



CS BrainSense
BRAIN • BODY • BALANCE



48 Studies on Micronutrient Formulations and Vitamin-Mineral Treatments for Mental Health Conditions and Whole Body Wellness

Vitamin-mineral treatment improves aggression and emotional regulation in children with ADHD: a fully blinded, randomized, placebo-controlled trial.

BACKGROUND:

Evaluation of broad-spectrum micronutrient (vitamins and minerals) treatment for childhood ADHD has been limited to open-label studies that highlight beneficial effects across many aspects of psychological functioning.

METHOD:

This is the first fully blinded randomized controlled trial of medication-free children (n = 93) with ADHD (7-12 years) assigned to either micronutrients (n = 47) or placebo (n = 46) in a 1:1 ratio, for 10 weeks. All children received standardized ADHD assessments. Data were collected from clinicians, parents, participants and teachers across a range of measures assessing ADHD symptoms, general functioning and impairment, mood, aggression and emotional regulation.

RESULTS:

Intent-to-treat analyses showed significant between-group differences favouring micronutrient treatment on the Clinical Global Impression-Improvement (ES = 0.46), with 47% of those on micronutrients identified as 'much' to 'very much' improved versus 28% on placebo. No group differences were identified on clinician, parent and teacher ratings of overall ADHD symptoms (ES ranged 0.03-0.17). However, according to clinicians, 32% of those on micronutrients versus 9% of those on placebo showed a clinically meaningful improvement on inattentive (OR = 4.9; 95% CI: 1.5-16.3), but no group differences on improvement in hyperactive-impulsive symptoms (OR = 1.0; 95% CI: 0.4-2.5). Based on clinician, parent and teacher report, those on micronutrients showed greater improvements in emotional regulation, aggression and general functioning compared to placebo (ES ranged 0.35-0.66). There were two dropouts per group, no group differences in adverse events and no serious adverse events identified. Blinding was successful with guessing no better than chance.

CONCLUSIONS:

Micronutrients improved overall function, reduced impairment and improved inattention, emotional regulation and aggression, but not hyperactive/impulsive symptoms, in this sample of children with ADHD. Although direct benefit for core ADHD symptoms was modest, with mixed findings across raters, the low rate of adverse effects and the benefits reported across multiple areas of functioning indicate micronutrients may be a favourable option for some children, particularly those with both ADHD and emotional dysregulation. Trial registered with the Australian New Zealand Clinical Trials Registry ACTRN12613000896774.

Vitamin-mineral treatment improves aggression and emotional regulation in children with ADHD: a fully blinded, randomized, placebo-controlled trial. Rucklidge JJ, Eggleston MJF, Johnstone JM, Darling K, Frampton CM. J Child Psychol Psychiatry. 2017 Oct 2.

[FULL TEXT](#)



KEY BENEFITS

CS BrainSense is designed to provide a solid nutritional foundation to help your brain and body perform optimally.*

- **Brain.** Powered by our proprietary CSTek™ mineral delivery technology, which combines each mineral with organic molecules. CSTek™ is intended to optimize mineral absorption and enable vital nutrients to cross the blood-brain barrier in order to support neuron structure and function.*
- **Body.** Delivers essential vitamins and minerals to fortify your body against chronic stress, anxiety, depression, and brain cell degeneration.*
- **Balance.** The level of each ingredient is calculated to maintain the natural ratios of nutrients in your body that are critical to promote optimal cognitive function, mental clarity, focus, and mood stability.*



Double-blind study: Micronutrient formulation is an effective and safe treatment for adult ADHD.

A micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy, showed “statistically robust improvements” in the first-ever double-blind study to test the effectiveness and safety of a multivitamin/mineral treatment for adult ADHD. Researchers from the University of Canterbury and the University of Otago, New Zealand, randomized 80 adults diagnosed with ADHD to take either the micronutrient formulation or identical-looking placebo pills for 8 weeks. Most of the study participants had at least one psychiatric diagnosis in addition to ADHD. Additional diagnoses included multiple anxiety disorders, major depressive disorder, dysthymia, bipolar disorder, reading disability, and alcohol/substance misuse or dependence. The nutrient group reported more than double the improvement in attention, hyperactivity, and impulsivity symptoms, compared with the placebo group. Clinical psychologists rated more than twice as many people in the nutrient group ‘very much’ or ‘much’ improved in overall symptoms. They also rated moderate and severely depressed participants in the nutrient group as having nearly double the improvement in depression symptoms. Researchers found that the micronutrients were completely safe; there were no differences in side effects between the two groups.

Vitamin–mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomised placebo-controlled trial. Rucklidge JJ, Frampton CMA, Gorman B, Boggis A. The British Journal of Psychiatry. 2014 Feb;204(2): doi: 10.1192/bjp.bp.113.132126 [Epub ahead of print]

[FULL TEXT](#)

Micronutrient formulation outperforms Berocca Performance in reducing depression, anxiety, and stress in 91 earthquake survivors.

Following a 6.3-magnitude earthquake in Christchurch, New Zealand, researchers randomized 91 earthquake survivors to take one of two vitamin mineral formulas (Berocca Performance or a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy. Then they measured symptoms of situation-induced depression, anxiety, and stress in these individuals, as well as 25 additional people who took no supplement (a control group). After 4 weeks, 20% of the control group, 43% of the Berocca Performance group, and 74% of the group taking the micronutrients showed significant improvement in depression, anxiety, and stress symptoms. Researchers concluded that this study supports micronutrients as an inexpensive and practical treatment for acute stress following a natural disaster, with a slight advantage to higher doses.

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

Rucklidge JJ, Andridge R, Gorman B, Blampied N, Gordon H, Boggis A. Human Psychopharmacology. 2012 Sep;27(5):440-54.

[FULL TEXT](#)

Supplement Facts

Serving Size: 4 Veggie Capsules
Servings Per Container: 30

| Amount Per Serving | Label Claim | %DV |
|--|-------------|--------|
| Vitamin A (as retinyl palmitate) | 576 mcg | 64% |
| Vitamin C (as ascorbic acid) | 200 mg | 222% |
| Vitamin D (as cholecalciferol) | 24 mcg | 120% |
| Vitamin E (as D-alpha tocopheryl succinate) | 78 mg | 520% |
| Vitamin K (as phyloquinone & menaquinone-7) | 40 mcg | 33% |
| Thiamin (as thiamine mononitrate) | 20 mg | 1667% |
| Riboflavin | 6 mg | 462% |
| Niacin (as niacinamide) | 30 mg | 188% |
| Vitamin B6 (as pyridoxine hydrochloride) | 23.3 mg | 1372% |
| Folate (as calcium L-5 methyltetrahydrofolate) | 444 mcg DFE | 111% |
| Vitamin B12 (as adenosylcobalamin & methylcobalamin) | 300 mcg | 12500% |
| Biotin | 360 mcg | 1200% |
| Pantothenic acid (as D-calcium pantothenate) | 10 mg | 200% |
| Choline (as bitartrate) | 64 mg | 12% |
| Calcium (as CSTek™ Chelation Complex) | 440 mg | 34% |
| Iron (as CSTek™ Chelation Complex) | 4.6 mg | 26% |
| Phosphorus (as CSTek™ Chelation Complex) | 280 mg | 22% |
| Iodine (as CSTek™ Chelation Complex) | 68 mcg | 45% |
| Magnesium (as CSTek™ Chelation Complex) | 200 mg | 48% |
| Zinc (as CSTek™ Chelation Complex) | 16 mg | 145% |
| Selenium (as CSTek™ Chelation Complex) | 68 mcg | 124% |
| Copper (as CSTek™ Chelation Complex) | 2.4 mg | 267% |
| Manganese (as CSTek™ Chelation Complex) | 3.2 mg | 139% |
| Chromium (as CSTek™ Chelation Complex) | 208 mcg | 594% |
| Molybdenum (as CSTek™ Chelation Complex) | 48 mcg | 107% |
| Potassium (as CSTek™ chelation complex) | 80 mg | 2% |
| Proprietary blend | 416 mg | † |

Alpha-lipoic acid, mineral wax, inositol, acetyl-L-carnitine, grape seed extract, ginkgo biloba leaf extract, N-acetyl-L-cysteine, L-methionine, trace minerals as CSTek™ chelation complex: boron, vanadium, nickel.

† Daily Value (%DV) not established.

Other ingredients: Vegetarian capsule (hypromellose), microcrystalline cellulose, magnesium stearate, silicon dioxide, titanium dioxide.



GMO-Free
Gluten Free
Vegetarian Friendly



Micronutrient formulation reduces depression, anxiety, and stress in 17 earthquake survivors with ADHD.

A 7.1-magnitude earthquake in Christchurch, New Zealand created a natural experiment for measuring the protective effects of a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy on mood, anxiety and stress. Prior to the earthquake, researchers had assessed mood, anxiety and stress levels in a group of 33 adults diagnosed with attention deficit hyperactivity disorder, and they chose to repeat the same measures after the earthquake. Scores showed that the 16 participants taking micronutrients were more resilient to the effects of the earthquake than the 17 individuals not taking any supplement. This effect was particularly marked for depression scores.

Post-earthquake psychological functioning in adults with attention-deficit/hyperactivity disorder: positive effects of micronutrients on resilience.
Rucklidge JJ, Blampied, NM. *New Zealand Journal of Psychology*. 2011;40(4):51.

[FULL TEXT](#)

Database analysis: Micronutrient formulation greatly improves bipolar symptoms in 358 adults.

Scientists analyzed data from 358 adults with a diagnosis of bipolar disorder who took a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy for 6 months or more. The adults' overall symptom severity was 41% lower than baseline after 3 months, and 45% lower after 6 months. In addition, at 6 months, 53% of adults experienced greater than 50% improvement in symptoms, with 32% of adults experiencing greater than 75% improvement in symptoms. Symptom improvements at 6 months suggested that benefits of micronutrient treatment were not attributable to placebo or expectancy effects. Of those taking psychiatric medications, nearly half were able to discontinue them over a 6-month period. The remainder reduced their medication usage by 54% during the same time period. Adults who gradually eliminated their medications and took full recommended levels of the vitamin-mineral formulation experienced the greatest improvements in symptoms.

Database analysis of adults with bipolar disorder consuming a micronutrient formula.
Gately D, Kaplan BJ. *Clinical Medicine Insights: Psychiatry*. 2009 Apr;4:3-16.

[FULL TEXT](#)

Database analysis: Micronutrient formulation greatly improves bipolar and ADHD symptoms in 161 children and adolescents.

Scientists analyzed data from 120 children with pediatric bipolar disorder who were treated with a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy for at least 6 months. 24% of these children also had a diagnosis of attention deficit hyperactivity disorder (ADHD). Their results were compared with an additional 41 children who were diagnosed with ADHD alone. Children with a bipolar diagnosis showed a 59% decline in symptoms, whereas children with ADHD showed a 40% decrease in symptoms. The duration of symptom reduction suggests that benefits of micronutrient treatment were not attributable to placebo or expectancy effects. Of those taking psychiatric medications, more than half were able to completely discontinue them over a 6-month period. Medication use by the remainder of children was reduced by 74% during the same time period.

Database analysis of children and adolescents with bipolar disorder consuming a micronutrient formula.
Rucklidge JJ, Gately D, Kaplan BJ. *BioMed Central Psychiatry*. 2010 Sep 28;10:74.

[FULL TEXT](#)



Micronutrient formulation outperforms medications in 88 patients with autism.

Researchers compared psychiatric medication and micronutrient treatment approaches in 88 children with autism spectrum disorder. The micronutrient group (taking predominately a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy) improved significantly more than the medication group in key ways, including notably reduced irritability, anger, and intensity of self-injurious behaviors. The micronutrient-treated group also had dramatically lower treatment side-effects.

Micronutrients versus standard medication management in autism: a naturalistic case-control study.

Mehl-Madrone L, Leung B, Kennedy C, Paul S, Kaplan BJ. *Journal of Child and Adolescent Psychopharmacology*. 2010 Apr;20(2):95-103.

[FULL TEXT](#)

Micronutrient formulation greatly improves bipolar symptoms in 23 adults, adolescents, and children.

After observing a 10-year-old boy's dramatic response to a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy, Dr. Charles Popper, a psychiatrist and psycho-pharmacologist at Harvard Medical School, treated 22 additional bipolar disorder-diagnosed 4 patients in his private practice (10 adults, 9 adolescents, and 3 preadolescents) with the micronutrients. Nineteen of the 22 patients (86%) showed a positive response to micronutrient treatment. Of the 15 patients being treated with medications when they began the nutritional supplement, 11 patients remained stable during a follow-up period of 6 to 9 months without psychiatric medications.

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

Popper CW. *The Journal of Clinical Psychiatry*. 2001 Dec;62(12):933-5.

[FULL TEXT](#)

Micronutrient formulation greatly improves bipolar symptoms in 19 adults.

Dr. Miles Simmons, a psychiatrist in private practice, followed nineteen patients diagnosed with bipolar I or bipolar II disorder for an average of 13 months while they took a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy. Sixteen of the 19 patients (84%) showed significant clinical improvement. Thirteen of 16 medicated patients were able to completely discontinue psychiatric medications over 3 to 10 weeks and maintain stability over an average follow-up period of 13 months.

Nutritional approach to bipolar disorder.

Simmons M. *The Journal of Clinical Psychiatry*. 2003 Mar;64(3):338; author reply 338-9.

[FULL TEXT](#)

Micronutrient formulation greatly improves ADHD and other psychiatric disorders in 14 adults.

Researchers documented the impact of a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy in the treatment of 14 medication-free adults with attention deficit hyperactivity disorder. The adults' additional psychiatric diagnoses included major depressive disorder, bipolar disorder II, generalized anxiety disorder, social phobia, obsessive compulsive disorder, posttraumatic stress disorder, panic disorder with agoraphobia, and psychotic disorder not otherwise specified. During 8 weeks of micronutrient treatment, mood and hyperactivity/impulsivity symptoms normalized. Researchers also noted significant improvements on measures of anxiety, attention, stress, and quality of life. In follow-up, those who continued to take the micronutrients for 2-6 months experienced sustained or improved symptom relief.

Effect of micronutrients on behavior and mood in adults with ADHD: evidence from an 8-week open label trial with natural extension.

Rucklidge J, Taylor M, Whitehead K. *Journal of Attention Disorders*. 2011 Jan;15(1):79-91.

[FULL TEXT](#)



Micronutrient formulation stabilizes mood in 11 bipolar adults.

Researchers treated 11 adults diagnosed with various types of bipolar disorder for an average of 44 weeks with a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy. The adults' additional diagnoses included attention deficit hyperactivity disorder, dysthymic disorder, and obsessive-compulsive disorder. The adults experienced a 55% reduction in depression symptoms, a 60% reduction in mania symptoms, and a 66% reduction in general psychiatric symptoms. Their psychiatric medication use decreased by more than 50%. The only reported side effect, nausea, was infrequent, minor, and transitory.

Effective mood stabilization with a chelated mineral supplement: an open-label trial in bipolar disorder.

Kaplan BJ, Simpson JS, Ferre RC, Gorman CP, McMullen DM, Crawford SG. *The Journal of Clinical Psychiatry*. 2001 Dec;62(12):936-44.

[FULL TEXT](#)

Micronutrient formulation greatly improves mood, behavior, and anxiety disorders in 9 children.

Researchers treated nine unselected children with mood and behavioral problems with a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy. The children's psychiatric diagnoses included attention deficit hyperactivity disorder, bipolar disorder, depression, oppositional defiant disorder, obsessive-compulsive disorder, generalized anxiety disorder, Asperger syndrome, and Prader-Willi syndrome. After a minimum of 8 weeks of micronutrient treatment, the children's behavior improved significantly in the following areas: anxious and depressed mood, thought problems, interpersonal relationship problems, attention problems, social problems, withdrawn behavior, disruptive behavior, delinquent behavior, aggressive behavior, and self-harm behavior.

Improved mood and behavior during treatment with a mineral-vitamin supplement: an open-label case series of children.

Kaplan BJ, Fisher JE, Crawford SG, Field CJ, Kolb B. *Journal of Child and Adolescent Psychopharmacology*. 2004 Spring;14(1):115-22.

[FULL TEXT](#)

Safety and tolerability of Micronutrient formulations.

Scientists compiled safety data from all published and unpublished studies that used a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy which has been widely researched in the mental health field. Biological safety data from six sources, including 144 children and adults, showed no occurrences of clinically 5 meaningful negative outcomes/effects or abnormal blood tests that could be attributed to toxicity. Adverse event information from six studies involving 157 children and adults included reports of minor, transitory headache and nausea. Only one of the studies permitted a direct comparison between tolerability of the micronutrient treatment and medications: children and adults treated with micronutrients showed significantly fewer adverse events and significantly less weight gain compared with those taking medications.

Systematic review of safety and tolerability of a complex micronutrient formula used in mental health.

Simpson JS, Crawford SG, Goldstein ET, Field C, Burgess E, Kaplan BJ. *BioMed Central Psychiatry*. 2011 Apr 18;11:62.

[FULL TEXT](#)



Micronutrient formulation greatly improves brain function in rats.

Researchers at the world-renowned Canadian Centre for Behavioural Neuroscience conducted a series of controlled studies with rats fed a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy to test its effects on brain injuries and brain-related disorders. Neuroscientists performed surgery on a group of young rats, removing either the entire frontal lobe of the brain or part of the parietal lobe. The researchers then fed one group of these rats Purina Rat Chow (considered to be an ideally fortified lab rat diet with 22 added vitamins and minerals) and another group the same base diet fortified with the more complete, specially-processed micronutrient formulation. Brain recovery was significantly enhanced in the micronutrient-fed rats. As the rats recovered, researchers observed that the micronutrient-fed rats showed significantly calmer behavior and dramatically improved cognitive function compared with Purina fed rats. The brain cells of micronutrient rats were also more complexly-branched and better connected with neighboring cells than the brain cells of Purina-fed rats. The calmer behavior and enhanced cognitive function of micronutrient-treated rats are consistent with results documented by researchers around the world in many people with mood, anxiety, and behavioral disorders. The enhanced brain cell connectivity observed by researchers supports the use of micronutrient formulations for human brain recovery in conjunction with brain rehabilitation therapies.

Factors influencing frontal cortex development and recovery from early frontal injury.

Halliwell C, Comeau W, Gibb R, Frost DO, Kolb B. *Developmental Neurorehabilitation*. 2009;12(5):269-78.

[FULL TEXT](#)

Successful treatment of bipolar disorder II and ADHD with a micronutrient formula: a case study.

Researchers documented the effects of a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy on psychiatric and neurocognitive functioning in a naturalistic off-on-off-on design. A 21-year old female with bipolar II disorder, attention deficit hyperactivity disorder (ADHD), social anxiety, and panic disorder began taking a vitamin-mineral formulation following a documented 8-year history of ongoing psychiatric symptoms that were not well managed by medications. After 8 weeks on the formula, she showed significant improvements in mood, anxiety, and hyperactivity/impulsivity. She then chose to come off the formula. After 8 weeks, her depression scores returned to pre-treatment levels, and anxiety and ADHD symptoms worsened dramatically. When the formula was reintroduced, all psychiatric symptoms showed gradual improvements. After one year, she was in remission of all mental illness diagnoses. Her neurocognitive changes mirrored behavioral changes, showing improved processing speed, variability in response, and verbal memory.

Successful treatment of bipolar disorder II and ADHD with a micronutrient formula: a case study.

Rucklidge JJ, Harrison R. *CNS Spectrums*. 2010 May;15(5):289-95.

[FULL TEXT](#)

Successful treatment of OCD with a micronutrient formula following partial response to Cognitive Behavioral Therapy (CBT): a case study.

Researchers detail an off-on-off-on trial of an 18-yearold male diagnosed with obsessive-compulsive disorder (OCD) and Asperger's disorder who took a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy. The young man first underwent cognitive behavioral therapy (CBT) for one year with a modest response. Within a year thereafter, his anxiety became severe again and he began to experience major depression. After 8 weeks of using a vitamin-mineral formulation, his mood stabilized, his anxiety reduced, and his obsessions were in remission. Treatment was then discontinued for 8 weeks, during which time his obsessions, anxiety, and mood worsened. Reintroduction of the micronutrient formula again improved mood, obsession and anxiety symptoms within 8 weeks. After taking the formulation for 6 months longer, he experienced further improvements in mood and anxiety symptoms.

Successful treatment of OCD with a micronutrient formula following partial response to Cognitive Behavioral Therapy (CBT): a case study.

Rucklidge JJ. *Journal of Anxiety Disorders*. 2009 Aug;23(6):836-40.

[FULL TEXT](#)



Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children.

Researchers describe two medication-free boys with unstable mood and explosive rage who took a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy followed by reversal and re-treatment. The boys' diagnoses included pervasive developmental disorder with Asperger characteristics, attention deficit hyperactivity disorder, obsessive compulsive-disorder, and autism. Both boys benefited significantly from the micronutrient formula: mood, angry outbursts, delinquent behavior, social and attention problems, and anxious/obsessional symptoms improved when initially treated, returned when they discontinued treatment, and remitted when the micronutrient treatment was reintroduced. During a follow-up of over 2 years, both boys continued to be stable while taking the micronutrient treatment.

Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children.

Kaplan BJ, Crawford SG, Gardner B, Farrelly G. *Journal of Child and Adolescent Psychopharmacology*. 2002 Fall;12(3):205-19.

[FULL TEXT](#)

Multinutrient supplement as treatment: literature review and case report of a 12-year-old boy with bipolar disorder.

Researchers describe a 12-year-old boy who was diagnosed at age 6 with bipolar disorder. His diagnosis evolved to include psychotic features, generalized anxiety disorder and obsessive-compulsive disorder. Although he was treated with psychiatric medications for 6 years, he continued to experience many debilitating mood, anxiety, and obsessive-compulsive symptoms. During treatment with a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy, the boy's global functioning notably improved. He began interacting more appropriately with peers, remained calm and playful throughout most of the day, slept throughout the night, remained focused and efficient while completing schoolwork, and experienced decreased compulsions. Eventually, his hallucinations also ceased and all diagnoses fully remitted. His symptoms remained stable during a 14-month follow-up period.

Multinutrient supplement as treatment: literature review and case report of a 12-year-old boy with bipolar disorder.

Frazier EA, Fristad MA, Arnold LE. *Journal of Child and Adolescent Psychopharmacology*. 2009 Aug;19(4):453-60.

[FULL TEXT](#)

Efficacy and cost of micronutrient treatment of childhood psychosis.

An 11-year-old boy with a 3-year history of mental illness and psychiatric medication treatment was transitioned to a micronutrient formulation co-developed[†] by Hardy Nutritionals[®] founder David Hardy. The boy was diagnosed with multiple psychiatric disorders, including obsessive-compulsive disorder, generalized anxiety disorder, social anxiety disorder, and psychosis—not otherwise specified. The boy's anxiety, obsessive-compulsive, and psychotic symptoms decreased significantly when he took the vitamin-mineral formulation, and his progress was maintained through a 4-year follow-up. A cost comparison revealed that the boy's micronutrient treatment cost less than 1% of his former inpatient mental health care.

Efficacy and cost of micronutrient treatment of childhood psychosis.

Rodway M, Vance A, Watters A, Lee H, Bos E, Kaplan BJ. *BMJ Case Reports*. 2012 Nov 9;2012.

[FULL TEXT](#)



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

Researchers investigated the therapeutic effects of a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy in 7 children with bipolar disorder. The children's additional psychiatric diagnoses included attention deficit hyperactivity disorder, oppositional defiant disorder, major depressive disorder, generalized anxiety disorder, conduct disorder, and obsessive-compulsive disorder. The children experienced a 37% decrease in depression scores and a 45% decrease in mania scores over 8 weeks. Side effects were minor and transient—mostly temporary gastric discomfort.

Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders.
Frazier EA, Fristad MA, Arnold LE. *Journal of Alternative and Complementary Medicine*. 2012 Jul;18(7):678-85.

[FULL TEXT](#)

Can micronutrients improve neurocognitive functioning in adults with ADHD and severe mood dysregulation? A pilot study.

Researchers studied the impact of a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy on neurocognitive functioning in 14 adults with attention deficit hyperactivity disorder (ADHD) and severe mood dysregulation over an 8-week period. Significant improvement was observed in the ADHD-micronutrient group, but not the control group, across a range of verbal 7 abilities, including verbal learning, verbal cognitive flexibility and fluency, and verbal inhibition. These neurocognitive improvements were large and consistent with improved psychiatric functioning.

Can micronutrients improve neurocognitive functioning in adults with ADHD and severe mood dysregulation? A pilot study.
Rucklidge JJ, Harrison R, Johnstone J. *Journal of Alternative and Complementary Medicine*. 2011 Dec;17(12):1125-31.

[FULL TEXT](#)

Could yeast infections impair recovery from mental illness? A case study using micronutrients and olive leaf extract for the treatment of ADHD and depression.

A 24-year-old woman who experienced dramatic improvement in her ADHD and depression symptoms for more than 2 years while taking a micronutrient formulation co-developed⁺ by Hardy Nutritionals[®] founder David Hardy later experienced a recurrence of her former psychiatric symptoms as a result of a severe yeast infection. Her physical symptoms included an overall flu-like feeling; a chronic sore throat and runny nose; cravings for sugary and starchy foods; gastrointestinal cramps; and rashes and itching on her legs, groin, genital and rectal areas. Psychiatric symptoms included severe moodiness, inability to experience pleasure, and chronic irritability. These physical and psychiatric symptoms persisted for several months despite her ongoing use of a prescription antifungal cream. The woman began taking four capsules of olive leaf extract (identical to our Hardy Nutritionals[™] Olive Leaf Extract) as well as two capsules of probiotics (identical to our Hardy Nutritionals[™] Greens & Probiotics) daily to treat the yeast infection, in addition to her regular therapeutic dose of the micronutrients. After a week and a half, the woman's physical and psychiatric symptoms both improved, including disappearance of her rashes, cessation of the chronic itching, elimination of her runny nose, and improved mood and energy levels. After 2 months, she had returned to her previous level of function. During a year of follow-up, researchers found that the woman continued to enjoy relief from the physical and psychiatric symptoms caused by the yeast infection as long as she continued to take the Olive Leaf Extract.

Could yeast infections impair recovery from mental illness? A case study using micronutrients and olive leaf extract for the treatment of ADHD and depression.
Rucklidge JJ. *Advances in Mind-Body Medicine*. 2013 Summer;27(3):14-8.

[FULL TEXT](#)



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

Scientists observed while conducting previous studies that many study participants whose psychiatric symptoms were treated successfully with a micronutrient formulation co-developed*by Hardy Nutritionals® founder David Hardy tended to reduce or eliminate use of alcohol, cigarettes and cannabis on their own. This study details one case in which on-off micronutrient use resulted in off-on cigarette and cannabis smoking as well as off-on psychiatric symptoms. Micronutrients provide the necessary precursors and cofactors for adequate neurotransmitter production and regulation. In this way, micronutrients assist with mood regulation, help reduce anxiety, and directly affect brain reward circuitry, all of which can help individuals to successfully stop drug use.

Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal design: a case study.
Harrison R, Rucklidge JJ, Blampied N. *Journal of Psychoactive Drugs*. 2013 Jun;45(2):168-178.

[FULL TEXT](#)

A randomised trial of nutrient supplements to minimise psychological stress after a natural disaster

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

A randomised trial of nutrient supplements to minimise psychological stress after a natural disaster
Kaplan BJ, Rucklidge JJ, Romijn AR, Dolph M. *Psychiatry Res*. 2015 Aug 30;228(3):373-9.

[FULL TEXT](#)



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

Following the devastating New Zealand earthquake of February 22, 2011, Dr. Rucklidge et al. conducted a 4 week randomized trial in which anxiety and stress were significantly reduced in adults given various doses of micronutrients when compared to untreated individuals. One year later Dr. Rucklidge followed up with the study participants to evaluate long-term outcomes.

Of the original 91 participants who took micronutrients in the original trial, 64 (70.3%) completed the follow-up questionnaires, as did 21 (72.4%) of the original control group. Both groups improved over their post-earthquake baseline scores, and the risk of PTSD declined drastically for both groups. However, the nutrient-treated group reported significantly lower stress and greater improvements in mood and energy than the control group one year later, even after adjusting for baseline differences ($p < 0.001$).

Those who stayed on micronutrients through to follow-up or who stopped all treatment reported better psychological functioning than those who switched to other treatments, including medications ($p < 0.023$). The researchers concluded that, while disaster survivors improve psychologically over time regardless of whether or not they receive an intervention, taking micronutrients during the acute phase immediately following a disaster might result in significantly better short and long-term outcomes.

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
Rucklidge JJ, Blampied N, Gorman B, Gordon HA, Sole E. Hum Psychopharmacol. 2014 May;29(3):230-43. doi: 10.1002/hup.2392. Epub 2014 Feb 19. PubMed PMID: 24554519.

[FULL TEXT](#)

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

Dr. Julia Rucklidge conducted nutrient assays on study participants in her 8 week double-blind RCT using micronutrient treatment for adult ADHD. Using this extensive data set, she performed a post-hoc analysis of the original study in an attempt to determine if blood levels of nutrients in adult ADHD patients could be used to predict whether or not they would respond to micronutrient treatment. The blood markers measured were Vitamin D, Vitamin B12, Folate, Iron, Zinc, Copper, and Ferritin.

With the exception of Vitamin d (27% of participants deficient), nutrient deficiencies were slight or non-existent for the majority of participants at the beginning of the trial. In spite of the fact that only one participant exhibited iron deficiency, low iron levels were associated with higher baseline depression scores ($p = 0.009$). No other nutrient significantly correlated with baseline psychiatric scores.

Throughout the course of the trial, micronutrient treatment was associated with significant increases in blood Vitamin D, Vitamin B12, and Folate (all $p < 0.001$), but only Vitamin D was also identified as one of the nutrient markers that showed a statistically significant effect on treatment response.

The nutrient markers affecting treatment response were: ferritin, vitamin D, and copper. Greater ferritin at baseline correlated with being an ADHD responder ($p = 0.027$). (ADHD response was defined as $\geq 30\%$ decrease in symptom scores for a comprehensive combination of outcome measures. Of the 64 original study participants with complete nutrient assays, 39 (60.9%) were identified as ADHD responders.) Lower baseline vitamin D was predictive of greater improvements in depression ($p = 0.011$) and global functioning ($p = 0.045$) scores, and lower baseline copper levels predicted greater response in the depression ($p = 0.002$) and clinical global improvement ($p = 0.007$) outcome measures.

From among the non-nutrient variables measured, the researchers identified developmental history as the only noticeable predictor of response. This means that people with a history of developmental risk factors (e.g., slow to talk, walk, read, toilet train) may benefit even more from micronutrient treatment than those who developed normally as a child. It is also worth noting that several participants who reported alcohol or drug use at baseline later reported a reduction or cessation of these behaviors during micronutrient treatment, suggesting the possible value of nutrients in addiction therapy.



Only a few significant associations were identified between baseline biomarkers and outcomes, but, despite the difficulty in predicting the outcome for any given person, micronutrient treatment proved very effective – providing substantial ADHD symptom reduction for over half of the adults in this study.

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

Rucklidge JJ, Johnstone J, Gorman B, Boggis A, Frampton CM. *Prog Neuropsychopharmacol Biol Psychiatry*. 2014 Apr 3;50:163-71. doi:10.1016/j.pnpbp.2013.12.014. Epub 2013 Dec 26. PubMed PMID: 24374068.

[FULL TEXT](#)

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

Researchers collected safety, tolerability, and serum micronutrient concentration data and their correlations with mood changes from an 8-week pilot feasibility study of a broad spectrum micronutrient formula.

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.

In this open prospective study, short-term use of the micronutrient formula 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.

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

Frazier EA, Gracious B, Arnold LE, Failla M, Chitchumroonchokchai C, Habash D, Fristad MA. *J Child Adolesc Psychopharmacol*. 2013 Oct;23(8):558-67. doi: 10.1089/cap.2012.0098.

[FULL TEXT](#)

Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/Hyperactivity Disorder

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.

Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/Hyperactivity Disorder

Rucklidge JJ, Johnstone J, Harrison R, Boggis A. 2011. *Psychiatry Research*, 189:281-87.

[FULL TEXT](#)



Clinically Significant Symptom Reduction in Children with Attention-Deficit/Hyperactivity Disorder Treated with Micronutrients: An Open- Label Reversal Design Study

In January 2014, The British Journal of Psychiatry published the results of a double-blind controlled trial which provided evidence of efficacy for micronutrients⁺ (vitamins and minerals) in the treatment of ADHD symptoms in adults, with a reassuring safety profile.

As a follow-up to the adult trial, and pilot study for a RCT in childhood ADHD, the Journal of Child and Adolescent Psychopharmacology recently published the results of a study which treated 14 children with Attention-Deficit/Hyperactivity Disorder (ADHD) using micronutrients⁺ instead of medication.

The study demonstrated the clinical benefit, feasibility, and safety of broad-spectrum micronutrients in the treatment of childhood ADHD.

In the recently published study, medication-free children were treated with a micronutrient formula⁺ for eight weeks and then taken off it for four weeks—with the on-off cycle repeating itself over a six-month period.

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 behaviors. The children's self-reports confirmed the improvements. Excellent adherence to treatment occurred throughout, 10 side effects were mild and transitory, and no safety issues were identified through blood analyses.

The researchers said the results were so effective that some parents were reluctant to take their children off the micronutrients⁺ for the full four weeks. They noted “When they came off the micronutrients⁺, some children's symptoms returned within days, which was a good indication of their effectiveness.”

Clinically Significant Symptom Reduction in Children with Attention-Deficit/Hyperactivity Disorder Treated with Micronutrients: An Open-Label Reversal Design Study

Gordon HA, Rucklidge JJ, Blampied NM, Johnstone JM. *J Child Adolesc Psychopharmacol*. 2015 Dec;25(10):783-98. doi: 10.1089/cap.2015.0105. PubMed PMID: 26682999; PubMed Central PMCID: PMC4702182.

[FULL TEXT](#)

Effect of Micronutrients on Insomnia in Adults: A Multiple-Baseline Study

Insomnia is a debilitating condition causing psychological distress and frequently comorbid with other mental health conditions. This study examined the effect of 8 weeks of treatment by broad spectrum micronutrients (Hardy Nutritionals[®] Daily Self Defense[™]) on insomnia using a multiple-baseline-across-participants open-label trial design. Seventeen adults were randomized to 1-, 2-, or 3-week baseline periods (14 completed). Self-report measures were the Consensus Sleep Diary–Morning (CSD-M), the Pittsburgh Insomnia Rating Scale (PIRS), and the Depression, Anxiety, Stress Scale (DASS). Baselines were generally stable. Treatment completers reported reliable and clinically significant change in insomnia severity (PIRS), in depression, stress, and anxiety (DASS), and on at least two aspects of sleep measured by the CSD-M. All completers were treatment-compliant, and side effects were minimal. Nutritional supplementation is shown to be a novel, beneficial treatment for insomnia in adults. Follow-up research using placebo-controlled designs as well as comparisons to cognitive-behavioral and other treatments is recommended.

Effect of Micronutrients on Insomnia in Adults: A Multiple-Baseline Study

Joanna Lothian, Neville M. Blampied, Julia J. Rucklidge. *Clinical Psychological Science*. May 23, 2016. doi:10.1177/2167702616631740

[FULL TEXT](#)



Vitamin-Mineral Treatment of ADHD in Adults: A 1-Year Naturalistic Follow-Up of a Randomized Controlled Trial

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. Results: 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.

Vitamin-Mineral Treatment of ADHD in Adults: A 1-Year Naturalistic Follow-Up of a Randomized Controlled Trial
Rucklidge JJ, Frampton CM, Gorman B, Boggis A. *J Atten Disord.* 2014.

[FULL TEXT](#)

Micronutrient Treatment of Emotional Dyscontrol Following Traumatic Brain Injury

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 11 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.

Micronutrient treatment resulted in resolution of this patient's long-standing 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.

Micronutrient Treatment of Emotional Dyscontrol Following Traumatic Brain Injury
Kaplan, B. J., Leaney, C., Tsatsko, E. *Annals of Psychiatry and Mental Health.* 29 August 2016.

[FULL TEXT](#)



Hospitalization cost of conventional psychiatric care compared to broad-spectrum micronutrient treatment: literature review and case study of adult psychosis

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.

Hospitalization cost of conventional psychiatric care compared to broad-spectrum micronutrient treatment: literature review and case study of adult psychosis
Kaplan BJ, Isaranuwachai W, Hoch JS. *Int J Ment Health Syst.* 2017 Jan 31;11:14.

[FULL TEXT](#)



Effects of dietary supplements on depressive symptoms in older patients: a randomized double-blind placebo controlled trial.

Gariballa S, Forster S.

“In this prospective, double-blind, placebo-controlled study, we randomly assigned 225 hospitalised acutely ill older patients to receive either normal hospital diet plus 400 mL oral nutritional supplements (106 subjects) or normal hospital diet plus a placebo (119 subjects) daily for 6 weeks. The composition of the supplement was such as to provide 995 kcal for energy and 100% of the Reference Nutrient Intakes for a healthy old person for vitamins and minerals. Outcome measures were 6 weeks and 6 months changes in nutritional status, depressive symptoms and cognitive state. There were significant differences in symptoms of depression scores in the supplement group compared with the placebo group at 6 months ($p = 0.021$ for between groups difference). The effect of supplement was seen in all patient groups including those with no symptoms of depression, mild depression and those with severe depression ($p = 0.007$).”

Clin Nutr. 2007 Oct;26(5):545-51.

[https://www.clinicalnutritionjournal.com/article/S0261-5614\(07\)00099-4/fulltext](https://www.clinicalnutritionjournal.com/article/S0261-5614(07)00099-4/fulltext)

[FULL TEXT](#)

Thiamine supplementation mood and cognitive functioning. Psychopharmacology (Berl) 129(1):66-71, 1997 9122365

Benton D, Griffiths R, Haller J:

One hundred and twenty young adult females took either a placebo or 50 mg thiamine, each day for 2 months. Before and after taking the tablets, mood, memory and reaction times were monitored. An improvement in thiamine status was associated with reports of being more clearheaded, composed and energetic. The taking of thiamine had no influence on memory but reaction times were faster following supplementation. These influences took place in subjects whose thiamine status, according to the traditional criterion, was adequate.

Psychopharmacology January 1997, Volume 129, Issue 1, pp 66-71

<https://link.springer.com/article/10.1007/s002130050163>

[FULL TEXT](#)

Clinically Significant Symptom reduction in children with attention deficit/ hyperactivity disorder treated with micronutrients: an open-label reversal design study. J Child Adolesc Psychopharmacol 25(10):783-798, 2015 26682999

Gordon HA, Rucklidge JJ, Blampied NM, Johnstone JM:

“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.”

J Child Adolesc Psychopharmacol 25(10):783-798, 2015 26682999
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4702182/pdf/cap.2015.0105.pdf>

[FULL TEXT](#)

The effects of multivitamins on cognitive performance: a systematic review and meta-analysis. J alzheimers Dis 29(3):561-569, 2012 22330823

Grima NA, Pase MP, Macpherson H, Pipingas A:

Complementary medicine use is becoming increasingly popular with multivitamins being the most commonly used vitamin supplement. Although adequate vitamin and nutrient concentrations are necessary for optimal health and cognitive functioning, there is no scientific consensus as to whether multivitamin use prevents cognitive decline or improves mental functioning. The aim of the present study was to determine if multivitamins can be used efficaciously to improve cognitive abilities. A systematic review of randomized controlled trials was performed. Meta-analysis was performed on those cognitive tests used across the largest number of studies. Multiple electronic databases were searched until July 2011 by two authors. Randomized, placebo-controlled trials were considered appropriate if they reported on the chronic effects (≥ 1 month) of oral multivitamin supplementation on any valid cognitive outcomes. Ten trials were included in review ($n = 3,200$). Meta-analysis indicated that multivitamins were effective in improving immediate free recall memory (SMD = 0.32; 95% CI: 0.09-0.56, $p < 0.01$) but not delayed free recall memory (SMD = -0.14; 95% CI: -0.43-0.14, $p = 0.33$) or verbal fluency (SMD = 0.06; 95% CI: -0.05-0.18, $p = 0.26$). There was no evidence of publication bias or heterogeneity. Other cognitive abilities sensitive to AD pathology, such as executive and visuospatial functions, were found to be under researched. In conclusion, multivitamins were found to enhance immediate free recall memory but no other cognitive domains.

J alzheimers Dis 29(3):561-569, 2012 22330823
<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad111751>

[FULL TEXT](#)

French adults’ cognitive performance after daily supplementation with antioxidant vitamins and minerals at nutritional doses: a post hoc analysis of the supplementation in vitamins and minerals antioxidants (SU.VLMAX) trial. Am J Clin Nutr 94(3):892-899, 2011 21775560

Kesse-Guyot E, Fezeu L, Jeandel C, Ferry M, Andreeva V, Amieva H,
Hercberg S, Galan P:

“BACKGROUND: Antioxidant properties of some vitamins and trace elements may help to prevent cognitive decline. OBJECTIVE:

The aim of the current study was to estimate the long-term effects of antioxidant nutrient supplementation on the cognitive performance of participants in the Supplementation in Vitamins and Mineral Antioxidants (SU.VI.MAX) study 6 y after the end of the trial. DESIGN:



This study included 4447 French participants aged 45-60 y who were enrolled in the SU.VI. MAX study (1994-2002), which was a double-blind, placebo-controlled, randomized trial. From 1994 to 2002, participants received daily vitamin C (120 mg), β -carotene (6 mg), vitamin E (30 mg), selenium (100 Qg), and zinc (20 mg) in combination or as a placebo. In 2007-2009, the cognitive performance of participants was assessed with 4 neuropsychological tests (6 tasks). Principal components analysis (PCA) was performed to identify cognitive-function summary scores. Associations between antioxidant supplementation and cognitive functions, in the full sample and by subgroups, were estimated through ANOVA and expressed as mean differences and 95% CIs. Subgroup analyses were performed according to baseline characteristics. RESULTS:

Subjects receiving active antioxidant supplementation had better episodic memory scores (mean difference: 0.61; 95% CI: 0.02, 1.20). PCA indicated 2 factors that were interpreted as showing verbal memory and executive functioning. Verbal memory was improved by antioxidant supplementation only in subjects who were nonsmokers or who had low serum vitamin C concentrations at baseline. CONCLUSION:

This study supports the role of an adequate antioxidant nutrient status in the preservation of verbal memory under certain conditions. This trial was registered at clinicaltrials.gov as NCT00272428.”

Am J Clin Nutr 94(3):892-899, 2011 21775560
<https://academic.oup.com/ajcn/article/94/3/892/4411870>

[FULL TEXT](#)

Effects of a multivitamin/ multimineral supplement on young males with physical overtraining: a placebocontrolled, randomized, double-blinded cross-over trial. Biomed Environ Sci 26(7):599-604, 2013 23895706

Li X, Huang WX, Lu Jm, Yang G, Ma FL, Lan YT, Meng JH, Dou JT:

“OBJECTIVE: To investigate the effects of vitamin-mineral supplement on young males with physical overtraining. METHODS:

Two hundred and forty male Chinese field artillery personnel who undertook large scale and endurance military training and were on ordinary Chinese diet were randomized to receive a multivitamin/multimineral supplement or a placebo for 1 week. After a 1-week wash-out period, a cross-over with 1 week course of a placebo or multivitamin/multimineral supplement was conducted. Blood and urine samples were analyzed for adrenal, gonadal and thyroid hormones. In addition, cellular immune parameters (CD3+, CD3+CD4+, CD3+CD8+, CD4/CD8, CD3-CD56+, CD3-CD19+) were examined and psychological tests were performed before and after the training program and nutrition intervention. RESULTS:

After a large scale and endurance military training, the participants showed significantly increased thyroid function, decreased adrenal cortex, testosterone and immunological function, and significantly increased somatization, anger and tension. Compared to placebo, multivitamin/ multimineral intervention showed significant effects on functional recovery of the pituitary - adrenal axis, pituitary-gonadal axis, pituitary-thyroid axis and immune system as well as psychological parameters. CONCLUSION:

High-intensity military operations have significant impacts on the psychology, physical ability and neuroendocrine-immune system in young males. Appropriate supplementation of multivitamin/multimineral can facilitate the recovery of the psychology, physical ability and neuroendocrine-immune system in young males who take ordinary Chinese diet.”

Biomed Environ Sci 26(7):599-604, 2013 23895706
<https://www.sciencedirect.com/science/article/pii/S0895398813600938>

[FULL TEXT](#)



Effects of vitamin and mineral supplementation on stress, mild psychiatric symptoms, and mood in nonclinical samples: a meta-analysis. Psychosom Med 75(2):144- 153,2013 23362497

Long SJ, Benton D:

“OBJECTIVE: Biochemical processes in the brain affect mood. Minor dietary inadequacies, which are responsible for a small decline in an enzyme’s efficiency, could cumulatively influence mood states. When diet does not provide an optimal intake of micronutrients, supplementation is expected to benefit mood. This meta-analysis evaluated the influence of diet supplementation on mood in nonclinical samples.

METHODS:

Databases were evaluated and studies were included if they considered aspects of stress, mild psychiatric symptoms, or mood in the general population; were randomized and placebo- controlled; evaluated the influence of multivitamin/mineral supplements for at least 28 days. Eight studies that met the inclusion criteria were integrated using meta-analysis.

RESULTS:

Supplementation reduced the levels of perceived stress (standard mean difference [SMD]=0.35; 95% confidence interval [CI]=0.47-0.22; $p=.001$), mild psychiatric symptoms (SMD=0.30; 95% CI=0.43-0.18; $p=.001$), and anxiety (SMD=0.32; 95% CI=0.48-0.16; $p<.001$), but not depression (SMD=0.20; 95% CI=0.42-0.030; $p<.089$). Fatigue (SMD=0.27; 95% CI=0.40-0.146; $p<.001$) and confusion (SMD=0.225; 95% CI=0.38-0.07; $p<.003$) were also reduced. CONCLUSIONS:

Micronutrient supplementation has a beneficial effect on perceived stress, mild psychiatric symptoms, and aspects of everyday mood in apparently healthy individuals. Supplements containing high doses of B vitamins may be more effective in improving mood states. Questions about optimal levels of micronutrient intake, optimal doses, and active ingredients arise.”

Psychosom Med 75(2):144-153,2013 23362497
<https://insights.ovid.com/pubmed?pmid=23362497>

[FULL TEXT](#)

Historical changes in the mineral content of fruits and vegetables. British Food Journal 99(6):207-211, 1997

Mayer AMB:

Implies that a balance of the different essential nutrients is necessary for maintaining health. The eight minerals that are usually analysed are Na, K, Ca, Mg, P, Fe, Cu, Zn. A comparison of the mineral content of 20 fruits and 20 vegetables grown in the 1930s and the 1980s (published in the UK Government’s Composition of Foods tables) shows several marked reductions in mineral content. Shows that there are statistically significant reductions in the levels of Ca, Mg, Cu and Na in vegetables and Mg, Fe, Cu and K in fruit. The only mineral that showed no significant differences over the 50 year period was P. The water content increased significantly and dry matter decreased significantly in fruit. Indicates that a nutritional problem associated with the quality of food has developed over those 50 years. The changes could have been caused by anomalies of measurement or sampling, changes in the food system, changes in the varieties grown or changes in agricultural practice. In conclusion recommends that the causes of the differences in mineral content and their effect on human health be investigated.

British Food Journal 99(6):207-211, 1997
<https://www.emeraldinsight.com/doi/abs/10.1108/00070709710181540>

[FULL TEXT](#)



Effect of supplementation with selenium on postpartum depression: a randomized double-blind placebocontrolled trial. J Matern Fetal Neonatal Med 24(1):104-108, 2011 20528216

Mokhber N, Namjoo M, Tara F, Boskabadi H, Rayman MP, Ghayour- Mobarhan M, Sahebkar A, Majdi MR, Tavallaie S, Azimi-Nezhad M, Shakeri MT, Nematy M, Oladi M, Mohammadi M, Ferns G:

“OBJECTIVE: Postpartum depression is a common complication of childbirth, and its prevention is an important public-health issue because of its negative effects on mother, infant, and family. The present randomized, double-blind, placebo-controlled trial was conducted to examine the effect of prenatal selenium supplementation on the postpartum depression level in Iranian women. DESIGN:

A total of 166 primigravid pregnant women in the first trimester of pregnancy, were randomized to receive 100 Qg of selenium (n = 83) or a placebo (n = 83) per day until delivery. The symptoms of postpartum depression were evaluated during the eight weeks following delivery by means of the Edinburgh Postnatal Depression Scale (EPDS). Serum selenium concentrations were measured at baseline and at the end of study. RESULTS:

There was no significant difference in demographic characteristics and perceived social support between the selenium and control groups at baseline ($p > 0.05$). There were 22 drop-outs in the selenium-supplemented group and 19 in the placebo group. Forty-four women in the selenium group and 41 women in the placebo group completed the trial and the EPDS questionnaire. Selenium supplementation was associated with a significant increase in mean serum selenium concentration at term ($p < 0.001$) but remained unchanged in the control group. The mean EPDS score in the selenium group was significantly lower than that of the control group ($p < 0.05$). CONCLUSION:

These findings suggest that supplementation with selenium during pregnancy might be an effective approach for the prevention of postpartum depression.”

<https://www.tandfonline.com/doi/full/10.3109/14767058.2010.482598?scroll=top&needAccess=true>

[FULL TEXT](#)

Effect of zinc supplementation on mood states in young women: a pilot study. Eur J Clin Nutr 64(3):331-333, 2010 20087376

Sawada T, Yokoi K:

The relation of zinc (Zn) nutriture to brain development and function has been elucidated. The purpose of this study is to examine whether Zn supplementation improves mood states in young women. The study used a double-blind, randomized and placebo-controlled procedure. The major outcomes were psychological measures, somatic symptoms and serum Zn. Thirty women were placed randomly and in equal numbers into two groups, and they ingested one capsule containing multivitamins (MVs) or MV and 7 mg Zn daily for 10 weeks. Women who took MV and Zn showed a significant reduction in anger-hostility score ($P=0.009$) and depression-dejection score ($P=0.011$) in the Profile of Moods State (POMS) and a significant increase in serum Zn concentration ($P=0.008$), whereas women who took only MV did not. Our results suggest that Zn supplementation may be effective in reducing anger and depression.

Eur J Clin Nutr 64(3):331-333, 2010 20087376

<https://www.nature.com/articles/ejcn2009158>

[FULL TEXT](#)



The effect of vitamin-mineral supplementation on juvenile delinquency among American schoolchildren: a randomized, double-blind placebo-controlled trial. J altern Complement Med 6(1):7-17, 2000 10706231

Schoenthaler SJ, Bier ID:

CONTEXT: Numerous studies conducted in juvenile correctional institutions have reported that violence and serious antisocial behavior have been cut almost in half after implementing nutrient- dense diets that are consistent with the World Health Organization's guidelines for fats, sugar, starches, and protein ratios. Two controlled trials tested whether the cause of the behavioral improvements was psychological or biological in nature by comparing the behavior of offenders who either received placebos or vitamin-mineral supplements designed to provide the micronutrient equivalent of a well-balanced diet. These randomized trials reported that institutionalized offenders, aged 13 to 17 years or 18 to 26 years, when given active tablets produced about 40% less violent and other antisocial behavior than the placebo controls. However, generalization could not be made to typical schoolchildren without a controlled trial examining violence and antisocial behavior in public schools. **Objectives:** To determine if schoolchildren, aged 6 to 12 years, who are given low dose vitamin- mineral tablets will produce significantly less violence and antisocial behavior in school than classmates who are given placebos. **Design:** A stratified randomized, double-blind, placebo-controlled trial with pretest and posttest measures of antisocial behavior on school property. **Settings and Subjects:** Two "working class," primarily Hispanic elementary schools in Phoenix, Arizona. Approximately half of the potential schoolchildren participated, i.e., 468 students aged 6 to 12 years. **Intervention:** Daily vitamin- mineral supplementation at 50% of the U.S. recommended daily allowance (RDA) for 4 months versus placebo. The supplement was designed to raise vitamin- mineral intake up to the levels currently recommended by the National Academy of Sciences for children aged 6 to 11 years. **Outcome Measure:** Violent and nonviolent delinquency as measured by official school disciplinary records. **Results:** Of the 468 students randomly assigned to active or placebo tablets, the 80 who were disciplined at least once between September 1st and May 1st served as the research sample. During intervention, the 40 children who received active tablets were disciplined, on average, 1 time each, a 47% lower mean rate of antisocial behavior than the 1.875 times each for the 40 children who received placebos (95% confidence interval, 29% to 65%, < 5 .020). The children who took active tablets produced lower rates of antisocial behavior in 8 types of recorded infractions: threats/fighting, vandalism, being disrespectful, disorderly conduct, defiance, obscenities, refusal to work or serve, endangering others, and nonspecified offenses. **Conclusions:** Poor nutritional habits in children that lead to low concentrations of water-soluble vitamins in blood, impair brain function and subsequently cause violence and other serious antisocial behavior. Correction of nutrient intake, either through a well-balanced diet or low-dose vitamin-mineral supplementation, corrects the low concentrations of vitamins in blood, improves brain function and subsequently lowers institutional violence and antisocial behavior by almost half. This paper adds to the literature by enabling previous research to be generalized from older incarcerated subjects with a history of antisocial behavior to a normal population of younger children in an educational setting.

J altern Complement Med 6(1):7-17, 2000 10706231
<https://www.nature.com/articles/ejcn2009158.pdf>

[FULL TEXT](#)



The effect of randomized vitamin-mineral supplementation on violent and non-violent antisocial behavior among incarcerated juveniles. J Nutr Environ Med 7(4):343-352, 1997

Schoenthaler Stephen J, Bier Ian D.

In a randomized controlled double-blind trial, the effects of vitamin3mineral supplementation on violence and other serious antisocial behavior were studied for 3 months on 62 con®ned delinquents aged 13 to 17 years. A signi®cant difference between 32 active and 30 placebo subjects was found for violent and non-violent antisocial behavior. The net difference in rule infractions between the active and placebo groups in violence was 28% (95% con®dence interval 15341%). This direction and magnitude of effect were seen with both violent and non-violent rule violations. Twenty-six habitually violent subjects donated pre- and post-intervention blood samples. Among 10 subjects who maintained their normal or low blood concentrations of vitamins throughout the trial, there was no marked change in violence (i.e. 39 acts during baseline and 37 during intervention). In contrast, the 16 subjects who corrected their low blood vitamin concentrations during intervention produced 131 violent acts during baseline and 11 during intervention. The correction of low blood vitamin concentrations with vitamin3mineral supplements improves brain function and signi®cantly reduces violence among delinquents con®ned in correctional facilities.

J Nutr Environ Med 7(4):343-352, 1997

https://www.researchgate.net/publication/232037321_The_Effect_of_Randomized_Vitamin-Mineral_Supplementation_on_Violent_and_Non-violent_Antisocial_Behavior_Among_Incarcerated_Juveniles

[FULL TEXT](#)

Serum zinc level in depressed patients during zinc supplementation of imipramine treatment. J Affect Disord 126(3): 447-452, 2010 20493532

Siwek M, Dudek D, Schlegel-Zawadzka M, Morawska A, Piekoszewski W, Opoka W, Zieba A, Pilc A, Popik P, Nowak G:

“BACKGROUND: Recurrent major depression is associated with decreased blood zinc concentrations that may be increased by effective antidepressant therapy. Some clinical investigations point to alterations of the zinc level in blood as a potential marker of depression. METHODS:

A placebo-controlled, double blind study of zinc supplementation to imipramine therapy was conducted on sixty patients fulfilling the DSM-IV criteria for major depression (18-55 years old, 40 females, 20 males). Moreover, a group of 25 healthy volunteers was recruited (16 females, 9 males). Blood samples were drawn for the assay of serum zinc once from the control subjects and four times (before, and then 2, 6 and 12 weeks after the beginning of treatment) from the depressed subjects. RESULTS:

We report that: 1) the serum zinc level was significantly lower (by 22%) in depressed patients than in healthy volunteers, 2) all groups demonstrated a gradual increase in zinc concentrations over the period of imipramine treatment with or without zinc supplementation, 3) treatment-resistant patients demonstrated lower concentrations of zinc (by 14%) than treatment-non-resistant patients, 4) zinc concentrations were higher in zinc-supplemented patients than in placebo-supplemented patients, 5) zinc supplementation increased zinc concentrations over the period of treatment, and 6) at a 12-week imipramine treatment, a significant negative correlation was demonstrated between the Montgomery-Asberg Depression Rating Scale and the serum zinc level together with a concomitant increase in serum zinc in patients in remission. CONCLUSIONS:

Serum zinc is a state marker of depression.”

J Affect Disord 126(3): 447-452, 2010 20493532

<https://www.sciencedirect.com/science/article/pii/S0165032710003605>

[FULL TEXT](#)



Influence of thiamin supplementation on the health and general well-being of an elderly Irish population with marginal thiamine deficiency. J Gerontol 46(1):M16-M22, 1991 1986037

Smidt LJ, Cremin FM, Grivetti LE, Clifford AJ:

The effect of thiamin supplementation on the health and general well-being of 80 randomly selected healthy elderly Irish women, from a population with marginal thiamin deficiency, was studied. Key variables affecting thiamin status were controlled. Weekly dietary intakes, subjective feelings, and activity assessments were measured during a 4-week baseline and 6-week double blind treatment period. Clinical assessments were performed during the last week of each period. For treatment, subjects were randomly assigned to either thiamin (10 mg daily) or placebo groups. Compared to baseline and placebo supplemented values, thiamin-supplemented women experienced significantly increased appetite, energy intake, body weight and general well-being, and decreased fatigue. Thiamin supplementation also tended to reduce daytime sleep time, improve sleep patterns, and increase activity. These data suggest that evaluation of thiamin status is indicated when nonspecific conditions such as anorexia, weight loss, fatigue, depression, and sleep disorders are present in elderly persons.

J Gerontol 46(1):M16-M22, 1991 1986037
<https://www.ncbi.nlm.nih.gov/pubmed/1986037>

[FULL TEXT](#)

Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. BMJ 318(7195):1375-1381, 1999 10334745

Wyatt KM, Dimmock PW, Jones PW, Shaughn O'Brien PM:

“OBJECTIVE: To evaluate the efficacy of vitamin B-6 in the treatment of premenstrual syndrome. DESIGN: Systematic review of published and unpublished randomised placebo controlled trials of the effectiveness of vitamin B-6 in the management of premenstrual syndrome. SUBJECTS:

Nine published trials representing 940 patients with premenstrual syndrome. MAIN OUTCOME MEASURES:

Proportion of women whose overall premenstrual symptoms showed an improvement over placebo. A secondary analysis was performed on the proportion of women whose premenstrual depressive symptoms showed an improvement over placebo. RESULTS:

Odds ratio relative to placebo for an improvement in overall premenstrual symptoms was 2.32 (95% confidence interval 1.95 to 2.54). Odds ratio relative to placebo for an improvement in depressive symptoms was 1.69 (1.39 to 2.06) from four trials representing 541 patients. CONCLUSION:

Conclusions are limited by the low quality of most of the trials included. Results suggest that doses of vitamin B-6 up to 100 mg/day are likely to be of benefit in treating premenstrual symptoms and premenstrual depression.”

BMJ 318(7195):1375-1381, 1999 10334745
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC27878/>

[FULL TEXT](#)