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Impact of the MTHFR C677T polymorphism on one-carbon metabolites: Evidence from a randomised trial of riboflavin supplementation.

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Abstract

Homozygosity for the C677T polymorphism in MTHFR (TT genotype) is associated with a 24-87% increased risk of hypertension. Blood pressure (BP) lowering was previously reported in adults with the TT genotype, in response to supplementation with the MTHFR cofactor, riboflavin. Whether the BP phenotype associated with the polymorphism is related to perturbed one-carbon metabolism is unknown. This study investigated one carbon metabolites and their responsiveness to riboflavin in adults with the TT genotype. Plasma samples from adults (n 115) screened for the MTHFR genotype, who previously participated in RCTs to lower BP, were analysed for methionine, S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), betaine, choline and cystathionine by liquid chromatography tandem mass spectrometry (LC-MS/MS). The one-carbon metabolite response to riboflavin (1.6 mg/d; n 24) or placebo (n 23) for 16 weeks in adults with the TT genotype was also investigated. Plasma SAM (74.7 ± 21.0 vs 85.2 ± 22.6 nmol/L, P = 0.013) and SAM:SAH ratio (1.66 ± 0.55 vs 1.85 ± 0.51, P = 0.043) were lower and plasma homocysteine was higher (P = 0.043) in TT, compared to CC individuals. In response to riboflavin, SAM (P = 0.008) and cystathionine (P = 0.045) concentrations increased, with no responses in other one-carbon metabolites. These findings confirm perturbed one-carbon metabolism in individuals with the MTHFR 677 TT genotype, and for the first time demonstrate that SAM, and cystathionine, increase in response to riboflavin supplementation in this genotype group. The genotype-specific, one-carbon metabolite responses to riboflavin intervention observed could offer some insight into the role of this gene-nutrient interaction in blood pressure.

KEYWORDS: Hypertension; MTHFR; One-carbon metabolism; Riboflavin; S-adenosylmethionine

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