

Abstract

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The methylation, neurotransmitter, and antioxidant connections between folate and depression.

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BACKGROUND: Depression is common - one-fourth of the U.S. population will have a depressive episode sometime in life. Folate deficiency is also relatively common in depressed people, with approximately one-third of depressed individuals having an outright deficiency. Folate is a water-soluble B-vitamin necessary for the proper biosynthesis of the monoamine neurotransmitters serotonin, epinephrine, and dopamine. The active metabolite of folate, 5-methyltetrahydrofolate (5-MTHF, L-methylfolate), participates in re-methylation of the amino acid metabolite homocysteine, creating methionine. S-adenosylmethionine (S-AMe), the downstream metabolite of methionine, is involved in numerous biochemical methyl donation reactions, including reactions forming monoamine neurotransmitters. Without the participation of 5-MTHF in this process, S-AMe and neurotransmitter levels decrease in the cerebrospinal fluid, contributing to the disease process of depression.

RESULTS: S-AMe supplementation was shown to improve depressive symptoms. 5-MTHF also appears to stabilize, enhance production of, or possibly act as a substitute for, tetrahydrobiopterin (BH4), an essential cofactor in monoamine neurotransmitter biosynthesis. There are few intervention studies of folic acid or 5-MTHF as a stand-alone treatment for depression related to folate deficiency; however, the studies that have been conducted are promising.

CONCLUSION: Depressed individuals with low serum folate also tend to not respond well to selective serotonin reuptake inhibitor (SSRI) antidepressant drugs. Correcting the insufficiency by dosing folate along with the SSRI results in a significantly better antidepressant response.

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