials in children.

## 35. Popper CW

Do vitamins or minerals (apart from lithium) have mood-stabilizing effects? [Commentary]

Journal of Clinical Psychiatry/published December 2001; 62, 933-935

### ABSTRACT

Dr. Charles Popper, psychopharmacologist and psychiatrist at Harvard University's McLean Hospital, published a commentary on the Kaplan et al. (2001) paper, in which he reported the results of his clinical experience with Truehope® EPowerplus.

**Result:** Of 22 patients (10 adults, 9 adolescents, 3 pre-adolescents) who clinically met criteria for bipolar disorder, 19 (86%) showed a positive response to the micronutrient treatment. Of 15 patients taking medications, 11 (73%) were able to gradually withdraw from their medications, and were stable taking the micronutrient treatment alone.