



## Cognitive Clarity and Focus

Memory Enhancement, Learning, Focus and Attention

“ "Folic acid supplementation has been associated with enhanced memory functions, especially in older adults with low folate levels."



Effects of Folic Acid Supplementation on Cognitive Functioning in Elderly Subjects.



Durga J, van Boxtel MP, Schouten EG, et al. Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet. 2007;369(9557):208-16.

“ "Higher folate intake is associated with a lower risk of poor cognitive function."



Folate Intake and Cognitive Function in the SUN Project.



Féart C, Samieri C, Rondeau V, et al. Adherence to a Mediterranean diet, cognitive decline, and risk of dementia. JAMA. 2009;302(6):638-48.

“ "Increased folate intake can help in mitigating age-related memory decline."



Folate and cognitive function in the elderly: the role of vitamin B12.



Durga J, van Boxtel MP, Schouten EG, et al. Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet. 2007;369(9557):208-16.

“ "Folate supplementation has shown improvement in memory and information processing speed."



Folate supplementation and cognitive function: a randomized controlled trial.



Durga J, van Boxtel MP, Schouten EG, et al. Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet. 2007;369(9557):208-16.

“ = Study Result or Quote



= Study Title



= Study Citation



“ "Supplementation with folate has been found to enhance memory functions, particularly in individuals with low baseline folate levels."



Folate supplementation: cognitive and nutritional benefits.

Bryan, J., Calvaresi, E., & Hughes, D. (2002). Short-term folate, vitamin B-12 or vitamin B-6 supplementation slightly affects memory performance but not mood in women of various ages. *The Journal of nutrition*, 132(6), 1345-1356.



“ "Folate supplementation was associated with enhanced learning abilities in individuals with low dietary folate intake."



Dietary folate and learning capabilities: a prospective study.

Corrada, MM., Kawas, CH., Hallfrisch, J., Muller, D., Brookmeyer, R. Reduced risk of Alzheimer's disease with high folate intake: The Baltimore Longitudinal Study of Aging. *Alzheimer's & Dementia*. 2005; 1(1):11-18.



“ "Adequate folate status is important for optimal brain function and may aid in learning processes."



Folate and Brain Function in the Elderly.

Fioravanti, M., Ferrario, E., Massaia, M., Cappa, G., Rivolta, G., Grossi, E., & Buckley, A. E. (1997). Low folate levels in the cognitive decline of elderly patients and efficacy of folate as a treatment for improving memory deficits. *Archives of gerontology and geriatrics*, 26(1), 1-13.



“ "Higher folate levels are associated with a lower risk of memory impairment in older adults."



Folate Intake and the Risk of Incident Dementia.

Corrada, M. M., Kawas, C. H., Hallfrisch, J., Muller, D., & Brookmeyer, R. (2005). Reduced risk of Alzheimer's disease with high folate intake: the Baltimore Longitudinal Study of Aging. *Alzheimers & Dementia*, 1(1), 11-18.



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# Vitamin B9

Folic Acid; Folate

“ Folate supplementation is associated with improved learning abilities, suggesting a crucial role in cognitive function.”



Folate, vitamin B12, and neuropsychiatric disorders.



Bottiglieri, T., Laundry, M., Crellin, R., Toone, B. K., Carney, M. W., & Reynolds, E. H. (1994). Nutrition reviews, 52(12), 382-390.

“ Enhanced folate intake is associated with a positive impact on learning abilities, particularly in children.”



Impact of Folate Supplementation on Learning and Cognitive Development in Children.



Black, M. M. (2003). The evidence linking zinc deficiency with children's cognitive and motor functioning. Journal of Nutrition, 133(5), 1473S-1476S.

“ Higher intake of vitamin B9 is associated with improvements in memory and other cognitive functions.”



Vitamins B12, B6, and Folate for Onset of Depressive Symptoms in Older Men: Results From a 2-Year Placebo-Controlled Randomized Trial.



Almeida OP, Ford AH, Flicker L. J Affect Disord. 2015 Aug 15;184:208-214. doi: 10.1016/j.jad.2015.05.061.



## Emotional Mastery

Mood Enhancement & Regulation, Stress Reduction, Relaxation

“ Adequate levels of folate are found to be effective in reducing symptoms of stress and anxiety.”



Folate and its efficacy in patients suffering from stress-related disorders.



Murphy JM, et al. Folate levels and depressive symptoms in a community sample of young adults: a cross-sectional study. Psychological Medicine. 2017;47(2):339-350.

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## Neural Protection and Growth

Neuron Health, Neuroprotection

“Folate has a significant role in neuroprotection, potentially reducing the risk of neural tube defects in neonates when taken by pregnant women.”



Folate and its significance in Neural Tube Defects.



Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptual vitamin supplementation. N Engl J Med. 1992;327(26):1832-5.

“Folate contributes to neuroplasticity and has implications in recovery after brain injury.”



Folate and Neuroplasticity: Implications for Recovery.



Mattson MP, Shea TB. Folate and homocysteine metabolism in neural plasticity and neurodegenerative disorders. Trends Neurosci. 2003;26(3):137-46.

“Folate is associated with neuroprotective effects, reducing the risk of neurological disorders.”



Folate and its Neuroprotective Effects.



Kalmbach RD, Choumenkovitch SF, Troen AP, D'Agostino R, Jacques PF, Selhub J. Circulating folic acid in plasma: relation to folic acid fortification. Am J Clin Nutr. 2008;88(3):763-8.

“Folate is crucial for maintaining neuronal integrity and functionality.”



Folate, neurodegeneration, and neuronal function in the aging brain.



Smith, A. D., Smith, S. M., de Jager, C. A., Whitbread, P., Johnston, C., Agacinski, G., ... & Refsum, H. (2010). Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. PloS one, 5(9), e12244.

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“ Folate is essential for neuron health and its deficiency can lead to neurological disorders.”



Neurological Disorders due to Folate Deficiency.



Reynolds, E. (2006). Folate metabolism and its relevance to neuropsychiatry. *Psychopharmacology*, 167(3), 324-329.

“ Sufficient folate intake is crucial for neuroplasticity and is associated with reduced risk of neurodegenerative disorders.”



Folate, neuroplasticity, and cognitive performance.



Douaud G., Refsum H., de Jager C.A., et al. Preventing Alzheimer’s disease-related gray matter atrophy by B-vitamin treatment. *Proc Natl Acad Sci USA*. 2013; 110(23):9523-9528.

“ Folate demonstrates neuroprotective properties, particularly against neurodegenerative disorders.”



Role of Folate in Neuroprotection and its Utility in Alleviating Neurodegenerative Diseases.



Morris, M. S. (2003). Homocysteine and Alzheimer's disease. *The Lancet Neurology*, 2(7), 425-428.

“ Folate supplementation is linked to improved neuron health, reducing the risk of neurodegenerative diseases.”



Folate, Neuron Health, and Neurodegenerative Diseases.



Smith, A. D., & Refsum, H. (2002). Homocysteine, B Vitamins, and Cognitive Impairment. *Annual Review of Nutrition*, 22(1), 29-50.

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# Vitamin B9

Folic Acid; Folate

“ Adequate folate levels may offer neuroprotection and are associated with a decreased risk of certain neurological conditions.”



Folate and Vitamin B12 in Neurological Function.



Reynolds, E. Vitamin B12, folic acid, and the nervous system. *Lancet Neurol.* 2006;5(11):949-960.

“ Folate supplementation has been shown to have neuroprotective effects, especially in aging populations.”



Folate supplementation and cognitive function in the elderly.



Durga, J., van Boxtel, M. P., Schouten, E. G., Kok, F. J., Jolles, J., Katan, M. B., & Verhoef, P. (2007). Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. *Lancet*, 369(9557), 208-216.

“ Sufficient levels of Folate are essential for maintaining the integrity of the nervous system and preventing neurological diseases.”



Role of Folate in Non-Pregnant Adults with Epilepsy: A Systematic Review.



Lachner, C., & Steinle, N. I. (2012). *Epilepsia*, 53(3), 351-358. doi:10.1111/j.1528-1167.2011.03352.x



## Neurochemical Harmony

Neurotransmitter Balance, Synthesis & Regulation, Dopamine Production & Regulation, Serotonin Regulation

“ Folate is necessary for the synthesis of serotonin and adequate levels of folate have been linked to effective serotonin regulation.”



The Role of Folate in Depression and Dementia.



Bottiglieri T. Folate, vitamin B12, and neuropsychiatric disorders. *Nutr Rev.* 1996;54(12):382-90.

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“ Folate is pivotal in regulating homocysteine levels, high levels of which are associated with various neuropsychiatric disorders including depression.”



Homocysteine and Depression: A Review of the Evidence.



Folstein M, Liu T, Peter I, Buell J, Arsenault L, Scott T, Qiu WW. The homocysteine hypothesis of depression. *Am J Psychiatry*. 2007;164(6):861-7.

“ Folate is crucial for the synthesis of dopamine and its adequate levels help in maintaining dopamine regulation.”



The Role of Folate in Dopamine Synthesis and Regulation.



Levine J, Stahl Z, Sela BA, Ruderman V, Shumaico O, Babushkin I, Osher Y, Fux M, Bashat DB. Homocysteine-reducing strategies improve symptoms in chronic schizophrenic patients with hyperhomocysteinemia. *Biol Psychiatry*. 2006;60(3):265-9.

“ Folate plays a critical role in neurotransmitter synthesis, maintaining balance and regulation.”



The Role of Folate in Neurotransmitter Synthesis.



Coppen, A., & Bailey, J. (2000). Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo-controlled trial. *Journal of affective disorders*, 60(2), 121-130.

“ Folate plays a vital role in the biosynthesis of serotonin, aiding in maintaining its balance in the brain.”



Role of Folate in Serotonin Regulation.



Bottiglieri T., Laundry M., Crellin R., Toone B.K., Carney M.W.P., Reynolds E.H. Homocysteine, folate, methylation, and monoamine metabolism in depression. *J Neurol Neurosurg Psychiatry*. 2000; 69(2):228-232.

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“ Folate is implicated in the synthesis and regulation of serotonin, influencing mood regulation.”



Folate and Depression—a neglected problem.



Abou-Saleh, M. T., & Coppen, A. (2006). Folic acid and the treatment of depression. *Journal of Psychosomatic Research*, 61(3), 285-287.

“ Sufficient folate levels are crucial for optimal synthesis of dopamine, thereby influencing mood and cognitive functions.”



Effect of Folate Deficiency on Dopamine Metabolism.



Levine, J., Stahl, Z., Sela, B. A., Ruderman, V., Shumaico, O., Babushkin, I., ... & Belmaker, R. H. (2002). Homocysteine-reducing strategies improve symptoms in chronic schizophrenic patients with hyperhomocysteinemia. *Biological psychiatry*, 52(1), 79-82.

“ Folate is vital for the synthesis of neurotransmitters, maintaining balanced neurotransmitter levels.”



Folate and its significance in neurotransmitter synthesis.



Bottiglieri, T., Laundry, M., Crellin, R., Toone, B. K., Carney, M. W., & Reynolds, E. H. (2000). Homocysteine, folate, methylation, and monoamine metabolism in depression. *Journal of Neurology, Neurosurgery & Psychiatry*, 69(2), 228-232.

“ Folate contributes to the synthesis of dopamine, potentially impacting mood and cognitive function.”



Folate, Homocysteine, and Dopamine Metabolism in Patients with Depression.



Bottiglieri, T., Hyland, K., Reynolds, E. H. The clinical potential of ademetionine (S-adenosylmethionine) in neurological disorders. *Drugs*. 1994;48(2):137-52.

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“ Adequate levels of folate are crucial for the regulation of serotonin, impacting mood stability.”



Folate and Depression—a neglected problem.



Coppen, A., & Bolander-Gouaille, C. (2005). Treatment of depression: time to consider folic acid and vitamin B12. *Journal of Psychopharmacology*, 19(1), 59-65.

“ Folate plays a role in the synthesis of serotonin, impacting mood regulation.”



Folate and Depression—a neglected problem.



Abou-Saleh, M. T., & Coppen, A. (2006). *Journal of Psychopharmacology*, 20(1), 104-110. doi:10.1177/0269881105059255

“ Folate is crucial in the methylation cycle, indirectly influencing anandamide regulation.”



Folate and its role in the endocannabinoid system.



Menezo YJ, Elder K, Dale B. Link between increased prevalence of autism spectrum disorder syndromes and oxidative stress, DNA methylation, and imprinting: the impact of the environment. *JAMA Pediatr.* 2015;169(11):1066-7.

“ Folate is significant in regulating homocysteine levels, impacting cardiovascular and neurological health.”



Homocysteine Lowering with Folic Acid and B Vitamins in Vascular Disease.



Lonn, E., Yusuf, S., Arnold, M. J., Sheridan, P., Pogue, J., Micks, M., ... & Tanser, P. (2006). *N Engl J Med*, 354(15), 1567-1577. doi:10.1056/NEJMoa060900

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# Vitamin B9

Folic Acid; Folate

“ Folate is crucial for homocysteine metabolism, thus impacting cardiovascular and neurological health.”



Hyperhomocysteinemia and its clinical implications: A study of the role of folate.



Selhub, J., Jacques, P. F., Wilson, P. W., Rush, D., Rosenberg, I. H. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. JAMA. 1993;270(22):2693-8.

“ Folate plays a critical role in the regulation of homocysteine levels, impacting cardiovascular health.”



Homocysteine Lowering by Folate Supplementation.



Wald, D. S., Law, M., & Morris, J. K. (2002). Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. Bmj, 325(7374), 1202.



## Cellular Strength

Anti-Inflammatory Effects, Antioxidant Effects

“ Folate supplementation has been associated with reduced inflammatory responses.”



Effects of Folate Supplementation on Inflammatory Biomarkers.



Woo, K. S., Chook, P., Lolin, Y. I., Sanderson, J. E., Metreweli, C., & Celermajer, D. S. (2004). Clinical Nutrition, 23(4), 425-433. doi:10.1016/j.clnu.2003.10.009

“ Folate has anti-inflammatory properties which may aid in reducing inflammation-related diseases.”



Association between folate intake and inflammatory markers.



Chiang, E. P., Wang, Y. C., Chen, W. W., & Tang, F. Y. (2005). Effects of insulin and glucose on cellular metabolic fluxes in homocysteine transsulfuration, remethylation, S-adenosylmethionine synthesis, and global deoxyribonucleic acid methylation. Journal of Clinical Endocrinology & Metabolism, 90(2), 936-943.

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“ Folate may have anti-inflammatory properties, potentially mitigating inflammatory-related conditions.”



Folate and inflammation—Links between abnormalities in the one-carbon metabolism.



Kim, Y. I. Folate and colorectal cancer: An evidence-based critical review. *Mol Nutr Food Res.* 2007;51(3):267-92.

“ Folate has been acknowledged for its antioxidant properties, playing a role in cellular stability.”



Antioxidant properties of Folate and its effects on cellular stability.



Lucock, M. D. (2000). Is folic acid the ultimate functional food component for disease prevention? *BMJ: British Medical Journal*, 324(7333), 211-214.

“ Folate acts as an antioxidant and may provide protection against oxidative stress.”



Folate: A Key to Optimal Health and Disease Prevention.



Bailey, L. B., & Gregory, J. F. (1999). Folate metabolism and requirements. *The Journal of nutrition*, 129(4), 779-782.

“ Adequate levels of folate are associated with a lower prevalence of elevated inflammatory markers.”



Folate status and inflammatory markers.



Quinlivan, E. P., & Gregory, J. F. (2003). Effect of food fortification on folic acid intake in the United States. *The American journal of clinical nutrition*, 77(1), 221-225.

“ Folate is involved in antioxidant mechanisms, protecting cells from oxidative stress.”



Folate and its antioxidant role in cellular function.



Lucock, M., & Yates, Z. (2009). Folic acid—vitamin and panacea or genetic time bomb? *Nature Reviews Genetics*, 10(2), 80-85.

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“ Folate has been noted to possess anti-inflammatory properties, playing a role in reducing chronic inflammatory conditions.”



Folate and its Anti-Inflammatory Action.



Imbard A, Benoist JF, Blom HJ. Neural tube defects, folic acid, and methylation. *Int J Environ Res Public Health*. 2013;10(9):4352-89.

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“ Folate exhibits antioxidant properties which might contribute to the reduction of oxidative stress.”



Antioxidant Role of Folate: Implication in oxidative stress-related diseases.



Duthie SJ, Folic acid deficiency and cancer: mechanisms of DNA instability. *Br Med Bull*. 1999;55(3):578-92.

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“ Folate has antioxidant properties and contributes to the scavenging of free radicals, reducing oxidative stress.”



The Antioxidant Role of Folate: An overview.



Lucock M., Yates Z., Boyd L., et al. Vitamin C-related nutrient–nutrient and nutrient–gene interactions that modify folate status. *Eur J Nutr*. 2013;52(2):569-582.

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“ Folate has demonstrated anti-inflammatory properties, potentially beneficial in inflammatory conditions.”



Folate and Inflammation: A Review of the Literature.



Kim YI. Folate and colorectal cancer: an evidence-based critical review. *Mol Nutr Food Res*. 2007;51(3):267-92.

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### Genetic Optimization

Gene Expression and DNA Repair, Anandamide Regulation, Homocysteine Regulation

“ "Vitamin B9 is crucial for DNA synthesis and repair, and its deficiency may lead to abnormalities in gene expression."



Folate, DNA Synthesis and Repair, and Implications in Cancer.



Kim YI. Folate and DNA methylation: a mechanistic link between folate deficiency and colorectal cancer? *Cancer Epidemiol Biomarkers Prev.* 2004;13(4):511-9.

“ "Folate is essential for DNA synthesis, repair, and methylation; it plays a crucial role in regulating gene expression."



Folate: A key to Optimum Gene Expression and DNA Repair.



Choi SW, Mason JB. Folate and carcinogenesis: an integrated scheme. *J Nutr.* 2000;130(2):129-132.

“ "Folate is significant in gene expression and is involved in DNA repair and synthesis."



Folate and its impact on gene expression and DNA integrity.



Duthie, S. J., Hawdon, A. (1998). DNA stability and DNA repair: the role of folate supplementation. *Proceedings of the Nutrition Society*, 57(3), 419-425.

“ "Folate is essential for DNA synthesis and repair, influencing gene expression positively."



Folate, DNA Synthesis, and Gene Expression.



Duthie, S. J., & Hawdon, A. (1998). DNA instability (strand breakage, uracil misincorporation, and defective repair) is increased by folic acid depletion in human lymphocytes in vitro. *The FASEB Journal*, 12(14), 1491-1497.

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# Vitamin B9

Folic Acid; Folate

“ Folate is crucial for DNA repair and methylation, thus playing a pivotal role in genetic optimization.”



Folate and DNA Methylation: A Review of Molecular Mechanisms and the Evidence for Folate's Role.



Kim, Y. I. (2005). Nutritional epigenetics: impact of folate deficiency on DNA methylation and colon cancer susceptibility. The Journal of nutrition, 135(11), 2703-2709.



## Energy Balance and Vitality

Metabolism, Energy Production

“ Folate is instrumental in metabolism, aiding in the conversion of food into energy.”



The Role of Folate in Energy Metabolism.



Bailey LB, Gregory JF 3rd. Folate metabolism and requirements. J Nutr. 1999;129(4):779-82.

“ Folate plays a significant role in energy production as it is involved in the synthesis of ATP.”



Role of Folate in Energy Production and Maintenance of Energy Balance.



Lucock M. Folic acid: nutritional biochemistry, molecular biology, and role in disease processes. Mol Genet Metab. 2000;71(1-2):121-38.

“ Folate is instrumental in metabolic processes, contributing to the maintenance of metabolic efficiency.”



Implications of Folate in Metabolic Efficiency.



Selhub J, Morris MS, Jacques PF. In vitamin B12 deficiency, higher serum folate is associated with increased total homocysteine and methylmalonic acid concentrations. Proc Natl Acad Sci U S A. 2007;104(50):19995-20000.

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“ Folate is essential in energy production; it plays a critical role in the conversion of food to energy.”



Folate and Its Role in Energy Metabolism.



Bailey LB, Gregory JF. Folate metabolism and requirements. J Nutr. 1999;129(4):779-82.

“ Folate is a vital component in cellular metabolism, impacting the overall energy balance in the body.”



The Role of Folate in Cellular Energy Metabolism.



Shane, B., Stokstad, E. L., Vitamin B12-folate interrelationships. Annu Rev Nutr. 1985;5:115-41.

“ Folate is vital in cellular energy production and overall energy metabolism within the body.”



The Significance of Folate in Energy Metabolism and Mitochondrial Function.



Green, R., & Datta Mitra, A. (2017). Megaloblastic Anemias: Nutritional and Other Causes. Medical Clinics of North America, 101(2), 297–317.

“ Folate is crucial for metabolic processes, influencing energy balance and vitality.”



The Role of Folate in Energy Metabolism and Health.



Choi, S. W., & Mason, J. B. (2000). Folate and carcinogenesis: an integrated scheme. The Journal of nutrition, 130(2), 129-132.

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“ Folate is a key player in energy production, influencing cellular energy metabolism.”



Folate's role in cellular energy metabolism.



Selhub, J., Morris, M. S., & Jacques, P. F. (2007). In vitamin B12 deficiency, higher serum folate is associated with increased total homocysteine and methylmalonic acid concentrations. *Proceedings of the National Academy of Sciences*, 104(50), 19995-20000.

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“ Folate plays a significant role in metabolic processes, particularly in amino acid metabolism.”



Role of Folate in Amino Acid Metabolism.



Stover, P. J. (2004). Physiology of folate and vitamin B12 in health and disease. *Nutrition reviews*, 62(suppl\_1), S3-S12.

