



Irish Section Meeting, 20–22 June 2018, Targeted approaches to tackling current nutritional issues

B-Vitamins, blood pressure and endothelial compliance in healthy adults stratified by *MTHFR* genotype

M. Rooney, M. Clements, C.F. Hughes, H. McNulty, J.J. Strain and M. Ward

Nutrition Innovation Centre for Food and Health (NICHE), Ulster University, Cromore Rd, Coleraine, BT55 1SA, Northern Ireland.

Hypertension affects 1 billion people worldwide and is a primary public health concern as the leading cause of premature mortality. A common polymorphism, the C677T mutation in the gene, *MTHFR*, encoding the enzyme methylenetetrahydrofolate reductase (MTHFR) affects 12% of the UK and Irish population and is associated with an increased risk of hypertension⁽¹⁾. The activity of MTHFR, which generates the predominant co-factor form of folate, 5 methyl-tetrahydrofolate, is dependent on flavin adenine dinucleotide (FAD), the co-enzyme form of riboflavin. Individuals homozygous for the *MTHFR* 677TT genotype have reduced MTHFR enzyme activity resulting in lower 5 methyl-THF concentrations⁽²⁾, however previous randomised controlled trials at our Centre have shown that blood pressure (BP) is highly responsive to riboflavin supplementation specifically in individuals with the TT genotype⁽³⁾. The mechanism explaining how this gene-nutrient interaction influences BP is unknown, but it may involve a nitric oxide (NO)-mediated effect on endothelial function⁽¹⁾. The aim of this study was to investigate BP and endothelial function in adults stratified by *MTHFR* genotype.

Healthy individuals, aged 18–60 years, were recruited from workplaces across Northern Ireland and screened for *MTHFR* genotype. Participants were invited to an appointment where health and lifestyle information, anthropometry, BP and endothelial function were assessed and a blood sample was taken. Pulse wave velocity (PWV) and augmentation index (AIx), which are indices of endothelial function, were measured with a SphygmoCor (AtCor Medical, Australia). BP, PWV and AIx were compared across the *MTHFR* genotypes.

	All (n = 108)		CC (n = 22)		CT (n = 24)		TT (n = 62)		P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	42.32	10.49	42.05	10.25	39.67	11.39	43.45	16.19	0.384
Male (%)	65 (60%)		14 (64%)		13 (54%)		38 (61%)		0.512
SBP mmHg	133.3	14.2	128.5 ^a	11.0	128.0 ^a	8.6	137.1 ^b	15.78	<0.001
DBP mmHg	81.0	10.7	77.7	7.7	80.4	9.4	82.5	9.4	0.112
AIx (%)	20.19	14.31	14.36	14.00	21.21	16.90	21.85	12.99	0.118
PWV (m/s)	7.13	1.44	6.42 ^a	1.15	7.33 ^{ab}	1.66	7.30 ^b	1.38	0.035

Differences between groups were assessed by ANOVA; values within a row with different superscript letters are significantly different, by Tuckey post-hoc test. Abbreviations: AIx, augmentation index; DBP, diastolic blood pressure; PWV, pulse wave velocity; SBP, Systolic BP.

Preliminary results in a subset of the study cohort, summarised in the table above, show that systolic BP is markedly higher in participants with the TT genotype, compared to CC and CT genotypes, with a similar, albeit non-significant, trend for diastolic BP. Pulse wave velocity was significantly higher in individuals with the TT compared to CC genotype, indicating poorer endothelial compliance in this genetically at-risk group.

In conclusion, this study has shown for the first time that individuals with the *MTHFR* TT genotype have poorer endothelial function compared to their age-matched CC genotype counterparts. Further research investigating the effect of riboflavin (and folate) status on measures of vascular function is required, in order to further our understanding of the mechanism explaining this novel gene-nutrient interaction in BP.

Acknowledgements

Northern Ireland Clinical Research Facility (NICRF), City Hospital, Belfast.

- McNulty H, Strain JJS, Hughes CF *et al.* (2017) *Mol Aspects Med* **53**, 2–9.
- Antoniades C, Shirodaria C, Leeson P *et al.* (2009) *Circulation* **119** (18), 2507–15.
- Horigan G, McNulty H, Ward M, *et al.* (2010) *J Hypertens* **28** (3), 478–86.