daily Essential Nutrients

RESEARCH SUMMARY

Dear Healthcare Professional,

Thank you for your interest in Hardy Nutritionals® **Daily Essential Nutrients (DEN)** – a unique vitamin-mineral formulation with independently validated efficacy for mood, anxiety, and behavioral symptoms.

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.

This summary lists the independent research backing **DEN** by category, 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. We also strongly recommend our training course for clinicians. These 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 Hardy Wellness Advisor or Scientist.

We appreciate working with you for your patients' health!

Sincerely,

The Hardy Nutritionals® team
www.GetHardy.com

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9:00 AM - 5:00 PM (MST)

Mental Wellness
— *Naturally*™ —

PROPRIETARY FORMULATION
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ADHD in Adults

In a double-blind randomized placebo-controlled trial conducted at the University of Canterbury in New Zealand, adults diagnosed with ADHD (DSM-IV criteria) who took 15 capsules/day of a predecessor formulation substantially similar to Daily Essential Nutrients† showed "statistically robust improvements in a variety of areas of psychological functioning" in just 8 weeks.[1]

Table 2 Baseline and post 8-week data on primary and secondary outcome measures[a]

	Micronutrient formula group ($n=42$)			Placebo group ($n=38$)					
Variable	Baseline Mean (s.e.)	Post Mean (s.e.)	Change from baseline[b]	Baseline Mean (s.e.)	Post Mean (s.e.)	Change from baseline[b]	Difference (95% CI)	*P*	Effect size[c]
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)[1]

Compared with placebo, those taking the broad-spectrum micronutrients† reported more than double the improvement in attention, hyperactivity, and impulsivity symptoms, with no side effects or safety signals.[1]

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).[1]

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.[2]

"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."[3]

- Charles W. Popper, M.D.

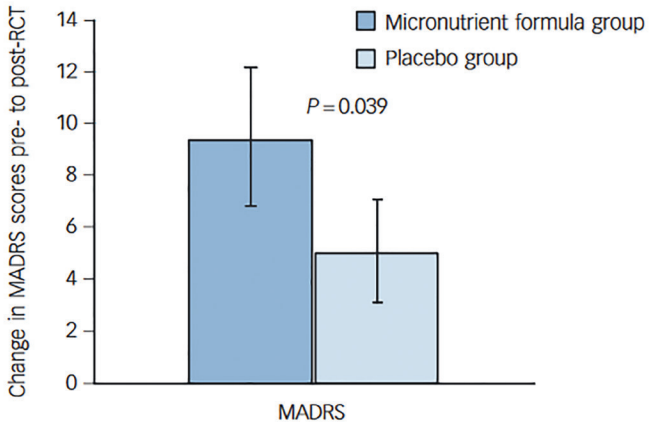

Fig. 4 Change in Montgomery–Åsberg Depression Rating Scale (MADRS) scores pre- to post-randomised controlled trial (RCT) for those who entered the trial moderately depressed across groups.

Source: (Rucklidge 2014)[1]

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

[2] Rucklidge 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.†

[3] 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.

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

ADHD in Children

A double-blind, placebo-controlled trial randomized unmedicated children with ADHD (age 7-12 years) to take 12 capsules/day of Daily Essential Nutrients (DEN) 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." (See Table 2).[1]

Table 2 Baseline and post 10-week data on primary and secondary outcome measures

	Micronutrients (n = 47)					Placebo (n = 46)							
	Baseline		Post		Change from	Baseline		Post		Change from	Difference		
Variable	Mean	*SE*	Mean	*SE*	baseline[a]	Mean	*SE*	Mean	*SE*	baseline[a]	(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	18.5	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**

[a]Adjusted for baseline.
[b]Cohen's d (effect size) measured as the mean difference in the change divided by the within-group *SD* of the difference in the change.
[c]Assesses change so not measured at baseline.
[d]$p < .05$ based on per-protocol.
[e]Based on completed questions (n = 72).
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.

The micronutrients also caused marked improvements in global functioning relative to placebo, with strong trends observed across both parent and teacher ratings for measures which "tapped into behaviors including hot tempers, fights with other children, explosive angry outbursts, and moods changing rapidly for no reason." The authors noted the practical significance of these findings by pointing out that "while poor self-control and emotional dysregulation are not considered core ADHD symptoms…[they] are often more impairing…" (See Figure 3).

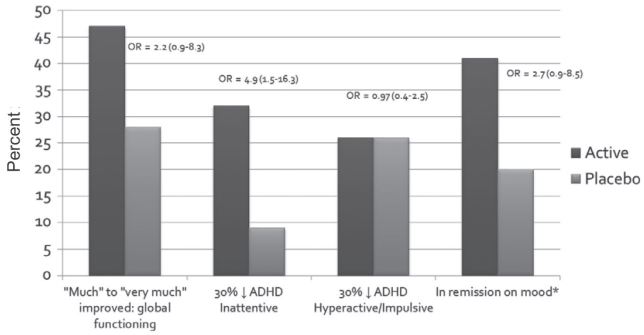

Figure 3. Percent of responders per group across different symptoms *based on children entering trial with severe mood dysregulation (n = 62). OR, odds ratio.[1]

"Many parents commented that...their child was calmer, more able to be reasoned with, and happier... These improvements bode well for improving life outcomes."

- Study authors

At one-year follow-up a much higher percentage of those children who stayed on DEN were "much" or "very much" improved overall relative to baseline functioning compared to those who switched to medications or discontinued treatment (p<0.001), and significantly more were considered in full remission (p<0.001). These outcomes clearly demonstrate that for some children with ADHD broad- spectrum micronutrients are likely to provide the best overall outcomes and that the benefits are robust in the long-term. (See Figure 5).

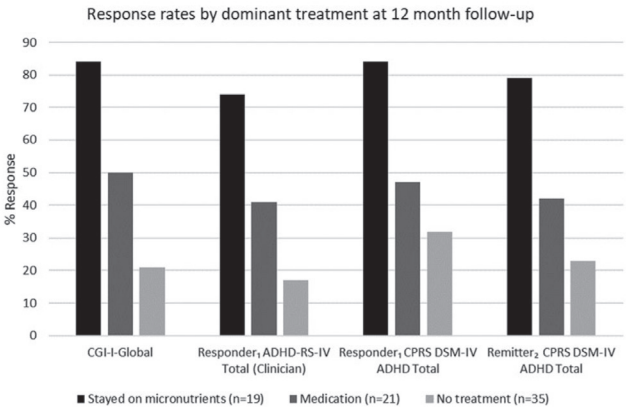

Figure 5. Response rates by dominant treatment at 12-month follow-up. Responder$_1$ defined as a decrease in symptoms of 30% or more. Remitter$_2$ defined as T-score <65.[2]

[1]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.

[2]Darling KA, Eggleston MJF, Retallick-Brown H, Rucklidge JJ. 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. J Child Adolesc Psychopharmacol. 2019 Nov;29(9):688-704.

ADHD in Children (MADDY study)

A larger, multi-center study replicated the previous double-blind, randomized controlled trial using DEN in children with ADHD (ages 6-12, 9-12 capsules/day), and the result was an even more impressive response rate in just 8 weeks: "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 defined as 'much improved' or 'very much improved' on clinician ratings, and did not include those who showed less dramatic clinical betterment.)[1]

Holistic benefit to global functioning beyond ADHD symptoms was again apparent, with trend towards betterment in parent ratings of disruptive mood dysregulation (p=0.09) and significantly reduced peer conflict (CASI-5 subscale, p=0.04) as rated by other non-parent adults who had high levels of interaction with the child (e.g. teachers).[1]

"This fully blinded RCT of micronutrients addresses several concerns related to existing ADHD treatment, including the possibility of counteracting height suppression and treating associated irritable mood, emotional dysregulation, and aggression."[1]

- MADDY Study Authors

As with the first study, "No serious adverse events nor clinically significant changes from baseline in blood and urine tests occurred."[1] In fact, side effects actually trended lower in the micronutrient group as measured by the Pediatric Adverse Events Rating Scale (PAERS) - apparently because it inadvertently captured efficacy, with DEN significantly reducing the mean anxiety combined score relative to placebo (p=0.005)![2] "Longer time on multinutrients did not result in greater adverse events."[3]

In stark contrast to stimulants which are known to suppress appetite and stunt growth, the DEN group grew statistically significantly taller than the placebo group during the 8 week study period (RCT; 6mm, p<0.01)![1] The trend of accelerated growth continued into the additional two months of open-label extension (OLE), although the difference between groups narrowed because the placebo group was also offered the micronutrients during this time. The response rate also significantly improved with the longer duration of use culminating in 2 out of every 3 children 'much' or 'very much' improved on clinician ratings after 4 months of DEN use (p=0.04).[3]

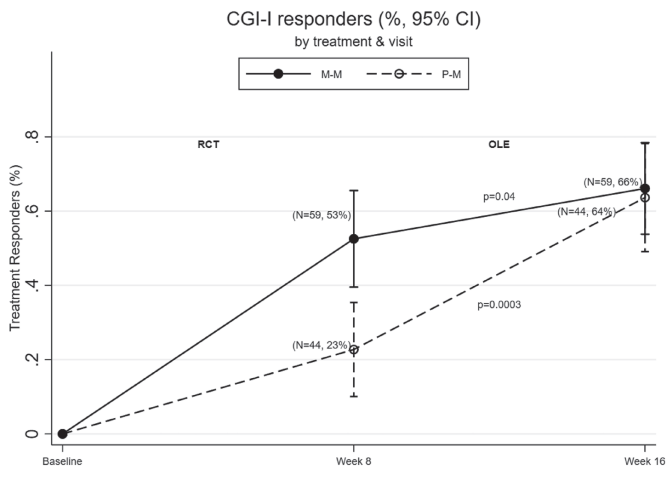

Fig. 2 Percent responders on clinician-rated Clinical Global Impression-Improvement Scale at week 8 (RCT) and week 16 (OLE).
M–M=Multinutrient– Multinutrient, P–M=Placebo–Multinutrient.[3]

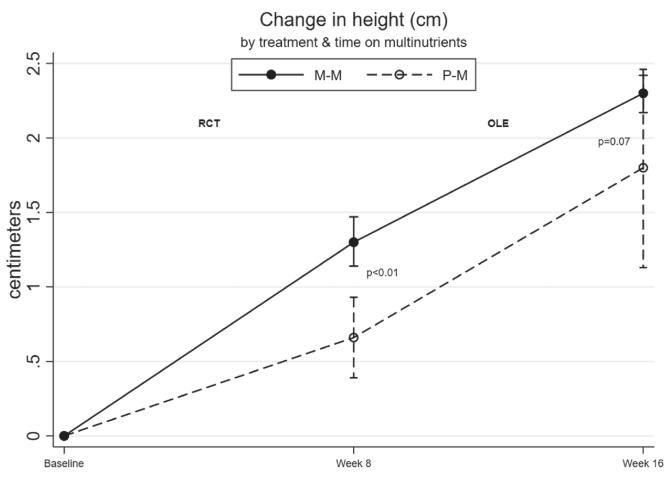

Fig. 3 Change in height (cm) by treatment group at RCT (week 8) and OLE (week 16).
M–M=Multinutrient–Multinutrient, P–M=Placebo–Multinutrient.[3]

"...secondary analysis found that the multinutrients, compared to placebo, were associated with improvements in parental concerns overall, and in two domains specifically: inattention (p=0.01, d=0.55) and internalizing symptoms (anxiety/depression; p=0.03, d=0.80)..."[4]

- Study Authors

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[1]Johnstone JM, Hatsu IE, Tost G, Srikanth P, Eiterman LP, Bruton AM, Ast HK, Robinette LM, Stern MM, Millington EG, Gracious BL, Hughes AJ, Leung BMY, Arnold LE. Micronutrients for Attention-Deficit/Hyperactivity Disorder in Youths: A Placebo-Controlled Randomized Clinical Trial. J Am Acad Child Adolesc Psychiatry. 2022 May;61(5):647-661.

[2]Leung BMY, Srikanth P, Gracious B, Hatsu IE, Tost G, Conrad V, Johnstone JM, Arnold LE. Paediatric adverse event rating scale: a measure of safety or efficacy? Novel analysis from the MADDY study. Curr Med Res Opin. 2022 Sep;38(9):1595-1602.

[3]Leung BMY, Srikanth P, Robinette L, Bruton AM, Tost G, Hatsu IE, Arnold LE, Johnstone JM. Micronutrients for ADHD in youth (MADDY) study; comparison of results from RCT and open label extension. Eur Child Adolesc Psychiatry. 2024 May;33(5):1355-1367.

[4]Tost G, Srikanth P, Bruton A, Hatsu IE, Leung BMY, Ast HK, Eiterman LP, Robinette LM, Williams C, Gracious B, Arnold LE, Johnstone JM. Problems most concerning to parents of children with ADHD and emotional dysregulation in a randomized controlled trial of multinutrients: MADDY secondary analysis. Eur Child Adolesc Psychiatry. 2024 May 31.

Antenatal Depression (NUTRIMUM study)

Researchers recruited 88 medication-free pregnant women at 12-24 weeks gestation with moderate to severe depression (EPDS ≥ 13). Participants were randomized 1:1 to either 12 capsules/day of Daily Essential Nutrients (DEN) or to an active placebo (containing iodine and riboflavin) for a minimum of 12 weeks (from recruitment until parity).[1]

The micronutrient group experienced significantly greater improvements in depression symptoms compared with the active placebo group, as rated by clinicians (CGI-I; p=0.0196) and self (M-CGI-I; p=0.0052), with the micronutrient group significantly more likely to identify as 'much' to 'very much' improved (68.8%) compared with active placebo (38.5%) (M-CGI-I; p=0.011). The women in the micronutrient group also outperformed the active placebo group on global assessment of functioning (GAF; p=0.0359), and sleep quality (PSQI; p=0.0224).[1]

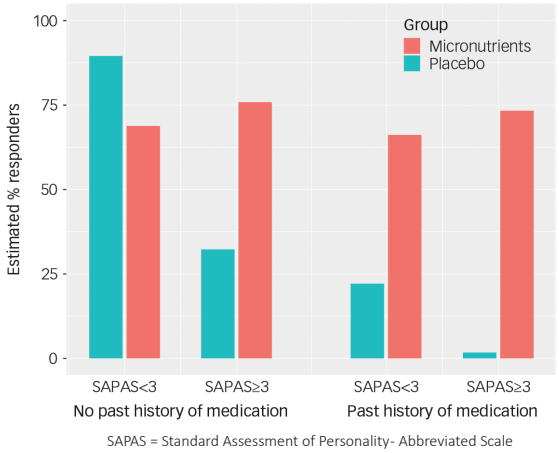
Table 4 Observed baseline and post-treatment change data and Cohen's *d* on primary and secondary outcomes for participants who provided both baseline and post-treatment data, and time and treatment only model estimates for the expected difference over the 12-week study period (on the log-scale, except for binary responses)

	Micronutrients				Active placebo								
	Baseline (*n* = 43)		Raw change (*n* = 32)		Baseline (*n* = 43)		Raw change (*n* = 36)						
Outcome	Mean	±s.d.	Mean	±s.d.	Mean	±s.d.	Mean	(±s.d.)	Cohen's *d*	Effect[c]	95% CI[c]	*P* (group)[d]	*n*(obs)[e]
EPDS (self-report depression)	13.95	4.08	−7.41	5.69	14.42	3.22	−6.78	4.76	0.12	0.165	(−0.033 to 0.363)	0.1018	478
CGI-I (clinician-rated)			2.13	1.10			2.59	1.28	0.39	0.245	(0.040–0.451)	**0.0196**	222
CGI-I (binary)[a]			68.8%				51.4%			1.360	(−0.167 to 2.880)	0.1267	222
M-CGI-I (self-report)			2.25[b]	1.14			3.08[b]	1.42	0.64	0.328	(0.101–0.555)	**0.0052**	71
M-CGI-I (binary)[a]			68.8%				38.5%			1.259	(0.292–2.279)	**0.0103**	71
GAF (global functioning)	60.93	6.84	11.22	8.13	59.49	6.63	9.57	9.00	0.19	−0.049	(−0.095 to −0.003)	**0.0359**	308
MADRS (clinician-rated depression)	18.23	7.96	−8.94	7.67	18.07	7.05	−7.78	7.40	0.15	0.085	(−0.156 to 0.324)	0.4893	305
SF-12 (quality of life)	31.58	5.81	2.16	5.86	30.83	4.63	3.50	5.41	0.24	0.000	(−0.066 to 0.066)	0.9997	293
PSS (stress)	22.36	5.20	−7.68	7.57	22.59	5.02	−7.14	6.48	0.08	0.034	(−0.136 to 0.204)	0.6968	289
PSQI (sleep)	9.09	3.38	−2.22	3.40	10.44	4.26	−2.28	3.95	0.02	0.202	(0.029–0.375)	**0.0224**	294
DERS-SF (emotional regulation)	46.33	12.10	−9.03	12.67	46.98	10.78	−9.58	9.81	0.05	0.009	(−0.083 to 0.101)	0.8555	294
GAD-7 (anxiety)	9.19	4.31	−5.47	5.67	9.91	4.52	−5.14	5.13	0.06	0.204	(−0.030 to 0.439)	0.0871	477
DASS (depression, anxiety and stress)	21.07	10.04	−10.66	11.83	19.51	9.81	−8.72	7.83	0.20	0.174	(−0.082 to 0.431)	0.1824	476
Suicidal ideation[f]	0.74	0.98	−0.47	1.02	0.47	0.85	−0.16	1.07	0.29	0.038	(−0.119 to 0.196)	0.6346	305
Self-harm[g]	0.51	0.74	−0.38	0.71	0.42	0.63	−0.31	0.47	0.12	0.056	(−0.051 to 0.163)	0.3073	476

In multivariate analysis, the researchers discovered two strong predictors of a good response to DEN: 1) Those with a history of psychiatric medication use showed significantly greater change on the EPDS (P = 0.0183) if taking DEN rather than active placebo, perhaps providing hope for those who are 'treatment resistant' to medications. 2) Those with personality difficulties (i.e. difficulty making & keeping friends, impulsive, untrusting, short-tempered, worriers, perfectionists) were more likely to respond to DEN over active placebo (P = 0.0122), which further demonstrates that the benefits of the micronutrients extend well beyond diagnosed psychiatric symptoms.[1]

Daily Essential Nutrients was safe, with no difference in treatment-emergent side effects between micronutrients and active placebo. Homocysteine, which is associated with multiple pregnancy complications, decreased significantly more in the micronutrient group (p<0.001), while serum vitamin B12 (p<0.001) and vitamin D (p<0.001) increased.[1] The micronutrients also prevented the vitamin C depletion typically seen in pregnant mothers.[2]

"Outcomes were comparable to those obtained using psychotherapy, but achieved with much less contact."[1]
- Study authors



SAPAS = Standard Assessment of Personality- Abbreviated Scale

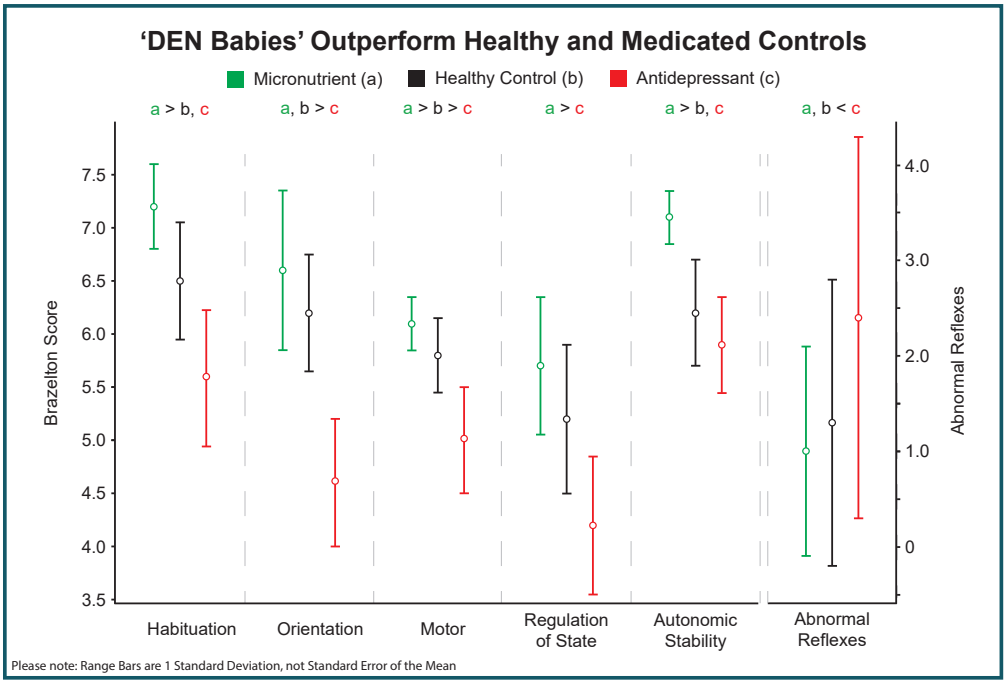
[1]Bradley HA, Moltchanova E, Mulder RT, Dixon L, Henderson J, Rucklidge JJ. Efficacy and safety of a mineral and vitamin treatment on symptoms of antenatal depression: 12-week fully blinded randomised blacebo-controlled trial (NUTRIMUM). BJPsych Open. 2024 Jun 3;10(4):e119..

[2]Carr AC, Bradley HA, Vlasiuk E, Pierard H, Beddow J, Rucklidge JJ. Inflammation and Vitamin C in Women with Prenatal Depression and Anxiety: Effect of Multinutrient Supplementation. Antioxidants (Basel). 2023 Apr 17;12(4):941.

Infant Health & Development

Researchers at the University of Canterbury evaluated a total of 103 infants, 37 exposed to Daily Essential Nutrients (DEN) in-utero (12 capsules/day; 50-182 days exposure), 18 exposed to antidepressants in-utero (exposure for full gestation), and 48 whose mothers received neither treatment nor experienced depressive symptoms. However, 64.6% of the healthy control moms, and 88.9% of the moms using antidepressants were also taking some other prenatal supplement during the pregnancy.[1]

Infants were assessed using the Brazelton Neonatal Behavioral Assessment Scale (NBAS) within 28 days of birth. Micronutrient-exposed infants performed better overall than antidepressant-exposed infants (d=1.0-1.7) and healthy control infants (d=0.5-1.1).[2] Micronutrient-exposed babies were significantly better off than newborns from moms taking pharmaceutical antidepressants on six out of seven physiological and neurological measures (habituation to disturbances, orientation to sights and sounds, motor control, regulation of state, autonomic stability, and normal reflexes; all $p < .01$). And in spite of the fact that their mothers were disadvantaged by antenatal depression, micronutrient-exposed babies also outperformed infants from otherwise healthy, unmedicated moms on three of the seven measures (habituation to disturbances, motor control, and autonomic stability; all $p < .05$)![1] The longer the mothers used DEN during the pregnancy the better off their infants appeared to be, as evidenced by a within-group association between duration of DEN use by the mother and better habituation ($p = .028$).[1]



The micronutrient-exposed infants were more likely to be carried to full term than infants from healthy, unmedicated mothers and mothers taking antidepressants (both $p<0.001$), thus reducing myriad risks associated with preterm birth.[1] Likely as a result of reaching a higher gestational age than antidepressant-exposed infants (d=0.74), the micronutrient-exposed infants also had significantly more body length (d=0.83) and lower rates of low birth weight.[2]

In further follow-up at 4, 6, and 12 months postpartum, the researchers attempted to determine the influence of in utero micronutrient exposure on infant temperament. DEN exerted small, positive effects on orienting/regulatory capacity (longitudinal change, $\beta = 0.266$) and negative affectivity (initial levels, $\beta s = -0.116$; longitudinal changes, $\beta = -0.235$). The direction of these correlations indicate that in-utero DEN exposure may exert a positive influence on infant temperament in the first year of life and may mitigate the known risks associated with antenatal depression, as DEN-exposed infants displayed temperamental characteristics on par with typical pregnancies where symptoms of depression were not present.[3] The researchers concluded, "Overall, our results indicate that micronutrient supplementation given above the Recommended Dietary Allowance during pregnancy appears safer relative to existing treatment options for women with depression and may even launch these infants to a better start in life."[1]

Not only did the micronutrients successfully improve psychological functioning and birth outcomes, but they also appear to have mitigated some of the risks associated with antenatal depression and poorer infant outcomes, particularly when taken at a higher dose and with a more balanced variety of nutrients compared to typical over-the-counter antenatal nutritional supplements"[1]

- Study authors

[1]Campbell SA, Bradley HA, Mulder RT, Henderson JMT, Dixon L, Haslett LC, Rucklidge JJ. Effect of antenatal micronutrient or antidepressant exposure on Brazelton neonatal behavioral assessment scale (NBAS) performance within one month of birth. Early Hum Dev. 2024 Mar;190:105948.

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Traumatic Brain Injury

A rat model study performed at the *Canadian Centre for Behavioural Neuroscience* provides exciting evidence that a predecessor formulation substantially similar to Daily Essential Nutrients† 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†.[1]

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 $p<0.001$).[1]

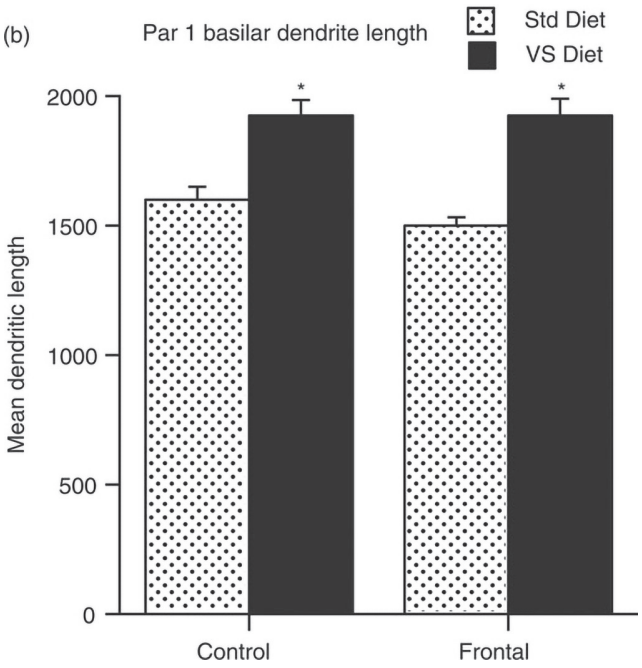
Frontal lesion regrowth with control (left) and supplemented† (right) diets. (actual pictures of study rat brains)

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 ($p<0.05$).[2]

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 ($p<0.05$).[2]

This same broad-spectrum multinutrient formula† delivered dramatic improvements in a human case of traumatic brain injury. Brain scans showed intra-cranial bleeds and supra-orbital lacerations to the right frontal lobe at the time of the injury. After more than 5 years of rehabilitation, a psychiatric report noted ongoing mood lability and aggressive outbursts which were expected to be permanent. However, the patient began to feel improvements in his emotional control within 2 weeks of starting the micronutrients at 8 capsules per day, and formal mood lability ratings by both clinician and self were markedly improved within 6 months, with measurable ongoing improvements for 12 months at the same dose.[3]

The proven ability of broad-spectrum micronutrients to increase cortical thickness and improve neuronal connectivity has broad clinical implications, including the potential to prevent cognitive decline, dementia, neurodegenerative disease, and any other condition where neuronal 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. (b) Dendritic length in perilesional cortex (microns).

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

Source: (Halliwell 2009)[2]

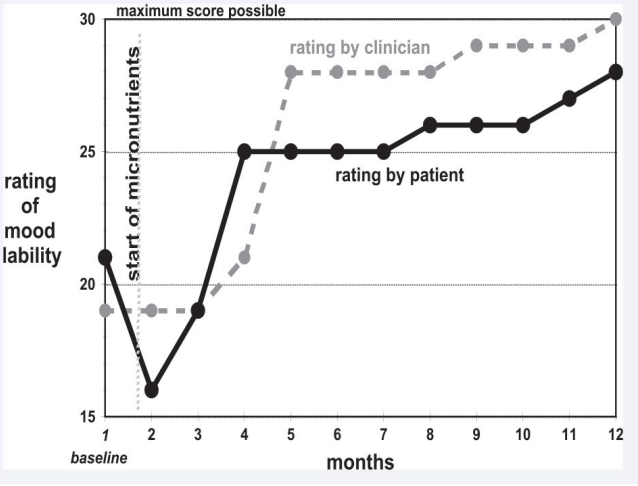


Figure 1 Mood lability ratings provided monthly for 12 months. Patient report is shown with the black line; clinician report is shown with a grey line [each blinded to the other's ratings].

Source: (Kaplan 2016)[3]

"These studies suggest a powerful neurotrophic effect of broad-spectrum micronutrients..."[4]

- Charles W. Popper, M.D.

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Product-specific Research by Symptom Category

Anxiety & Stress

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

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