Biochimie. 2020 Apr 22. pii: S0300-9084(20)30077-8. doi: 10.1016/j.biochi.2020.04.007. [Epub ahead of print]

Riboflavin supplementation alters global and gene-specific DNA methylation in adults with the MTHFR 677 TT genotype.

Amenyah SD[1], McMahon A[2], Ward M[2], Deane J[3], McNulty H[2], Hughes CF[2], Strain JJ[2], Horigan G[2], Purvis J[4], Walsh CP[3], Lees-Murdock DJ[5].

Author information

Abstract

DNA methylation is important in regulating gene expression and genomic stability while aberrant DNA methylation is associated with disease. Riboflavin (FAD) is a cofactor for methylenetetrahydrofolate reductase (MTHFR), a critical enzyme in folate recycling, which generates methyl groups for homocysteine remethylation to methionine, the pre-cursor to the universal methyl donor S-adenosylmethionine (SAM). A polymorphism (C677T) in MTHFR results in decreased MTHFR activity and increased homocysteine concentration. Previous studies demonstrated that riboflavin modulates this phenotype in homozygous adults (MTHFR 677 TT genotype), however, DNA methylation was not considered. This study examined DNA methylation, globally and at key MTHFR regulatory sites, in adults stratified by MTHFR genotype and the effect of riboflavin supplementation on DNA methylation in individuals with the 677 TT genotype. Samples were accessed from participants, screened for the MTHFR C677T polymorphism, who participated in observational (n = 80) and targeted riboflavin (1.6 mg/day) RCTs (n = 80). DNA methylation at LINE-1 and key regulatory regions of the MTHFR locus were analysed by pyrosequencing in peripheral blood leukocytes. LINE-1 (+1.6%; $p = 0.011$) and MTHFR south shelf (+4.7%, $p < 0.001$) were significantly hypermethylated in individuals with the MTHFR 677 TT compared to CC genotype. Riboflavin supplementation resulted in decreased global methylation, albeit only significant at one CpG. A significant reduction in DNA methylation at the MTHFR north shore (-1.2%, $p < 0.001$) was also observed in TT adults following intervention with riboflavin. This provides the first RCT evidence that DNA methylation may be modulated by riboflavin in adults with the MTHFR 677 TT genotype.

KEYWORDS: DNA methylation; MTHFR C677T polymorphism; One-carbon metabolism; Riboflavin

PMID: 32334045 DOI: 10.1016/j.biochi.2020.04.007