

prevalence of riser pattern was also higher in summer than in winter (in summer, 27.2%; vs. in winter, 10.1%, $p < 0.05$). When the interaction between BP parameters and each season for the association with TOD was assessed, an association between riser pattern and UACR and an association between nighttime home DBP and BNP were stronger in winter compared to those in other seasons (both p for interaction < 0.05).

	UACR		BNP	
	Winter N=601	Other seasons N=1944	Winter N=601	Other seasons N=1944
Office SBP, 10 mmHg	0.066 (0.039, 0.092)	0.078 (0.064, 0.091)	-0.002 (-0.024, 0.020)	0.017 (0.005, 0.030)
	$P_{int} = 0.216$		$P_{int} = 0.147$	
Office DBP, 10 mmHg	0.103 (0.059, 0.147)	0.078 (0.055, 0.101)	-0.030 (-0.066, 0.006)	-0.036 (-0.056, -0.016)
	$P_{int} = 0.203$		$P_{int} = 0.551$	
Daytime home SBP, 10 mmHg	0.059 (0.024, 0.094)	0.063 (0.045, 0.082)	0.038 (0.010, 0.067)	0.014 (-0.003, 0.032)
	$P_{int} = 0.246$		$P_{int} = 0.579$	
Daytime home DBP, 10 mmHg	0.057 (-0.006, 0.119)	0.054 (0.020, 0.089)	0.047 (-0.005, 0.098)	-0.015 (-0.045, 0.015)
	$P_{int} = 0.314$		$P_{int} = 0.034$	
Nighttime home SBP, 10 mmHg	0.061 (0.026, 0.097)	0.032 (0.013, 0.052)	0.037 (0.007, 0.066)	0.016 (-0.001, 0.033)
	$P_{int} = 0.787$		$P_{int} = 0.160$	
Nighttime home DBP, 10 mmHg	0.071 (0.011, 0.130)	0.056 (0.023, 0.090)	0.049 (0.004, 0.094)	0.016 (-0.014, 0.046)
	$P_{int} = 0.267$		$P_{int} = 0.019$	
Riser pattern	0.164 (0.003, 0.326)	0.003 (-0.072, 0.079)	-0.099 (-0.234, 0.036)	0.045 (-0.023, 0.114)
	$P_{int} = 0.035$		$P_{int} = 0.346$	

This table shows non-standardized coefficient (95% confidence interval) of each of the BP parameters for log-transformed UACR and BNP in multivariable linear regression models in the subjects categorized in winter (N=601) versus other seasons (N=1944). The model in Office SBP/DBP was adjusted for traditional host factors (age, sex, body mass index, prevalent CVD, current smoking, alcohol consumption, diabetes, dyslipidemia, chronic kidney disease, and use of antihypertensive medications). The models in daytime home SBP/DBP (Mean of morning and evening home SBP) were adjusted for traditional host factors and office SBP or DBP. The model in nighttime home SBP/DBP was adjusted for traditional host factors, office SBP or DBP, and daytime home SBP or DBP. The model in riser pattern was adjusted for traditional host factors, office SBP, daytime home SBP, and nighttime home SBP. The values of p for interaction were calculated from the analysis model in all participants (N=2545), which included each BP parameter, winter (vs. other seasons), the interaction between each BP parameter and winter (vs. other seasons), and traditional host factors. Abbreviations: BNP, b-type natriuretic peptide; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; SBP, systolic blood pressure; UACR, urine albumin creatinine ratio. $P_{int} = p$ for interaction, $^*p < 0.05$; $^{**}p < 0.01$

Conclusions: In the present study, we revealed the association of nighttime home BP and TOD was stronger in winter than in other seasons.

DIURNAL RHYTHM AND SALT RESPONSIVE RESHAPING OF GUT MICROBIOTA CORRELATES WITH HYPERTENSION

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Objective: Aberrant diurnal rhythms of Blood Pressure (BP) are well known to be associated with hypertension, however, whether rhythmicity of microbial composition is associated with salt sensitive hypertension remains unknown. We hypothesized that BP and gut microbial composition follow synchronous rhythms in high salt fed Dahl Salt-Sensitive (S) rats and contribute to the progression of hypertension.

Design and method: To test this hypothesis, we examined groups of Dahl S rats for their diurnal rhythms of both the gut microbiota and blood pressure in low salt (0.3%) and high salt (2%) conditions.

Results: In high salt fed animals, Firmicutes/Bacteroidetes (F/B) ratio significantly changed between the dark (active) and light (rest) phases, which correlated with the diurnal rhythmicity of BP suggesting salt mediated rhythmic regulation of microbiota. Diurnal rhythms of Firmicutes, Bacteroidetes and Actinobacteria were independently associated with BP and significant in high salt fed animals. Discrete genera were observed to correlate independently or interactively with one or more of the following 3 factors- 1) BP rhythm, 2)

dietary salt, 3) amplitude of BP. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUST) analysis revealed diurnal rhythmicity of microbial pathways. During the active phase of the host, microbiota upregulated biosynthetic processes whereas during the resting phase of the host, microbiota upregulated degradation pathways of metabolites. These diurnal changes in microbiota, their functional pathways and BP response were prominently associated with a concerted rhythmicity of renal Lipocalin 2 and Endothelin 1.

Conclusions: Collectively, these data demonstrated the existence of synchronous diurnal rhythms of BP and renal inflammation with diurnal reshaping of gut microbiota in salt-sensitive hypertension. Such a concerted rhythmicity with peaks observed at the mid-active phase suggests that targeting this timepoint to reshape microbiota and/or intervene with medication could benefit hypertensives.

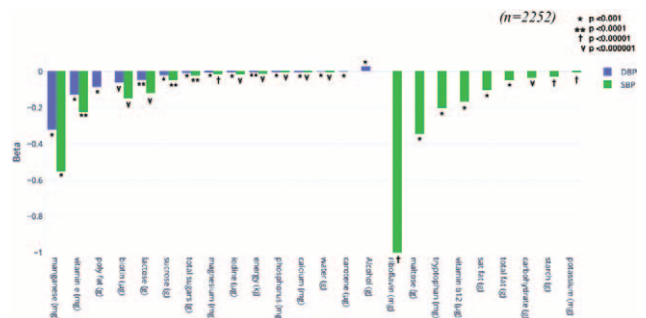
DIETARY INFLUENCE OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE IN THE TWINSUK COHORT

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Objective: Hypertension is a major modifiable risk factor for cardiovascular morbidity and mortality. Clinical and population-based studies show that several dietary components affect blood pressure and modification of these nutritional factors provide an important strategy to control blood pressure and reduce rates of hypertension. In this study, we examined the association between different nutrient intake and blood pressure in a cohort of adult twins.

Design and method: We included 2252 adults from the TwinsUK registry not on hypertensive treatments with concurrent clinical blood pressure measurements. All subjects completed a Food Frequency Questionnaire facilitating estimated intake of 45 nutrients. Linear mixed models were used to investigate nutrient intake on systolic and diastolic blood pressure adjusting for age, gender, BMI and family relatedness. A Bonferroni correction was applied for multiple testing. A backward linear regression was then used to determine independently associated nutrients.

Results: We identified 24 nutrients significantly associated with blood pressure after adjusting for covariates and multiple testing (Figure.1). Of those nutrients, 21 were negatively associated with SBP, 14 were negatively associated with DBP and one was positively associated with DBP. Among those with the greatest association with SBP were: riboflavin (Beta(SE): -1.39(0.34), $p=1.11 \times 10^{-6}$), manganese (-0.55(0.2), $p=1.25 \times 10^{-4}$) and maltose (-0.35(0.13), $p=1.35 \times 10^{-4}$). Intake of manganese (-0.32(0.14), $p=3.85 \times 10^{-4}$), vitamin e (-0.13(0.05), $p=3.12 \times 10^{-4}$) and polyunsaturated fats (-0.09(0.04), $p=5.76 \times 10^{-4}$) had the largest negative correlation with DBP, while, alcohol intake showed a positive correlation with DBP (0.03(0.01), $p=4.16 \times 10^{-4}$). From the multivariable model, the following six nutrients were independently associated with systolic blood pressure, explaining 22% of the variance: vitamin b12 (-0.19), biotin (-0.12), total fat (-0.13), starch (-0.03), total sugars (-0.04) and energy intake (-0.01). Five nutrients were independently associated with diastolic blood pressure and explained 14% of the variance, those were biotin (-0.08), magnesium (-0.01), energy intake (-0.00), carotene (-0.00) and alcohol (-0.06).



Conclusions: Our findings confirm current understanding and extend the panel of dietary nutrients implicated in blood pressure regulation. Our new findings of dietary factors that affect blood pressure after validation offer additional diet and lifestyle approaches in hypertension prevention and management.

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