Essential Lutrients

RESEARCH SUMMARY





Dear Healthcare Professional,

Thank you for your interest in Hardy Nutritionals® **Daily Essential Nutrients (DEN)** – a unique technology-enhanced vitamin-mineral formulation for the treatment of mood, anxiety, and behavioral symptoms.

This summary lists the independent research backing **DEN** by indication, and also provides detailed information about select studies.

For Treatment Guidelines and other information relevant to clinical applications, please refer to the Clinical Reference Guide for Healthcare Professionals and the Frequently Asked Questions Guide on our website. Both resources bring together a wealth of knowledge accumulated through extensive research and valuable feedback from healthcare professionals, and are designed to facilitate the clinical use of **DEN**.

We welcome any feedback, questions or concerns you may have. Please feel free to call us and speak with a Product Specialist.

We appreciate working with you for your patients' health!

Sincerely,

The Hardy Nutritionals® team www.GetHardy.com

Toll free: 1-855-955-1114 Fax: 1-587-271-1117

Email: info@GetHardy.com

Office Hours: Monday - Friday 9:00 AM - 5:00 PM (MST)



Daily Essential Nutrients is the result of a long history of independent medical research and extensive clinical experience. This broad-spectrum micronutrient therapy[†] has been used successfully to alleviate the symptoms of almost everything neurological - from brain injury and autism to attention, anxiety, mood, and other psychiatric disorders. The following are summaries of 2 of the nearly 30 medical journal publications.

Traumatic Brain Injury

A rat model study performed at the *Canadian Centre for Behavioural Neuroscience* provides exciting evidence that micronutrient treatment[†] could revolutionize recovery from traumatic brain injuries and neurodegenerative disorders. ^{1, 2}

At 4 days old, researchers administered either medial frontal or posterior parietal lesions to the treatment rats. From surgery to adulthood, half of the control animals and half of the injured animals received vitamin & mineral supplementation.

After 100 days, both parietal and frontal lesion animals fed the micronutrient formula[†] exhibited significantly less anxiety in open field tests as measured by mean distance and horizontal activity (treatment effects for both groups p<0.001).



Frontal lesion regrowth with control (left) and supplemented[†] (right) diets. (actual pictures of study rat brains)

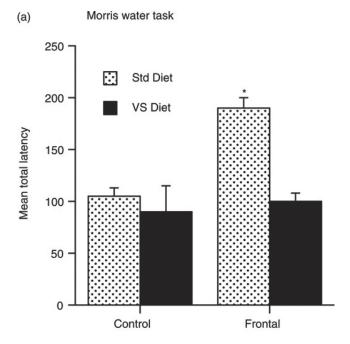
Amazingly, brains of frontal lesion rats were completely regrown with micronutrient supplementation[†], and cognitive function was restored to a level statistically not different from normal as measured by Morris water maze tests (p<0.05).

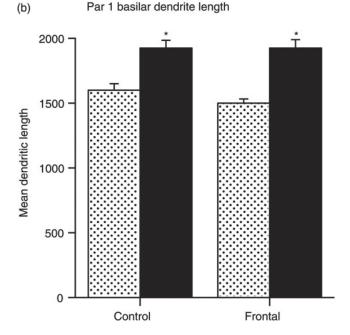
The brains of both lesioned and unlesioned animals fed micronutrients[†] had greater mean cortical thickness than unsupplemented

animals in post-mortem examinations (p<0.05), and the neurons of the supplemented rats also had longer, more complexly-branched dendritic endings (p<0.05).

This breakthrough research has broad clinical application. The enhanced brain cell health in the micronutrient-fed[†] rats may explain why micronutrients have produced dramatic results in people with brain injuries such as stroke or concussion.

The proven ability of micronutrient therapy[†] to increase cortical thickness and connectivity also speaks to its potential to prevent and treat neurodegenerative disease, including Alzheimer's, Autism, Parkinsons and any other condition where brain cell deterioration and loss of cortical thickness are evident.





Effects of vitamin supplements on recovery from medial prefrontal lesions on post-natal day 3 in rats. (a) Performance on the Morris water task (total time swam in seconds over 5 attempts). (b) Dendritic length in perilesional cortex (microns).

VS Diet = vitamin†-supplemented standard diet Std Diet = standard diet (Purina Rat Chow)

Source: (Halliwell 2009)

¹ Halliwell C. Dietary choline and vitamin/mineral supplement for recovery from early cortical injury [master's thesis]. [Lethbridge (AB)]: University of Lethbridge; 2003. 191 p.[†]

² Halliwell C, Comeau W, Gibb R, Frost DO, Kolb B. Factors influencing frontal cortex development and recovery from early frontal injury. Developmental Neurorehabilitation. 2009;12(5):269-78.[†]

ADHD in Adults

In 2014, the British Journal of Psychiatry published a double-blind randomized placebo-controlled trial conducted at the University of Canterbury in New Zealand, which provides evidence of efficacy for micronutrient therapy[†] in the treatment of ADHD symptoms in adults, with a reassuring safety profile.³

Adults diagnosed with ADHD (DSM-IV criteria) who took the nutrient treatment[†] showed "statistically robust improvements in a variety of areas of psychological functioning" in just 8 weeks.

	Micronutrie	nt formula g	roup (<i>n</i> = 42)	Place	ebo group (<i>n</i>	= 38)			
	Baseline	Post	Change from	Baseline	Post	Change from			Effec
Variable	Mean (s.e.)	Mean (s.e.)	baseline ^b	Mean (s.e.)	Mean (s.e.)	baseline ^b	Difference (95% CI)	P	sizec
Primary outcomes									
CAARS DSM-IV ADHD									
symptoms total									
Self-report	79.4 (1.5)	67.3 (2.2)	-11.81	75.3 (1.9)	70.5 (2.3)	-5.10	-6.71 (-11.72 to -1.70)	0.009	0.61
Observer	69.5 (2.0)	61.4 (2.3)	-8.44	70.5 (2.0)	66.9 (2.1)	-3.30	-5.14 (-9.65 to -0.63)	0.026	0.59
Clinician	73.4 (1.4)	65.0 (1.7)	-7.69	69.0 (1.4)	64.1 (1.7)	-5.64	-2.05 (-6.21 to 2.12)	0.331	0.23
CGI-I-ADHD ^c		2.8 (0.2)	2.83		3.4 (0.2)	3.40	-0.56 (-1.03 to -0.09)	0.020	0.53
CGI-I – Overall Impression ^d		2.8 (0.2)	2.79		3.5 (0.2)	3.50	-0.71 (-0.16 to -1.27)	0.012	0.57
MADRS, total	17.2 (1.1)	11.5 (1.3)	-5.32	14.2 (1.1)	12.0 (1.3)	-2.65	-2.66 (-5.64 to 0.31)	0.078	0.41

ADHD, attention-deficit hyperactivity disorder; CAARS, Conners Adult ADHD Rating Scale (all raw scores are converted to *T*-scores based on age and gender; CGI-I, Clinical Global Impressions – Improvement (the score for the CGI-I ranges from 1 (very much improved) to 7 (very much worse) as compared with baseline functioning); MADRS, Montgomery–Åsberg Depression Rating Scale; GAF, Global Assessment of Functioning (rated 1–100); LIFE-RIFT, Longitudinal Interval Follow-up Evaluation – Range Impaired Functioning Tool. a. Results in bold are significant.

- b. Adjusted for baseline.
- c. Cohen's d (effect size) measured as the mean difference in the change divided by the within-group standard deviation of the difference in the change.
- d. Assesses change so not measured at baseline.

CGI-I-ADHD, CGI-I-Overall Impression, and MADRS, total are all clinician-scored rating scales. Source: (Rucklidge 2014)3

Compared with placebo, those taking the micronutrient treatment[†] reported more than double the improvement in attention, hyperactivity, and impulsivity symptoms.

Post-hoc analysis also revealed nearly double the improvement in moderate or severe depression, as rated by clinical psychologists, and more than twice as many people were 'very much improved' or 'much improved' overall, compared with the placebo group as rated by the Clinical Global Impressions – Improvement in attention-deficit hyperactivity disorder symptoms scores (CGI-I-ADHD).

A one year follow-up to this trial showed that those remaining on the micronutrient treatment[†] continued to experience improved mood whereas those who discontinued it or reverted to medications worsened.⁴

"I have many patients who previously required close medication management on conventional drugs, but who now check in every 3 to 12 months with little symptomatology to report."

- Charles W. Popper, M.D.

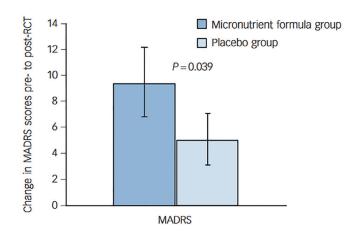


Fig. 4 Change in Montgomery–Åsberg Depression Rating Scale (MADRS) scores pre- to post-randomised controlled trial (RCT) for those who entered the trial moderately depressed across groups.

Source: (Rucklidge 2014)³

³ Rucklidge JJ, Frampton CMA, Gorman B, Boggis A. Vitamin–mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomised placebocontrolled trial. The British Journal of Psychiatry. 2014 Feb;204(2).†

⁴Rucklidge JJ, Johnstone J, Gorman B, Boggis A, Frampton CM. Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement. Prog Neuropsychopharmacol Biol Psychiatry. 2014 Apr 3;50:163-71.†

⁵ Popper CW. Single-micronutrient and broad-spectrum micronutrient approaches for treating mood disorders in youth and adults. Child Adolesc Psychiatr Clin N Am. 2014 Jul;23(3):591-672.

ADHD in Children

Double-blind research conducted at five universities has investigated the safety and efficacy of micronutrient therapy in the treatment of ADHD and related symptoms in children.

A 2018 double-blind, placebo-controlled study[†] randomized unmedicated children diagnosed with ADHD, together with significant mood, aggression and emotional dysregulation symptoms, to take Hardy Nutritionals® Daily Essential Nutrients or matching placebo for 10-weeks. Clinician ratings revealed "significant between-group differences favoring 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." An additional 22% in the micronutrient group showed less dramatic clinical improvement.

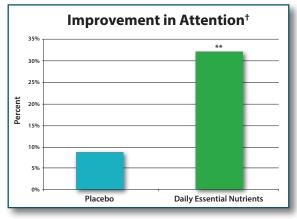
A 2021 multi-center, randomized, placebo-controlled trial[‡] replicated these results, with a higher response rate: "For the Clinical Global Impression-Improvement, 54% of the micronutrient and 18% of the placebo group were responders (Risk Ratio=2.97, 97.5% CI: 1.50, 5.90, p<0.001)." 'Responders' were rated 'much improved' or 'very much improved' by clinicians and does not include those who showed less dramatic clinical improvement. As with the first study, "No serious adverse events nor clinically significant changes from baseline in blood and urine tests occurred." Researchers also reported that during the 8-week trial, "The micronutrient group grew six millimeters more than the placebo group (p=0.002)."

	Micronutrients ($n = 47$)					Placebo ($n = 46$)							
	Baseline		Post		Change	Baseline		Post		Change	D: CC		
Variable	Mean	SE	Mean	SE	from baseline ^a	Mean	SE	Mean	SE	from baseline ^a	Difference (confidence interval)	p	ES^b
Primary outcomes													
CGI-I-Overall ^c			2.8	0.2	2.83			3.3	0.1	3.26	-0.47 (-0.05 to -0.90)	0.029^{d}	0.46
Clinician ADHD-RS-IV Symptoms Total	44.8	1.0	37.1	1.6	7.75	45.1	0.8	38.7	1.4	6.32	-1.43 (-4.91 to 2.05)	0.415	0.17
Parent CPRS-R:L DSM-IV ADHD Symptoms Total	42.5	1.0	33.4	1.6	9.08	42.4	1.1	34.6	1.6	7.79	-1.29 (-5.45 to 2.88)	0.540	0.13
Additional measures													
CGI-I-ADHD ^c			2.9	0.2	2.87			3.4	0.1	3.37	-0.50 (-0.88 to -0.11)	0.012^{d}	0.53
CGI-I-Mood ^c			2.9	0.2	2.92			3.4	0.1	3.43	-0.52 (-0.10 to -0.95)	0.017^{d}	0.51
C-GAS	48.1	0.9	54.2	1.4	6.07	48.8	0.9	51.8	1.3	2.97	3.10 (0.45 to 5.75)	0.022^{d}	0.48
CMRS-P	25.0	1.7	15.2	1.5	9.46	23.4	1.6	17.3	1.7	6.45	-3.00 (-6.64 to 0.62)	0.100	0.35
Clinician ADHD-RS-IV													
DSM-IV Inattention	24.1	0.5	20.0	0.8	4.05	23.7	0.4	21.6	0.7	2.10	-1.95 (-3.94 to 0.04)	0.055^{d}	0.41
DSM-IV H/I	20.7	0.8	17.1	1.0	3.67	21.4	0.7	17.2	1.0	4.24	0.54 (-1.46 to 2.55)	0.591	0.11
Teacher CTRS-R:L DSM-IV Total ^e	34.7	1.8	32.8	1.7	1.95	34.4	1.7	33.2	2.1	1.23	-0.33 (-5.08 to 4.42)	0.889	0.03
Parent SDQ – total problem score	23.0	0.7	18.1	0.9	5.09	21.9	0.8	19.3	0.9	2.79	-1.95 (-4.0 to 0.10)	0.062	0.41
Parent SDQ - Conduct problems score	5.3	0.3	4.2	0.3	1.10	5.0	0.4	4.8	0.4	0.14	-0.87 (-1.57 to -0.17)	0.015^{d}	0.52
Teacher SDQ – total problem score	18.6	1.0	16.0	1.1	3.36	17.7	0.9	17.1	0.9	0.33	-1.78 (-3.88 to 0.32)	0.064	0.45
Teacher SDQ - Conduct problems score	4.0	0.4	2.9	0.4	1.13	3.8	0.4	3.6	0.5	0.27	-0.86 (-1.74 to 0.18)	0.055^{d}	0.47
Teacher BRIEF - Behavioural Regulation Index	62.6	1.0	58.6	1.0	4.01	60.8	2.6	61.5	2.3	-0.30	-4.31 (-8.68 to -0.07)	0.053	0.48
Teacher BRIEF - Emotional Control Subscale		2.6	16.6	2.4	1.91	18.2	0.9	18.5	1.0	-0.24	-2.15 (-3.74 to -0.60)	0.009^{d}	0.66

aAdjusted for baseline.

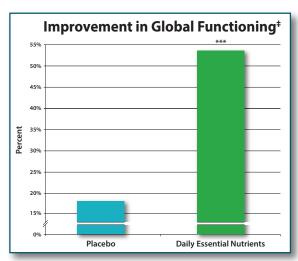
Results in bold are significant.

H/I, hyperactivity/impulsivity; C-GAS, Child Global Assessment Scale; CGI-I, Clinical Global Impression-Improvement; SDQ, Strengths and Difficulties Questionnaire; CMRS-P, Child Mania Rating Scale – Parent; CPRS-R, Conners Parent Rating Scale-Revised:Long version; CTRS, Conners Teacher Rating Scale-Revised:Long version; BRIEF, Behaviour Rating Inventory of Executive Function.



^{**}Percent of participants who experienced a 30% or greater reduction in clinician-rated ADHD lnattention Subscale scores (DSM-IV), p=0.005; n=93.

Source: Rucklidge JJ, Eggleston MJF, Johnstone JM, Darling K, Frampton CM. Vitamin-mineral treatment improves aggression and emotional regulation in children with ADHD: a fully blinded, randomized, placebo-controlled trial. J Child Psychol Psychiatry, 2018 Mar; 59(3):232-246.



***Percent of participants rated by clinicians as "much improved" or "very much improved" on the Overall Clinical Global Impression-Improvement assessment in per-protocol analysis, p<0.001; n=126

Source: Johnstone JM, Hatsu I, Tost G, Srikanth P, Eiterman LP, Bruton A, Ast HK, Robinette LM, Stern MM, Millington EG, Gracious B, Hughes AJ, Leung BM, Arnold LE. Micronutrients for Attention-Deficit/ Hyperactivity Disorder in Youth: A Placebo-Controlled Randomized Clinical Trial. J Am Acad Child Adolesc Psychiatry. 2021 Jul 21:50890-8567(21)00473-1.

bCohen's d (effect size) measured as the mean difference in the change divided by the within-group SD of the difference in the change

^cAssesses change so not measured at baseline.

 $^{^{\}rm d}p$ < .05 based on per-protocol.

eBased on completed questions (n = 72)

Product-specific Research by Indication

Anxiety & Stress

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.

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.

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.

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.

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.

Attention & Hyperactivity

Micronutrients for Attention-Deficit/Hyperactivity Disorder in Youth: A Placebo-Controlled Randomized Clinical Trial.

Johnstone JM, Hatsu I, Tost G, Srikanth P, Eiterman LP, Bruton A, Ast HK, Robinette LM, Stern MM, Millington EG, Gracious B, Hughes AJ, Leung BM, Arnold LE. J Am Acad Child Adolesc Psychiatry. 2021 Jul 21:S0890-8567(21)00473-1.

Mineral-vitamin treatment associated with remission in attention-deficit/hyperactivity disorder symptoms and related problems: 1-year naturalistic outcomes of a 10-week randomized placebo-controlled trial.

Darling KA, Eggleston MJ, Retallick-Brown H, Rucklidge JJ. Journal of Child and Adolescent Psychopharmacology. 2019 Jul 25.

Can we predict treatment response in children with ADHD to a vitamin-mineral supplement? An investigation into pre-treatment nutrient serum levels, MTHFR status, clinical correlates and demographic variables.

Rucklidge JJ, Eggleston MJ, Darling KA, Stevens AJ, Kennedy MA, Frampton CM. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2019 Mar 8;89:181-92.

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

Rucklidge JJ, Eggleston MJ, Johnstone JM, Darling K, Frampton CM. Journal of Child Psychology and Psychiatry. 2018 Mar;59(3):232-46.

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. Journal of Attention Disorders. 2017 Apr;21(6):522-32.

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.

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).

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.†

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.

Autism Spectrum

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

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

Brain Injury

Micronutrient treatment of emotional dyscontrol following traumatic brain injury.

Kaplan BJ, Leaney C, Tsatsko E. Ment Health. 2016;4(5):1078.

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.

Dietary choline and vitamin/mineral supplement for recovery from early cortical injury [master's thesis].

Halliwell C. [Lethbridge (AB)]: University of Lethbridge; 2003. 191 p.

Insomnia

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

Joanna Lothian, Neville M. Blampied, Julia J. Rucklidge. Clinical Psychological Science. Published online before print May 23, 2016.

Mood & Behavior

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.

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.

Database analysis of adults with bipolar disorder consuming a micronutrient formula.

Gately D, Kaplan BJ. Clinical Medicine Insights: Psychiatry. 2009 Apr;4:3-16.[†]

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.[†]

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.†

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.

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.

Nutritional approach to bipolar disorder.

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

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.

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.

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

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

Psychosis

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

Kaplan BJ, Isaranuwatchai W, Hoch JS. International journal of mental health systems. 2017 Dec;11(1):14.

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.

Other

Addiction/Dependency

Novel Mineral-Vitamin Treatment for Reduction in Cigarette Smoking: A Fully Blinded Randomized Placebo-Controlled Trial.

Reihana PK, Blampied NM, Rucklidge JJ. Nicotine & Tobacco Research. 2018 Aug 23.

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.

Limiting Factors of Micronutrient Therapy

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.

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.[†]

Safety

An observational preliminary study on the safety of long-term consumption of micronutrients for the treatment of psychiatric symptoms.

Rucklidge JJ, Eggleston MJ, Ealam B, Beaglehole B, Mulder RT. The Journal of Alternative and Complementary Medicine. 2019 Jun 1;25(6):613-22.

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.

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.

Mechanism

Human gut microbiome changes during a 10 week Randomised Control Trial for micronutrient supplementation in children with attention deficit hyperactivity disorder.

Stevens AJ, Purcell RV, Darling KA, Eggleston MJ, Kennedy MA, Rucklidge JJ. Scientific Reports. 2019 Jul 12;9(1):10128.

Resting-state networks and neurometabolites in children with ADHD after 10 weeks of treatment with micronutrients: results of a randomised placebo-controlled trial.

Borlase N, Melzer TR, Eggleston MJ, Darling KA, Rucklidge JJ. Nutritional Neuroscience. 2019 Feb 13:1-1.

Methylomic changes in response to micronutrient supplementation and MTHFR genotype.

Stevens AJ, Rucklidge JJ, Darling KA, Eggleston MJ, Pearson JF, Kennedy MA. Epigenomics. 2018 Sep 4;10(09):1201-14.

The micronutrient formulation studied was a pre-2013 version of EMPowerplus which was co-formulated by Daily Essential Nutrients formulator, David Hardy.

[‡]The micronutrient formulation studied was Daily Self Defense-for Women which was formulated by David Hardy.

