

# Central Blood Pressure Responses to Dietary Sodium and Potassium Interventions

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## BACKGROUND

To explore how central hemodynamics respond to dietary sodium and potassium interventions, and whether the responses are associated with metabolic traits.

## METHODS

We conducted a dietary intervention study including a 7-day low-sodium (51.3 mmol sodium/day) intervention, a 7-day high-sodium (307.8 mmol sodium/day) intervention, and a 7-day high-sodium with potassium supplementation (60.0 mmol potassium/day) intervention among 99 northern Chinese subjects aged 18–60 years. Five metabolic traits included abdominal obesity, high triglycerides, low HDL cholesterol, raised blood pressure (BP), and high glucose. Central hemodynamics were measured at baseline and during each intervention.

## RESULTS

Central systolic BP (SBP), diastolic BP (DBP), pulse pressure (PP), and augmentation index (AIx@75) significantly decreased during low-sodium intervention, increased during high-sodium intervention, and then decreased during potassium supplementation. We observed potential linear trends toward significance of central SBP and PP responses to low-sodium intervention, and significant linear trends of responses

to high-sodium intervention as the number of metabolic traits grows. For example, among participants with 0 or 1, 2 or 3, and 4 or 5 metabolic traits, central SBP responses to high-sodium intervention were 8.8 [95% confidence interval (5.8, 11.8)], 9.3 (7.1, 11.6), and 14.0 (11.6, 16.3) mmHg, respectively (*P* for trend = 0.009). Significant linear trends of central SBP and DBP responses to potassium supplementation were also observed.

## CONCLUSIONS

Central BP and AIx@75 were lowered by sodium reduction and potassium supplementation, and elevated by sodium-loading. The responses of central BP were pronounced among individuals with metabolic traits clustering.

## CLINICAL TRIALS REGISTRATION

Trial Number NCT00721721 (The current study is registered on ClinicalTrials.gov; <https://clinicaltrials.gov>).

**Keywords:** blood pressure; central blood pressure; hypertension; metabolic traits; sodium; potassium.

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Central blood pressure (BP) does not correspond to brachial BP due to pressure pulse amplification from the aorta to the periphery.<sup>1</sup> Accumulating studies have suggested that central systolic BP (SBP) and pulse pressure (PP) are more closely related to subclinical organ damage<sup>2–4</sup> and cardiovascular diseases<sup>4–7</sup> than brachial BP, indicating a better predictive ability of central BP.

Low-sodium and high-potassium diets have been well documented to lower brachial BP.<sup>8,9</sup> Currently, several randomized controlled trials have also examined the effects of dietary sodium or potassium intervention on central BP<sup>10–14</sup>; however, the effects of sodium or potassium on central BP independent of peripheral BP have not been evaluated. Besides, central augmentation index (AIx) response to dietary sodium restriction and potassium supplementation

remains controversial.<sup>11–18</sup> Thus, clarifying the responses of central hemodynamics to dietary sodium and potassium interventions is needed.

BP responses to sodium intake vary among individuals, and this phenomenon was called “salt sensitivity”.<sup>19</sup> Previous studies have uncovered that insulin resistance<sup>20</sup> and metabolic syndrome<sup>21</sup> (MS) increase salt sensitivity of brachial BP. However, there is no study investigating how metabolic traits influence salt sensitivity of central BP up to present. Moreover, the relationship between metabolic traits and brachial or central BP responses to potassium supplementation has not been evaluated.

Therefore, we conducted this dietary intervention study to investigate the responses of central hemodynamics to dietary sodium and potassium interventions, and whether the

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responses are associated with metabolic traits. The current study may be helpful to elucidate whether dietary sodium and potassium interventions are more effective among individuals with more metabolic traits.

## METHODS

### Study participants

The present study was conducted in rural areas of Shandong province in northern China from June to October 2010. The study participants were a part of the Genetic Epidemiology Network of Salt Sensitivity (GenSalt) study. Details of the study population and methods for the GenSalt study have been published elsewhere.<sup>22</sup> In brief, a community-based BP screening was conducted among persons aged 18–60 years to identify potential probands. Those with mean brachial SBP of 130–160 mm Hg and/or diastolic BP (DBP) of 85–100 mm Hg were recruited, along with their parents, siblings, spouses, and offspring aged 16 years or older. Individuals with stage-2 hypertension, secondary hypertension, a history of clinical cardiovascular disease, diabetes, or chronic kidney disease, using antihypertensive medications, pregnant, heavy alcohol users, or currently on a low-sodium diet were excluded from the study. A total of 108 participants were recruited at baseline, among whom 7 did not take central hemodynamic measurements during low-sodium intervention, 1 during high-sodium intervention, and another one during high-sodium with potassium supplementation intervention. Thus, 99 participants were eligible and included in the current analysis. This study was approved by the institutional review board of Fuwai Hospital and participating institutions. Written informed consent was obtained from each participant before data collection.

### Dietary intervention

After a 3-day baseline examination, study participants received a 7-day low-sodium diet (3 g salt or 51.3 mmol sodium per day), followed by a 7-day high-sodium diet (18 g salt or 307.8 mmol sodium per day). During these 2 intervention periods, potassium intake remained consistent. Although not recorded, the potassium intake was monitored by the 24-hour urinary potassium excretion data. In the final week, participants maintained a high-sodium diet and took a 60 mmol potassium supplement daily. Although dietary sodium intake was the same for all study participants during each intervention, dietary total energy intake varied according to their baseline energy intake level. Participants were categorized into 5 energy intake levels (1,600; 2,100; 2,600; 3,100; and 3,600 kcal/day) based on baseline 24-hour Dietary Recall data. All meals were prepared without salt by full-time chefs in onsite kitchens. Prepackaged salt was added to each participant's meal by study staff when it was served. All participants were required to have their meals at the study kitchen under the supervision of the study staff during the entire study period, and were instructed to avoid consuming any foods that were not provided by the study. Besides, 3-timed urinary specimens (1 24-hour and 2 overnight) were collected at baseline and in each intervention

period to monitor participants' compliance with dietary interventions. The overnight urinary excretions of sodium and potassium were converted to 24-hour values on the basis of formulas developed from data obtained in the GenSalt study. The results showed good compliance with the interventions. The mean (SD) 24-hour urinary excretions of sodium and potassium were 214.4 (52.0) and 42.0 (10.9) mmol at baseline, 55.3 (18.3) and 35.7 (9.1) mmol during low-sodium intervention, 234.4 (31.6) and 44.2 (9.3) mmol during high-sodium intervention, and 230.3 (24.5) and 77.5 (10.8) mmol during high-sodium intervention with potassium supplement, respectively.

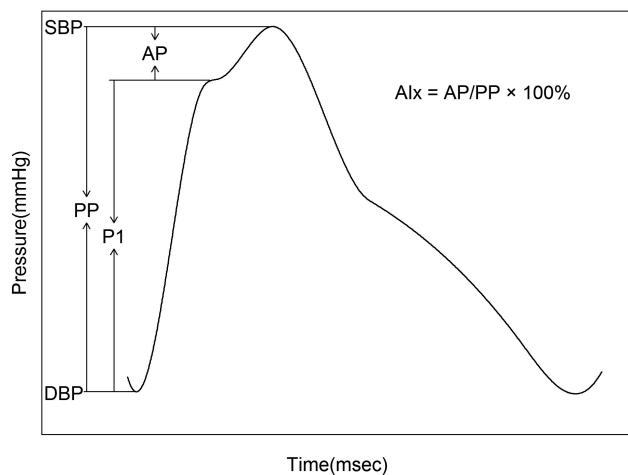
### Data collection

A standard questionnaire was administered by trained staff at the baseline examination to collect information on demographic characteristics, personal and family medical history, and lifestyle risk factors. We adapted the Paffenbarger Physical Activity Questionnaire to collect information on the physical activity.<sup>23</sup> The physical activity information obtained from the questionnaire was converted to metabolic equivalent hours per day. Body weight and height were measured twice in light indoor clothing without shoes. Body mass index was calculated as kilograms per square meter ( $\text{kg}/\text{m}^2$ ). Waist circumference was measured 1 cm above the participant's navel during light breathing. Overnight ( $\geq 8$  hour) fasting blood specimens were obtained for measurement of glucose and lipid concentrations. Plasma glucose concentration was measured with a modified hexokinase enzymatic method (Hitachi automatic clinical analyser, model 7060, Tokyo, Japan). Concentrations of HDL cholesterol and triglycerides were assessed enzymatically with commercially available reagents.

Three brachial BP measurements were obtained in every morning of the 3-day baseline examination by certified technicians using a random-zero sphygmomanometer according to a standard protocol. Pulse wave analysis was performed using the SphygmoCor CP system (AtCor Medical Ltd, Australia) in the morning of baseline examination and day 6 of each intervention. The radial pressure wave was obtained using applanation tonometry at the right radial artery, and then converted to central aortic pressure wave by a validated generalized transfer function.<sup>24</sup> Central hemodynamics included central SBP, DBP, PP, forward wave amplitude (P1), and augmentation pressure normalized to a heart rate of 75 bpm (AP@75). Central AIx was calculated as  $\text{AP}/\text{PP} \times 100\%$ , and then normalized to a heart rate of 75 bpm<sup>25</sup> (AIx@75) (Figure 1). Peripheral (that is, radial artery) SBP, DBP, PP, and heart rate were also obtained. All participants were measured in sitting position after 5-minute rest. Additionally, participants were advised to avoid smoking, consuming alcohol, coffee or tea, and physical activity for at least 30 minutes before measurement.

### Statistical analysis

Five metabolic traits included abdominal obesity (waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women), high triglycerides (serum concentration of triglycerides



**Figure 1.** Typical central aortic pressure waveform from a middle-aged subject. Abbreviations: Alx, augmentation index; AP, augmentation pressure; DBP, diastolic blood pressure; PP, pulse pressure; P1, forward wave amplitude; SBP, systolic blood pressure.

$\geq 150$  mg/dl), low HDL cholesterol (HDL cholesterol concentration  $< 40$  mg/dl in men and  $< 50$  mg/dl in women), raised brachial BP (SBP  $\geq 130$  mm Hg or DBP  $\geq 85$  mm Hg), and high glucose (plasma glucose concentration  $\geq 100$  mg/dl).<sup>26</sup> Participants were divided into 3 groups according to the number of metabolic traits: 0 or 1, 2 or 3, and 4 or 5. The responses of central hemodynamics were defined as follows: responses to low-sodium intervention = values on low-sodium diet – values at baseline; responses to high-sodium intervention = values on high-sodium diet – values on low-sodium diet; responses to potassium supplementation = values on high-sodium diet with potassium supplementation – values on high-sodium diet.

Continuous variables were presented as mean  $\pm$  SD or median with interquartile range based on normality of data and categorical variables as frequency with percentage. Baseline characteristics among 3 groups were compared by 1-way analysis of variance for normal variables and by Kruskal–Wallis test for nonnormal variables, using Student–Newman–Keuls test for *post hoc* contrast. Chi-square test was used to compare differences in categorical variables. Central and peripheral hemodynamics between 2 consecutive interventions were compared by paired *t* test. The responses of central BP independent of corresponding peripheral BP were assessed by linear mixed-effects model. We performed multivariable linear regression analysis to test linear trends of the responses of central hemodynamics as the number of metabolic traits increasing, adjusted for age, gender, body mass index, physical activity, smoking and drinking status, as well as baseline 24-hour urinary excretion of sodium and potassium. We additionally calculated the standardized  $\beta$  coefficients of each metabolic trait with the central hemodynamics responses to interventions, and the false discovery rate was used to adjust the results for multiple comparisons. A 2-tailed  $P < 0.05$  was considered statistically significant. All statistical analyses were performed with SAS software version 9.4 (SAS Institute, Inc., Cary, NC).

## RESULTS

A total of 99 participants completed the dietary sodium and potassium interventions, and the majority had 4 or 5 (38.4%) or 2 or 3 (36.4%) metabolic traits. As shown in Table 1, participants with more metabolic traits were more likely to be women. As expected, brachial SBP and DBP, body mass index, waist circumference, fasting concentration of triglycerides and glucose were significantly higher, whereas HDL cholesterol concentration was significantly lower, in participants with more metabolic traits. There were no significant differences in age, physical activity, and 24-hour urinary excretion of sodium and potassium by the number of metabolic traits.

Central and peripheral hemodynamics at baseline and during each intervention are presented in Table 2. Central SBP, DBP, PP, AP@75, and AIx@75 significantly decreased during low-sodium diet, increased during high-sodium diet, and then decreased during high-sodium diet with potassium supplement. Peripheral SBP, DBP, and PP significantly decreased during low-sodium diet and increased during high-sodium diet. However, only peripheral SBP significantly decreased during potassium supplementation. After adjustment for corresponding peripheral BP, we observed a  $-2.7$  [95% confidence interval ( $-3.9, -1.5$ )] mm Hg decrease and a  $2.0$  ( $1.0, 3.0$ ) mm Hg increase of central SBP, as well as a  $-2.2$  ( $-3.3, -1.0$ ) mmHg decrease and a  $1.7$  ( $0.8, 2.6$ ) mm Hg increase of central PP, during low-sodium and high-sodium intervention, respectively (all  $P < 0.001$ ) (Supplementary Table S1).

After multivariable adjustment, we observed potential linear trends toward significance of central SBP, PP, and P1 responses to low-sodium intervention, and significant linear trends of the responses to high-sodium intervention with the increment number of metabolic traits (Figure 2). For example, among participants with 0 or 1, 2 or 3, and 4 or 5 metabolic traits, the responses of central SBP were  $-8.1$  ( $-13.7, -2.4$ ),  $-10.5$  ( $-14.7, -6.3$ ), and  $-14.8$  ( $-19.2, -10.3$ ) mm Hg during low-sodium intervention ( $P$  for trend = 0.079), and  $8.8$  ( $5.8, 11.8$ ),  $9.3$  ( $7.1, 11.6$ ), and  $14.0$  ( $11.6, 16.3$ ) mm Hg during high-sodium intervention ( $P$  for trend = 0.009). Moreover, significant linear trends of central SBP and DBP responses to potassium supplementation were also observed (both  $P$  for trend  $< 0.05$ ) (Figure 2). In addition, we found that glucose was significantly correlated to central SBP, PP and P1 responses to low-sodium intervention, and brachial SBP was significantly associated with central PP response to high-sodium intervention. During potassium supplementation, waist circumference and HDL cholesterol significantly related to the responses of central SBP and DBP, and triglyceride was significantly associated with the response of central SBP. However, only waist circumference remained significantly associated with central DBP response to potassium supplementation after adjustment for multiple comparisons (Supplementary Table S2–S4).

## DISCUSSION

The present dietary intervention study in a group of northern Chinese individuals suggested that central BP and

**Table 1.** Baseline characteristics of study participants by the number of metabolic traits

	Overall (n = 99)	Number of metabolic traits			P
		0 or 1 (n = 25)	2 or 3 (n = 36)	4 or 5 (n = 38)	
Age (years)	53.4 ± 6.6	54.2 ± 5.9	52.2 ± 8.1	54.0 ± 5.3	0.396
Male, n (%)	60 (60.6%)	19 (76.0%)	24 (66.7%)	17 (44.7%)	0.030
Body mass index (kg/m <sup>2</sup> )	25.1 ± 3.4	22.2 ± 2.2 <sup>b</sup>	25.0 ± 3.2 <sup>c</sup>	27.0 ± 2.8 <sup>d</sup>	<0.001
Physical activity (METs <sup>a</sup> per day)	57.2 ± 19.9	62.5 ± 21.4	58.5 ± 21.2	52.5 ± 16.9	0.132
Current smoking, n (%)	23 (23.2%)	8 (32.0%)	11 (30.6%)	4 (10.5%)	0.061
Current drinking, n (%)	31 (31.3%)	6 (24.0%)	15 (41.7%)	10 (26.3%)	0.240
Brachial SBP (mm Hg)	134.3 ± 20.4	119.7 ± 12.7 <sup>b</sup>	128.4 ± 14.1 <sup>c</sup>	136.2 ± 11.6 <sup>d</sup>	<0.001
Brachial DBP (mm Hg)	83.0 ± 9.0	77.2 ± 8.4 <sup>b</sup>	79.8 ± 8.0	84.6 ± 8.0 <sup>d</sup>	0.002
Waist circumference (cm)	87.8 ± 10.6	78.6 ± 7.4 <sup>b</sup>	87.5 ± 10.0 <sup>c</sup>	94.1 ± 8.2 <sup>d</sup>	<0.001
HDL cholesterol (mg/dl)	42.6 (35.4~50.9)	49.1 (43.0~52.1) <sup>b</sup>	44.5 (40.5~58.1)	35.0 (31.6~39.6) <sup>d</sup>	<0.001
Triglyceride (mg/dl)	157.8 (112.5~255.6)	93.8 (82.9~119.8) <sup>b</sup>	137.8 (119.0~198.6) <sup>c</sup>	263.5 (201.8~345.8) <sup>d</sup>	<0.001
Glucose (mg/dl)	104.1 (93.9~121.9)	92.3 (88.0~97.8) <sup>b</sup>	102.0 (95.1~110.2) <sup>c</sup>	115.4 (105.7~135.9) <sup>d</sup>	<0.001
Urinary excretion (mmol per 24-hour)					
Sodium	214.4 ± 52.0	201.9 ± 49.1	221.2 ± 48.2	216.3 ± 56.9	0.351
Potassium	42.0 ± 10.9	37.9 ± 7.3	44.0 ± 9.6	42.8 ± 13.3	0.083

Values are mean ± SD or median (IQR) for continuous variables and frequency (%) for categorical variables. Abbreviations: DBP, diastolic blood pressure; HDL, high-density lipoprotein; MET, metabolic equivalent; SBP, systolic blood pressure.

<sup>a</sup>One MET is equivalent to a metabolic rate consuming 1 kcal per kg of body weight per hour.

<sup>b</sup>0 or 1 vs. 4 or 5, *P* < 0.05.

<sup>c</sup>0 or 1 vs. 2 or 3, *P* < 0.05.

<sup>d</sup>2 or 3 vs. 4 or 5, *P* < 0.05.

**Table 2.** Central and peripheral hemodynamics of study participants at baseline and during dietary interventions

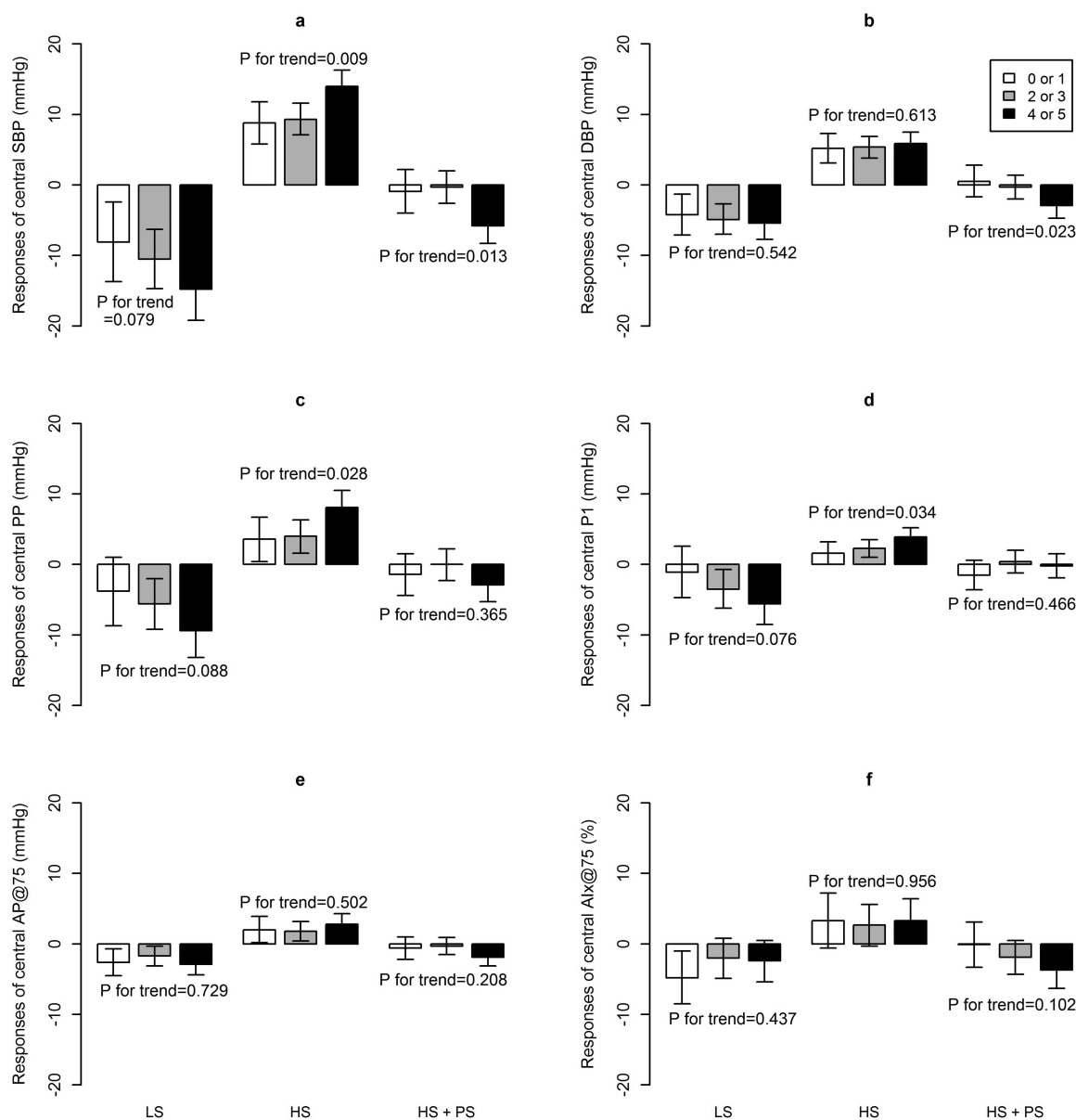
	Baseline	Low sodium	High sodium	High-sodium + potassium supplementation
SBP, mm Hg				
Central	123.2 ± 17.2	111.6 ± 12.9 <sup>a</sup>	122.6 ± 14.2 <sup>b</sup>	120.0 ± 13.4 <sup>c</sup>
Peripheral	134.3 ± 20.4	123.1 ± 14.3 <sup>a</sup>	133.2 ± 15.2 <sup>b</sup>	131.1 ± 14.8 <sup>c</sup>
DBP, mm Hg				
Central	84.3 ± 9.1	79.4 ± 8.6 <sup>a</sup>	84.9 ± 8.9 <sup>b</sup>	83.8 ± 8.3 <sup>c</sup>
Peripheral	83.0 ± 9.0	78.1 ± 8.6 <sup>a</sup>	83.7 ± 8.9 <sup>b</sup>	82.7 ± 8.2
PP, mm Hg				
Central	38.9 ± 14.1	32.2 ± 9.4 <sup>a</sup>	37.7 ± 11.4 <sup>b</sup>	36.2 ± 10.1 <sup>c</sup>
Peripheral	51.3 ± 17.6	45.0 ± 11.4 <sup>a</sup>	49.6 ± 12.6 <sup>b</sup>	48.5 ± 11.5
Central P1, mm Hg	28.7 ± 10.1	25.0 ± 6.7 <sup>a</sup>	27.7 ± 7.3 <sup>b</sup>	27.4 ± 6.9
Central AP@75, mm Hg	10.1 ± 5.2	7.7 ± 4.4 <sup>a</sup>	9.9 ± 5.0 <sup>b</sup>	8.9 ± 4.6 <sup>c</sup>
Central Alx@75, %	25.5 ± 8.4	22.6 ± 10.7 <sup>a</sup>	25.7 ± 9.5 <sup>b</sup>	23.5 ± 9.3 <sup>c</sup>
Heart rate, bpm	75.9 ± 11.5	78.7 ± 10.4 <sup>a</sup>	76.3 ± 10.1	76.7 ± 8.9

Values are mean ± SD. Abbreviations: Alx@75, augmentation index normalized to a heart rate of 75 bpm; AP@75, augmentation pressure normalized to a heart rate of 75 bpm; DBP, diastolic blood pressure; PP: pulse pressure; P1, forward wave amplitude; SBP, systolic blood pressure.

<sup>a</sup>*P* < 0.05 vs. baseline.

<sup>b</sup>*P* < 0.05 vs. low-sodium intervention.

<sup>c</sup>*P* < 0.05 vs. high-sodium intervention.



**Figure 2.** Multivariable-adjusted<sup>a</sup> mean responses of central hemodynamics to low-sodium (LS), high-sodium (HS), and high-sodium with potassium supplementation (HS + PS) intervention by the number of metabolic traits for central SBP (a), DBP (b), PP (c), P1 (d), AP@75 (e), and AIx@75 (f). <sup>a</sup>Adjusted for age, gender, body mass index, physical activity, smoking and drinking status, and baseline 24-hour urinary excretion of sodium and potassium. Error bars show 95% confidence intervals. Abbreviations: AP@75 and AIx@75, augmentation pressure and augmentation index normalized to a heart rate of 75 bpm; DBP, diastolic blood pressure; PP: pulse pressure; P1: forward wave amplitude; SBP, systolic blood pressure.

AIx@75 could be lowered by sodium reduction and potassium supplementation, and elevated by sodium-loading. Furthermore, we found central SBP and PP responses to low-sodium and high-sodium interventions remained significant even after adjustment for corresponding peripheral BP. Additionally, central BP responses to high-sodium intervention and potassium supplementation significantly increased as the number of metabolic traits growing, and these associations were independent of important covariates.

Previous observational studies have suggested that dietary sodium intake, indicated by 24-hour urinary sodium or sodium/potassium ratio, is positively associated with central SBP and PP in African<sup>27</sup> and Asian<sup>28</sup> population. Meanwhile,

a randomized controlled trial conducted in Dutch adults found that high-sodium diet significantly increased central SBP, DBP, and PP,<sup>11</sup> with which our results are consistent. Gates *et al.*<sup>14</sup> also reported that sodium restriction significantly lowered central SBP and DBP. The effect of potassium supplement on central BP remains controversial in western population, with 1 study observed significant decrease of central SBP and DBP,<sup>13</sup> however, the other 2 did not.<sup>11,12</sup> In addition, Hu *et al.*<sup>10</sup> reported that replacing 35% dietary sodium with 25% potassium and 10% magnesium significantly lowered central SBP and PP but not DBP after 12-month intervention in northern Chinese. In Hu's trial, participants' meals were cooked by themselves with salt



substitute or usual salt provided by the study, thus the investigators failed to assess the exact consumed amount of the salt substitute or salt. While our study had a better quality control strategy that all meals were prepared by full-time chefs and prepackaged salt was added to each participant's meal by study staff. The present study suggested that both sodium reduction and potassium supplementation lowered central SBP, DBP, and PP in northern Chinese population.

Although previous studies have suggested a potential decrease of central BP by dietary sodium reduction, whether the effects are independent of corresponding peripheral BP has not been investigated. In our analysis, we observed an approximate 2 mm Hg response of central SBP and PP during dietary sodium intervention after adjustment for corresponding peripheral BP. These findings could provide additional evidence to the opinion that central BP may serve as a better intervention target in clinical practice.<sup>1</sup>

Despite of the doubt of central AIx being used as an indicator of arterial stiffness, it independently predicts cardiovascular events and mortality.<sup>29</sup> Therefore, interventions to lower central AIx could be of significance. Previous studies have evaluated the effects of short-term dietary sodium intervention on central AIx; however, the results differ cross studies.<sup>11,14-16</sup> The inconsistency across studies may lie in the different sample characteristics,<sup>14,16</sup> magnitude of sodium reduction,<sup>11,14</sup> and length of intervention period.<sup>15,16</sup> Besides, most studies in western population<sup>11-13,18</sup> and a meta-analysis<sup>17</sup> found no significant effect of potassium supplement on central AIx. In the present study, however, we found central AIx@75 significantly decreased during low-sodium intervention and potassium supplementation, indicating that dietary sodium and potassium interventions may be helpful to lower central AIx.

The association between MS and salt sensitivity of brachial BP has been demonstrated in previous studies. In 56 Japanese patients, Uzu *et al.*<sup>30</sup> reported a significant higher prevalence of salt-sensitive hypertension among patients with MS than those without (70.6% vs. 36.0%,  $P = 0.017$ ). In 301 participants from Venezuela, Hoffmann and Cubeddu<sup>31</sup> observed significant greater responses of SBP and DBP to salt restriction among those with more metabolic traits, which was subsequently confirmed by Chen *et al.* in a large population of China.<sup>21</sup> However, no study has investigated the relationship between metabolic traits and central BP responses to dietary sodium intervention so far. We are the first to find central SBP and PP responses to high-sodium intervention increase as the number of metabolic traits grows. Moreover, we for the first time reported that central SBP and DBP responses to potassium supplementation were also greater among those with more metabolic traits. Our findings may have potential clinical relevance, that is, dietary sodium reduction and potassium supplementation are especially effective in lowering central BP among individuals with metabolic traits clustering.

The underlying mechanism of the associations between metabolic traits and salt sensitivity of BP is not fully understood. Insulin resistance and obesity are the most important mechanisms involved in MS.<sup>26</sup> Previous studies have suggested that insulin resistance-related hyperinsulinemia, sympathetic overdrive, and rennin-angiotensin system activation

contribute to sodium retention, and thereby increasing BP responses to sodium intake.<sup>32-34</sup> Besides, the enhanced salt sensitivity of BP in obesity has been noted<sup>35</sup> and might be explained by increased renal tubular reabsorption of sodium in obese individuals.<sup>36</sup> The variation in BP responses to potassium supplementation among individuals has been reported by the GenSalt collaborative research group, and the responses are associated with baseline brachial BP levels.<sup>37</sup> The present study further demonstrated that central BP responses to potassium supplementation varied according to the number of metabolic traits, which could be partly interpreted by the positive effect of potassium on salt-induced insulin resistance.<sup>32</sup>

Our study is the first free-living population-based dietary intervention study in which the central hemodynamics responses to dietary sodium and potassium interventions were examined according to metabolic risk status. We excluded patients with chronic kidney disease, who had increased salt sensitivity, and adjusted for important covariates in analysis to minimize study bias. The compliance with dietary interventions was excellent as measured by 24-hour urinary excretion of sodium and potassium. Nevertheless, 3 potential limitations should be addressed. First, the 24-hour sodium measured was lower than the prescribed sodium intake during high-sodium intervention, probably due to the fact that urinary sodium is usually less than dietary sodium intake.<sup>38</sup> However, some participants may not have finished their meals, so 24-hour urinary sodium excretion was estimated using a regression coefficient when only an overnight urine was collected. Second, our study might slightly underestimate the associations between metabolic traits clustering and central BP responses to dietary sodium intervention. To avoid potential adverse effects of a high-sodium diet, we excluded patients with stage 2 hypertension. Since hypertensive patients are more likely to have MS and salt sensitivity, the exclusion of stage 2 hypertensive patients is prone to bias the associations toward the null. Third, central and peripheral hemodynamics were measured only once in each intervention period, and the 30-minute abstention from smoking, consuming alcohol, coffee or tea, and physical activity prior to measurements was not long enough. However, the lack of restrictions which could affect the hemodynamic parameters is more likely to bias the results toward the null. Further studies with repeated measurements are needed to validate our findings.

In summary, the current study suggested that central BP and AIx@75 could be lowered by sodium reduction and potassium supplement, and elevated by sodium-loading. Moreover, we for the first time revealed significant effects of dietary sodium intervention on central SBP and PP independent of corresponding peripheral BP, which supports the opinion that central BP is a superior intervention target over peripheral BP. In addition, we found the responses of central BP increased with the number of metabolic traits, indicating that dietary sodium and potassium interventions are especially beneficial among individuals with metabolic traits clustering.

#### SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

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## DISCLOSURE

The authors declared no conflict of interest.

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