Folate and Vitamin $B_{12}$: Function and Importance in Cognitive Development

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The importance of the B vitamins folate and vitamin $B_{12}$ for healthy neurological development and function is unquestioned. As essential cofactors for one-carbon metabolism, folate and vitamin $B_{12}$ are required for biological methylation and DNA synthesis. Vitamin $B_{12}$ also participates in the mitochondrial catabolism of odd-chain fatty acids and some amino acids. Disrupting these pathways can have wide-ranging direct and indirect consequences for neural tissue. Inborn errors of their metabolism and severe nutritional deficiencies in humans and in animal models cause serious neurological as well as hematological pathology. Although these conditions underscore the importance of folate and vitamin $B_{12}$ for neurological function, they are relatively rare. More commonly, individuals who fall in the lower range of population folate and vitamin $B_{12}$ intake and plasma concentrations, but who are not clinically deficient, have significantly higher risk of poor neurological outcomes. These include increased risk of neural tube defects among children born to mothers with low folate status, increased risk of cognitive impairment, depression, Alzheimer’s disease and stroke among older adults. The mandatory fortification of food with folic acid has been a highly successful public health intervention with respect to reduction of incident neural tube defects, and encouraging data from recent clinical trials suggest that B vitamin supplementation may help to prevent cognitive decline and brain atrophy in some older adults. In comparison, far less is known about folate and vitamin $B_{12}$ requirements for optimal brain development and long-term cognitive health in newborns, children and adolescents. And while improving sub-optimal nutritional status among mothers and children is undoubtedly beneficial, the limits of excessive intake and its long-term influence on cognition are unclear. Emerging data suggest that dietary manipulation of one-carbon metabolism can have significant and enduring effects on epigenetic regulation of neural gene
expression in ways that may shape brain and behavior. Caution is warranted given several observations of unfavorable health indicators in children and adults exposed to high folic acid intake with and without regard for $B_{12}$ status. Resolving these issues will require a far more detailed understanding of the mechanisms relating folate and $B_{12}$ to development and cognitive health than is currently available.