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Investigating the association between the *MTHFR* C677 T polymorphism and blood pressure as measured by ambulatory blood pressure monitoring

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Hypertension is the world's leading risk factor for preventable premature death and uncontrolled blood pressure (BP) rates remain high despite the widespread availability of anti-hypertensive drugs[(1)]. The C677 T polymorphism in the gene encoding methylenetetrahydrofolate reductase (MTHFR) is associated with hypertension[(2)]. Riboflavin, in the form of flavin adenine dinucleotide is required as a co-factor for MTHFR and has been shown in a number of randomised controlled trials, conducted at this centre, to significantly decrease clinic BP in adults who are homozygous (TT genotype) for the *MTHFR* C677 T polymorphism[(4)]. Ambulatory blood pressure monitoring (ABPM) is a more objective means of confirming the diagnosis of hypertension as ABPM can identify those with white coat hypertension, masked and resistant hypertension and has been shown to be a better predictor of mortality compared to clinic BP[(4)].

The aim of the current investigation is to explore the association between the *MTHFR* 677TT genotype and BP using ABPM. Adults recruited to the ongoing RIBOGENE study (NCT02463513) were screened for the TT genotype and were age and sex matched against those with the non-TT genotype. Following consent, participants provided a blood sample and had BP measured by both clinic BP and ABPM, in accordance with NICE guidelines[(5)]. Analysis of preliminary data indicates that individuals with the TT genotype have significantly higher clinic systolic blood pressure (SBP; $p < 0{\cdot}001$) and diastolic blood pressure (DBP; $p = 0{\cdot}001$) (Table). Overall mean 24hr SBP, as measured by ABPM, was found to be 5·5mmHg higher ($p = 0{\cdot}021$) in those with the TT genotype and this difference remained significant during awake and rest periods.

	MTHFR 677 C→T genotype				*P value*
	Non-TT (*n35*) Mean	SD	TT (*n35*) Mean	SD	
Age (y)	42·0	12·7	42·2	12·3	0·947
Clinic					
SBP (mmHg)	121·8	13·6	134·8	12·6	<0·001
DBP(mmHg)	71·7	7·7	78·9	10·3	0·001
24hr					
SBP(mmHg)	119·4	10·0	124·9	9·7	0·021
DBP(mmHg)	74·1	6·5	76·7	6·8	0·112
Awake					
SBP(mmHg)	123·9	10·5	128·9	9·8	0·040
DBP(mmHg)	77·6	7·2	79·9	7·1	0·186
Rest					
SBP(mmHg)	106·3	11·1	111·9	11·4	0·043
DBP(mmHg)	63·7	7·3	65·5	7·2	0·281

Data analysed using Independent T Test. P < 0·05 considered significant.

No previous study has investigated BP by ABPM in relation to this polymorphism. These preliminary results support the phenotype of elevated BP in adults with the *MTHFR* 677TT genotype as reported previously using clinic BP. Further ABPM studies are required to confirm these findings and to investigate circadian patterns by *MTHFR* genotype in the larger cohort and the effect of riboflavin intervention on BP in these genetically at risk adults.

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