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ORIGINAL CONTRIBUTION

# Prospective relevance of fruit and vegetable consumption and salt intake during adolescence for blood pressure in young adulthood

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**Abstract**
*Purpose* Fruit and vegetable (FV) consumption and salt intake are known dietary influences on blood pressure (BP) in adults, but data on their long-term relevance during growth for later BP are rare. We aimed to examine the independent and concomitant influences of adolescent FV and salt intakes on BP in young adulthood.
*Methods* In total, 206 participants (108 males) provided a plausible BP measurement in young adulthood (18–25 years) as well as three repeated 3-day weighed dietary records, 24-h urine samples and BP measurements during adolescence (11–16 years). FV intake was assessed based on dietary records and its urinary biomarkers such as potassium, oxalate and hippuric acid. Urinary sodium chloride (NaCl) was used to estimate salt intake. Prospective associations of adolescent FV and salt intake with adult BP were examined in sex-stratified linear regression models.
*Results* In multivariable models, a 100 g higher FV intake during adolescence was prospectively related to 0.9 mmHg lower systolic BP in young adult females ($P = 0.02$), but not in males ($P = 0.8$). Biomarkers supported the findings for FV regarding systolic BP. Concurrently, a 1 g higher salt intake was related to 1.7 mmHg higher systolic BP in young men only ($P = 0.01$). For diastolic BP, results were inconsistent.
*Conclusions* Our findings suggest that in adolescent healthy girls, a higher FV intake may be more relevant for BP than a reduced salt intake and the opposite appears to apply for boys. The physiological implications of the observed sex-specific diet–BP relationships need deeper examination.

**Keywords** Fruit and vegetables · Salt · Blood pressure · Adolescents · Prospective · Biomarker

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## Introduction

Due to its impact on chronic, especially cardiovascular diseases, high blood pressure (BP) is a leading risk factor for mortality worldwide [1]. Moreover, it has been demonstrated that higher BP at a young age may independently contribute to an increased cardiovascular risk later in life [2].

There is convincing evidence that diet markedly influences blood pressure in adults [3], and a large number of studies have demonstrated that a lower salt intake [4] as well as a higher fruit and vegetable (FV) consumption [5] might reduce BP in hypertensive and normotensive individuals. Nevertheless, data on the long-term relevance of these dietary factors during growth for BP later in life are rare. In a small longitudinal study [6], a higher FV intake in early childhood (3–6 years), especially when combined with a high dairy intake, was associated with a smaller BP increase and a lower absolute BP until early adolescence (13 years). Similar associations were found in a larger group of slightly older females [7]. A higher vegetable (but not fruit) consumption from adolescence to adulthood was

also longitudinally associated with lower mean arterial BP in the same timeframe in another recent study [8]. In two other studies, a higher vegetable intake during childhood [9] and a higher plant food intake in young adulthood [10] were related to a lower risk of elevated BP in later adulthood. A recent meta-analysis of randomized controlled trials showed that also in children, a reduction in salt intake might have beneficial effects on BP [11]. Regarding the prospective relevance of habitual salt intake for later BP, a higher sodium intake at 4 months of age was associated with a higher BP at age 7 years in one study [12], while in another study with children aged 5–17 years at baseline, urinary sodium was not associated with BP change during 7 years of follow-up [13]. In the latter study, however, a higher ratio of urinary sodium to potassium excretion was directly associated with systolic BP change [13].

Adolescence may be a vulnerable period for dietary influences on BP, especially because—throughout the life course—the steepest BP increases are observed during puberty [14]. Moreover, unfavorable changes in dietary habits, including a decrease in regular FV consumption and an increased intake of fast food and salty snacks, often occur in this age group [15].

Although some carefully conducted longitudinal studies have investigated the relevance of either FV consumption [6, 8] or salt intake [12, 13] for BP development at a young age, none of the above-mentioned studies directly evaluated the long-term relevance of both usual FV and salt intake during adolescence for BP levels in young adulthood. Therefore, the aim of our current analysis was to estimate the strengths of associations with future BP in young healthy subjects, concomitantly for both dietary components.

## Methods

### Study population

For the present prospective analysis, young adult participants with available data during adolescence were selected from the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study. The DONALD Study is an ongoing open-cohort study that was started in 1985 and investigates the relationship between diet, metabolism and development in healthy volunteers from infancy until young adulthood [16]. Detailed regular assessments, beginning at 3 months of age, include 3-day weighed dietary records, medical and anthropometric examinations as well as interviews on lifestyle. Beginning at the age of 3–4 years, 24-h urine samples are usually collected in parallel with the dietary records. The DONALD Study was approved by the Ethics Committee of the University of Bonn (Germany), and all assessments were performed with parental and, later on, children's written consent.

Among the 371 DONALD participants who have already reached adult age, 349 subjects had a BP measurement and parallely assessed anthropometric data available between 18 and 25 years of age. Of these, 215 participants had provided ≥3 parallel plausible dietary records and 24-h urine samples and ≥3 BP measurements during adolescence (11–16 years). Further, six participants were excluded because they were not born term (<36 weeks gestation) or because of missing data on birth weight or gestational age. In addition, three participants were excluded because of implausible BP data, resulting in a final study sample of 206 subjects (108 males). For each of these 206 participants, three repeated urinary, dietary and BP measurements during adolescence as well as one BP measurement in young adulthood were used in our analyses.

### Nutritional assessment

Food consumption in the DONALD Study is assessed annually using 3-day weighed dietary records. On three consecutive days, all consumed foods and beverages as well as leftovers are weighed on electronic food scales to the nearest 1 g. When exact weighing is not possible, household measures (e.g., number of spoons, cups) are allowed for semiquantitative reporting. Mean 3-day energy, nutrient and food group intakes were calculated from the records using our in-house nutrient database LEBTAB [17], which is continuously updated. For the current analysis, mean 3-day FV intake was calculated as the sum of FV consumed either separately or as part of composite foods with >50 % FV content. In this food group—referred to as FVJ—100 % FV juices were also included. This approach of calculating FV intake, omitting minor amounts of FV from composite foods with <50 % FV content such as fruit yoghurts, lemonades or pizza, was intended to be more reflective of dietary pattern or behavior. Potatoes, legumes and nuts were not considered as FV in our analyses.

### Urine sampling and urinary variables

Parents and children received detailed instructions on how to collect complete 24-h urine samples, which are usually performed at the last day of the 3-day dietary records [16]. During the collection period, all micturitions are immediately stored frozen ≤−12 °C in Extran-cleaned (Extran, MA03; Merck, Darmstadt, Germany), preservative-free, 1-L plastic containers before being transferred to the research institute where they are further stored at ≤−20 °C until analyzed. In the urine samples, 24-h creatinine excretion was quantified with a creatinine analyzer (Beckman-2; Beckman Instruments, Fullerton, CA) using the kinetic

**Table 1** Spearman's correlation coefficients for different urinary biomarkers with FVJ intake from dietary records

| | All | Boys | Girls |
|---|---|---|---|
| Hippuric acid ($n = 206$) | 0.54 | 0.61 | 0.45 |
| Potassium ($n = 206$) | 0.40 | 0.35 | 0.46 |
| Oxalate ($n = 184$) | 0.43 | 0.36 | 0.49 |
| Potassium + oxalate ($n = 184$) | 0.46 | 0.40 | 0.53 |

Data represent means of three repeated measurements per individual

*FVJ* fruit and vegetables including 100 % juices

Jaffé procedure. To minimize possible errors in urine collection, urine samples with a creatinine excretion below a body weight-related cutoff of 0.1 mmol/kg [16] were not considered in the present analysis. Kjeldahl technique (Buechi 430 Digestor and Buechi distillation unit B-324) was used to measure 24-h nitrogen excretion (as biomarker of dietary protein intake). Urinary sodium and potassium were determined by flame atomic absorption spectrometry (Perkin Elmer 1100 Spectrometer; Perkin Elmer, Überlingen, Germany), while 24-h excretions of chloride and oxalate were measured with a Dionex 2000 i/SP ion chromatograph with an ion Pac AS4A column (Dionex GmbH, Idstein, Germany). The arithmetic mean of urinary sodium chloride (NaCl) excretion was used as a biomarker for dietary salt intake. Since both, higher potassium [18, 19] and oxalate [19], excretions have been observed on FV-rich diets, a combined biomarker based on these two components served as urinary indicator of general FV intake in our analyses. The selection of this combined biomarker for the BP analyses was based on the stronger correlation of this indicator with recorded FVJ intake compared with urinary potassium or oxalate excretion alone (Table 1). Additionally, urinary hippuric acid (HA) excretion, a potential biomarker specifically related to the consumption of polyphenol-rich FV [20–22], was quantified with a direct colorimetric method according to Tomokuni and Ogata [23] with minor modifications as previously described [20].

## Blood pressure measurements

In the DONALD Study, BP measurements are usually scheduled every 2 years. Seated systolic and diastolic BP was measured by trained nurses with a random-zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer thereafter. Because BP values determined with random-zero devices are systematically lower compared with those derived from standard mercury sphygmomanometers [24], BP values obtained before 1994 were multiplied with an internally validated conversion factor (e.g., 1.056 for systolic BP) to harmonize both measurement methods. At each measurement occasion, two consecutive BP readings were taken at the right arm after a 5-min rest and appropriate cuff sizes were used according to arm circumferences. In all analyses, the arithmetic mean of both measurements at the same occasion was used. For the systolic and diastolic BP outcomes in young adulthood, absolute BP values were used. However, as BP rises physiologically during growth, we calculated sex-, age- and height-independent BP SDS values according to German reference percentiles [25] for adolescent BP values. For the determination of each subject's BP SDS, the standardized deviation of the individually measured BP from the mean BP of a representative German pediatric population [25] was derived according to age-, sex- and height-specific data. Thus, a lower (more negative) BP SDS indicated a lower BP for the child's current developmental status.

## Anthropometric and additional variables

Anthropometric measurements, scheduled at every assessment, are performed by trained nurses according to standard procedures. With the participants barefoot and dressed in underwear only, standing height was determined to the nearest 0.1 cm by using a digital stadiometer (Harpenden Ltd, Crymych, United Kingdom) and body weight was measured to the nearest 0.1 kg with an electronic scale (Seca 753E, Seca Weighing and Measuring Systems, Hamburg, Germany). From these height and weight data, individual BMI in kg/m$^2$ was calculated. For adolescent BMI and height, we additionally determined sex- and age-independent SDS values using German reference data [25].

On their child's admission to the DONALD Study, parents were interviewed about family characteristics, and anthropometric and medical examinations (including BP measurements) were performed with the same equipment as used for the children. Information on size at birth and gestational age were abstracted from the "Mutterpass," a standardized document given to all pregnant women in Germany. The duration of exclusive breast-feeding was assessed during the first visit until complementary feeding was initiated.

## Statistical analyses

SAS software (version 9.2, SAS Institute, Cary, NC, USA) was used for all analyses. A $P$ value $< 0.05$ was defined as significant in all statistical tests except for analyses of interaction, where $P < 0.1$ was considered statistically relevant. For the combined potassium–oxalate biomarker, 24-h potassium and oxalate excretion were internally standardized (mean = 0, SD = 1) by age group and sex. The standardized excretion rates were then averaged for each participant to obtain a marker for general FV intake. Adolescent nutritional, urinary and anthropometric data were included

in the analyses as individual arithmetic means of three repeated measurements. If a participant provided more than three measurements between 11 and 16 years of age, the first three measurements in this timeframe were used. To characterize usual BP during adolescence, BP SDS values for the first three measurements between 11 and 16 years were also averaged for each participant. Descriptive adolescent and adult characteristics as well as parental and early life factors are presented separately for males and females as means (±SD) or medians (25th, 75th percentiles) for continuous variables and as absolute and relative frequencies for categorical variables. Sex differences were tested using unpaired *t* tests or the Wilcoxon rank sum test for normally or non-normally distributed continuous variables and Chi-square test for categorical variables.

Multiple linear regression models (PROC GLM) were used to analyze the prospective associations between adolescent (biomarkers of) dietary intakes and adult BP. In these models, NaCl excretion, FVJ intake or FV-related urinary markers were included as continuous predictors, while adult systolic or diastolic BP were used as the continuous outcome variables. Separate models were constructed for systolic and diastolic BP. If necessary, variables included in the regression models were log transformed to achieve normal distribution. Tests for interactions indicated that the association of adolescent salt ($P = 0.08$) and FVJ intakes ($P = 0.09$) with adult systolic BP differed between males and females. Hence, all subsequent analyses were sex stratified. Basic models (Model 1, Tables 4, 5) for investigation of the adolescent diet–adult BP associations included the respective dietary or urinary predictor as well as adult age and pubertal BP SDS as individual covariates and young adults' BP as outcome. In a further step, standardized energy intake and maternal BP were included in the regression models. Besides, models with NaCl excretion as the main predictor were adjusted for FVJ intake, whereas models examining FVJ intake, HA excretion or the combined potassium–oxalate biomarker as main predictors were adjusted for NaCl excretion. Potential confounders that were additionally considered included adolescent height SDS as well as several dietary [intake of protein (or its biomarker 24-h nitrogen excretion), saturated fat, calcium and dairy products], early life (gestational age, birth weight, duration of breast-feeding) and parental (maternal overweight and educational level, smoking in the household) characteristics. Only those confounders who substantially modified the investigated diet–BP associations were retained in the final models (Model 2). Because adolescent dietary factors may influence adult BP through their effects on adult BMI or body fat, we additionally included adult BMI in the last, separate model (Model 3). To illustrate mean differences in adult BP according to categories of adolescent dietary intake, we computed sex-specific adjusted least square means of systolic BP at low (the first quartile), medium (the second and the third quartile) and high (the fourth quartile) levels of NaCl excretion, FVJ intake and the FV-related urinary predictors.

## Results

Nutritional, urinary and anthropometric characteristics during adolescence are given as means of three repeated measurements in Table 2. Mean age at the adolescent assessments was about 12 years and did not differ between boys and girls. Boys had a higher total energy intake and consumed a higher percentage of energy from protein compared with girls. While absolute dietary salt intake, but not FVJ intake, was higher in male participants, energy-adjusted intakes of both, salt and FVJ, did not differ by sex. Absolute 24-h urinary excretion rates of all investigated analytes except for HA and oxalate were higher in boys. While absolute height was slightly higher in male adolescents, all other anthropometric measures did not differ between the sexes. Regarding parental and early life characteristics (Table 2), only birth weight was significantly higher in boys. There were no sex differences in absolute and standardized systolic and diastolic BP during adolescence (Table 3), while in young adulthood, systolic and diastolic BP were about 11 mmHg and 5 mmHg higher, respectively, in males than in females. Male participants also showed a significantly higher adult BMI (Table 3). At the time of the BP measurement in adulthood, no study participant reported taking any antihypertensive medication.

In multivariable linear regression models, adjusted for adult age, adolescent BP SDS, adolescent height SDS, maternal BP and maternal education as well as for dietary intakes of energy, saturated fat and FVJ, a higher NaCl excretion was prospectively associated with higher systolic BP in males ($P = 0.01$) but not in females ($P = 0.1$) (Table 4, Model 2). Adjusted (Model 2) least square means of systolic BP were on average 7.5 mmHg higher in males with high (the fourth quartile) compared to those with low (the first quartile) NaCl excretion (Fig. 1). Concurrently, linear regression models revealed an inverse association ($P = 0.02$, Table 4, Model 2) between adolescent FVJ intake and adult systolic BP among women only. A significant inverse association with female systolic BP was also observed for the combined potassium–oxalate biomarker ($P = 0.002$), while HA was only in trend ($P = 0.06$) related to systolic BP in women. As can be seen in Fig. 1, females in the highest compared with the lowest quartile of FVJ intake, potassium–oxalate and HA excretion had 4.3, 5.9 and 3.5 mmHg lower mean systolic BP, respectively. Considering FV intake from all composite foods (instead of only those food items with >50 % FV content) changed these results only marginally (data not shown).

**Table 2** Nutritional, urinary and anthropometric data during puberty (11–16 years) as well as early life and parental characteristics of 206 DONALD participants

| | Boys ($n = 108$) | Girls ($n = 98$) | $P$ for difference |
|---|---|---|---|
| Age, years | 12.4 (12.1, 13.0)[a] | 12.3 (12.0, 13.0) | 0.4 |
| *Dietary intake* | | | |
| Energy, MJ | 9.1 (±1.5)[b] | 7.9 (±0.9) | <0.0001 |
| FVJ, g/day | 407 (268, 563) | 388 (274, 524) | 0.8 |
| FVJ, g/MJ | 45 (29, 62) | 51 (37, 67) | 0.1 |
| Salt[c], g/day | 6.7 (±1.5) | 6.1 (±1.9) | 0.006 |
| Salt[c], g/MJ | 0.75 (±0.16) | 0.77 (±0.22) | 0.3 |
| Protein, E % | 13.2 (±1.4) | 12.8 (±1.9) | 0.05 |
| Carbohydrate, E % | 51.3 (±4.3) | 51.5 (±4.9) | 0.8 |
| Fat, E % | 35.5 (±4.1) | 35.8 (±4.3) | 0.6 |
| Saturated fat, E % | 15.5 (±2.1) | 15.7 (±2.4) | 0.5 |
| *Urinary parameters* | | | |
| Creatinine, mmol/kg BW | 0.18 (±0.02) | 0.17 (±0.02) | <0.0001 |
| Nitrogen, mmol/day | 684 (±129) | 570 (±132) | <0.0001 |
| Sodium chloride[d], mmol/day | 116 (±27) | 105 (±32) | 0.006 |
| Potassium, mmol/day | 56 (±14) | 51 (±13) | 0.008 |
| Oxalate[e], mmol/day | 0.63 (0.47, 0.78) | 0,61 (0.47, 0.86) | 0.9 |
| Hippuric acid, mmol/day | 2.9 (2.4, 3.5) | 2.7 (2.4, 3.3) | 0.3 |
| *Anthropometric data* | | | |
| Weight, kg | 49.4 (±10.0) | 47.4 (±9.3) | 0.1 |
| Height, cm | 161 (±9) | 158 (±7) | 0.05 |
| Height SDS | 0.46 (±0.93) | 0.29 (±1.05) | 0.2 |
| BMI, kg/m$^2$ | 18.9 (±2.3) | 18.7 (±2.7) | 0.6 |
| BMI SDS | −0.17 (±0.74) | −0.32 (±0.89) | 0.2 |
| *Early life/parental data* | | | |
| Birth weight, g | 3,574 (±480) | 3,355 (±431) | 0.0007 |
| Gestational age, week | 40 (39, 40) | 40 (39, 40) | 0.5 |
| Breast-fed > 2 week, $n$(%) | 80 (74) | 77 (79) | 0.4 |
| Maternal overweight, $n$(%)[f, g] | 28 (26) | 32 (33) | 0.3 |
| Maternal school education ≥ 12 years, $n$(%) | 54 (50) | 47 (48) | 0.8 |
| Smoking in the household, $n$(%) | 39 (36) | 31 (32) | 0.5 |
| Maternal systolic BP[g], mmHg | 114 (±13) | 113 (±12) | 0.5 |
| Maternal diastolic BP[g], mmHg | 73 (± 10) | 73 (± 10) | 0.7 |

Pubertal data represent means of three measurements

*BP* blood pressure, *BW* body weight, *E %* percentage of energy intake, *FVJ* fruit and vegetables including 100 % juices, *SDS* standard deviation score

[a] All such data represent medians (25th, 75th percentiles)

[b] All such data represent means (±SD)

[c] Salt intake estimated from 24-h urinary sodium chloride excretion: 1 mmol sodium chloride corresponds to 0.058 g salt intake

[d] Sodium chloride excretion was calculated as [sodium (mmol/day) + chloride (mmol/day)]/2

[e] Data available for 87 girls and 97 boys

[f] BMI > 25

[g] Two missing values for maternal BMI, five missing values for maternal blood pressure, the missing data were amended using population median values for the regression analyses

Regarding diastolic BP in young adulthood (Table 5), no associations in basic or adjusted (Table 5, Model 2) models were seen with adolescent NaCl, FVJ intake or HA, neither among women nor among men. The potassium–oxalate biomarker, however, was inversely related to diastolic BP in males ($P = 0.04$). Additional adjustment for BMI in young

**Table 3** Blood pressure data during puberty (11–16 years) and anthropometric and blood pressure data in young adulthood (18–25 years) of 206 DONALD participants

| | Males ($n = 108$) | Females ($n = 98$) | $P$ for difference |
|---|---|---|---|
| *Adolescent BP* | | | |
| Systolic[a], mmHg | 104 (±7) | 103 (±8) | 0.3 |
| Systolic[b] SDS | −0.62 (±0.85) | −0.78 (±0.90) | 0.2 |
| Diastolic[a], mmHg | 62 (±6) | 61 (±6) | 0.3 |
| Diastolic[b] SDS | −0.52 (±0.92) | −0.71 (±0.94) | 0.1 |
| *Adult data* | | | |
| Age, years | 19.6 (18.0, 22.6) | 19.0 (18.1, 19.4) | 0.3 |
| BMI, kg/m$^2$ | 23.2 (20.9, 25.7) | 21.7 (20.1, 23.3) | 0.0007 |
| Systolic BP, mmHg | 122 (±11) | 111 (±9) | <0.0001 |
| Diastolic BP, mmHg | 74 (±9) | 69 (±8) | <0.0001 |

Pubertal data represent means of three measurements

*BP* blood pressure, *SDS* standard deviation score

[a] Data for the random-zero sphygmomanometer were multiplied by an internally validated conversion factor to account for differences in measurement systems

[b] SDS derived from German reference values according to participants age, sex and height [29]

adulthood (Model 3; Tables 4, 5) did not change the associations between dietary or urinary predictors and the BP outcomes.

In further analyses using change in BP (in mmHg/year) from adolescence until adulthood instead of absolute BP in young adulthood as an outcome, most associations were slightly attenuated. Nevertheless, results for both analyses were broadly comparable and adjustment for change in BMI from adolescence until adulthood did not alter these findings (data not shown). A change in dietary pattern (as well as, for example, in regular physical activity) occurring from adolescence until adulthood might also have influenced our BP results, but only 99 of our 206 study participants (48 %) had plausible urinary and dietary data in young adulthood as well. Therefore, specific longitudinal associations between changes in dietary intakes and changes in BP from adolescence to young adulthood could not be examined in the present study.

## Discussion

In the current analysis, we examined the concurrent long-term relevance of dietary salt and FVJ intake during adolescence for young adult BP. Our results suggest that adolescent dietary characteristics are related to later BP, but these relations probably differ by sex. According to findings in our study population, a higher dietary salt intake may be more relevant for systolic BP in young men, while a higher FVJ intake may be beneficial for systolic BP development predominantly in females. These findings were supported by biomarker analyses. The mutual adjustment of salt and FVJ in the linear regression models did not modify our results. According to the β-coefficients of our adjusted regression models (Table 4, Model 2), a 1 g increase of salt intake in adolescent boys was associated with a 1.7 mmHg higher systolic BP in young adulthood, while a 100 g higher FVJ consumption predicted a 0.9 mmHg lower systolic BP in young women.

In contrast to our findings for systolic BP, neither NaCl excretion nor FVJ intake or 24-h urinary HA was related to young adult diastolic BP. Nevertheless, a higher potassium–oxalate excretion, as well as a higher potassium excretion alone (data not shown), was associated with a lower diastolic BP in males. Because the correlation between dietary FVJ intake and potassium excretion in our male study participants was only moderate ($r = 0.35$, Table 1) and recorded FVJ consumption itself was not related to diastolic BP, we suppose that total potassium intake per se may be responsible for the observed BP association in young men. In general, it seems also possible that small dietary effects on diastolic BP could not be detected due to the lower proportion of BP variability explained by the fully adjusted models, indicated by lower $R^2$ values in Table 5 compared with Table 4: While >30 % of the variability in systolic BP was explained by the adjusted models for all investigated predictors in both sexes, $R^2$ values of only 15 % indicated that especially in women, other undetected factors importantly contribute to diastolic BP variation in our cohort. Measurement errors in the exposure as well as the outcome variables might also have affected our results. Although overestimation of BP in the clinical setting (i.e., white coat hypertension) may more often occur in subjects with higher BP levels, errors in BP measurement are unlikely to be related to the levels of dietary intake in our prospective analysis. With respect to dietary intake assessment, it seems possible that subjects with unfavorable dietary habits more frequently overestimate FV intake due to social desirability, which could lead to an underestimation of the investigated diet–BP associations. Our findings that BP associations based on dietary intake data are similar to those based on urinary biomarkers indicate, however, that this aspect seems to be of minor relevance in our study population.

To the best of our knowledge, so far only two other epidemiological studies have examined associations between adolescent FV intake and young adult BP in healthy subjects. In the study of Moore et al. [7], in which dietary FV intake, but not salt consumption, between 9 and 17 years of age and BP at the age of 18–20 years were assessed in more

**Table 4** Results of the linear regression models on the association between NaCl excretion, FVJ intake and FV-related biomarkers with *systolic BP* in 206 DONALD participants

| Outcome | Boys ($n = 108$) | | | Girls ($n = 98$) | | |
|---|---|---|---|---|---|---|
| Systolic BP (mmHg) | β (95 % CI) | *P* | $R^2$ | β (95 % CI) | *P* | $R^2$ |
| *NaCl excretion (mmol/day)* | | | | | | |
| Model 1[a] | 0.06 (−0.01, 0.14) | 0.09 | 0.22 | −0.02 (−0.07, 0.03) | 0.5 | 0.22 |
| Model 2[b] | 0.10 (0.03, 0.18) | 0.01 | 0.34 | −0.05 (−0.10, 0.01) | 0.1 | 0.31 |
| Model 3[c] | 0.10 (0.03, 0.18) | 0.01 | 0.35 | −0.05 (−0.11, 0.02) | 0.1 | 0.31 |
| *FVJ intake (100 g/day)* | | | | | | |
| Model 1 | 0.26 (−0.56, 1.09) | 0.5 | 0.20 | −0.69 (−1.44, 0.06) | 0.07 | 0.25 |
| Model 2 | 0.11 (−0.73, 0.96) | 0.8 | 0.34 | −0.92 (−1.72, −0.13) | 0.02 | 0.31 |
| Model 3 | 0.10 (−0.75, 0.94) | 0.8 | 0.35 | −0.92 (−1.73, −0.12) | 0.02 | 0.31 |
| *Ln Hippuric acid (mmol/day)* | | | | | | |
| Model 1 | 2.32 (−4.12, 8.76) | 0.5 | 0.20 | −3.55 (−9.54, 2.44) | 0.2 | 0.23 |
| Model 2 | −0.18 (−6.64, 6.29) | >0.9 | 0.34 | −6.39 (−12.95, 0.18) | 0.06 | 0.30 |
| Model 3 | −0.03 (−6.50, 6.45) | >0.9 | 0.35 | −6.68 (−13.42, 0.06) | 0.05 | 0.30 |
| *Sum of standardized potassium and oxalate*[e] | | | | | | |
| Model 1 | 1.02 (2.06, 4.09) | 0.5 | 0.18 | −2.59 (−5.36, 0.19) | 0.07 | 0.19 |
| Model 2 | 0.15 (−3.24, 3.54) | 0.9 | 0.36 | −5.00 (−8.16, −1.84) | 0.002 | 0.33 |
| Model 3 | 0.18 (−3.23, 3.58) | 0.9 | 0.36 | −4.96 (−8.15, −1.78) | 0.003 | 0.33 |

*BP* blood pressure, *FVJ* fruit and vegetables including 100 %-juices, *Ln* logarithmus naturalis, *NaCl* sodium chloride, *SDS* standard deviation score

[a] Adjusted for mean pubertal systolic BP SDS and adult age

[b] Model 1 additionally adjusted for standardized energy intake, intake of saturated fat (g/day), height SDS, maternal education, maternal BP and for NaCl excretion in models with FV-related predictors or for FV intake in the model with NaCl as the predictor

[c] Model 3(Mediator model): Model 2 additionally adjusted for adult BMI

[e] Data available for 97 boys and 87 girls

than 2,000 healthy girls, subjects in the highest category of FV consumption had a 0.4 mmHg lower systolic BP and a 1.1 mmHg lower diastolic BP as well as a 32 % reduction in the risk of elevated BP compared with those participants with the lowest FV intake, but these findings were not significant. In contrast, in the study of van de Laar et al. [8], significant longitudinal associations were observed between a higher vegetable (but not fruit) intake and a lower mean arterial BP during a 24-year timeframe covering adolescence and young adulthood. Another prospective study on the association of FV and BP in younger children [6] found a difference of 4.2 and 1.5 mmHg in systolic and diastolic BP in young adolescence, respectively, between children with low and high preschool FV consumption, which is in accordance with the 4.3-mmHg difference in systolic BP between the lowest and the highest category of FV intake in females in our study. In the prospective study of Brion et al. [12], in which a significant association between infant sodium intake and BP at the age of 7 years was observed, a 9 mmol higher sodium intake (corresponding to a 0.5 g increase in salt) predicted a 4 mmHg higher childhood systolic BP. In our study, a 9 mmol higher NaCl excretion was associated with a 0.9 mmHg higher systolic BP in boys, but the different age ranges investigated in our study and the population of Brion et al. [12], implying a great difference in dietary sodium intake, limits the direct comparability of both studies. In another recent observational study in older children and adolescents [26], a 1 g higher salt intake was cross-sectionally related to a 0.46 mmHg higher systolic BP in 14 to 18-year-old adolescents.

Our analyses show sex differences for the investigated diet–BP associations, with a significant direct relationship between dietary salt and systolic BP observable in male participants only. Varying salt–BP associations have been observed for adult males and females in other studies [27, 28], but conclusions on which sex may be more sensitive to a change in dietary salt intake are inconclusive. In a Chinese population, in which low- and high-salt interventions were performed in nearly 2,000 middle-aged adults, BP was more responsive to both salt treatments in women compared to men [27]. In contrast, in a cohort of more than 10,000 Japanese adults, a habitually higher dietary salt intake was related to higher systolic BP in men but not in women [28]. Mechanistic evidence supporting a stronger effect of dietary salt on BP in men comes from animal models suggesting that female sex hormones are able to

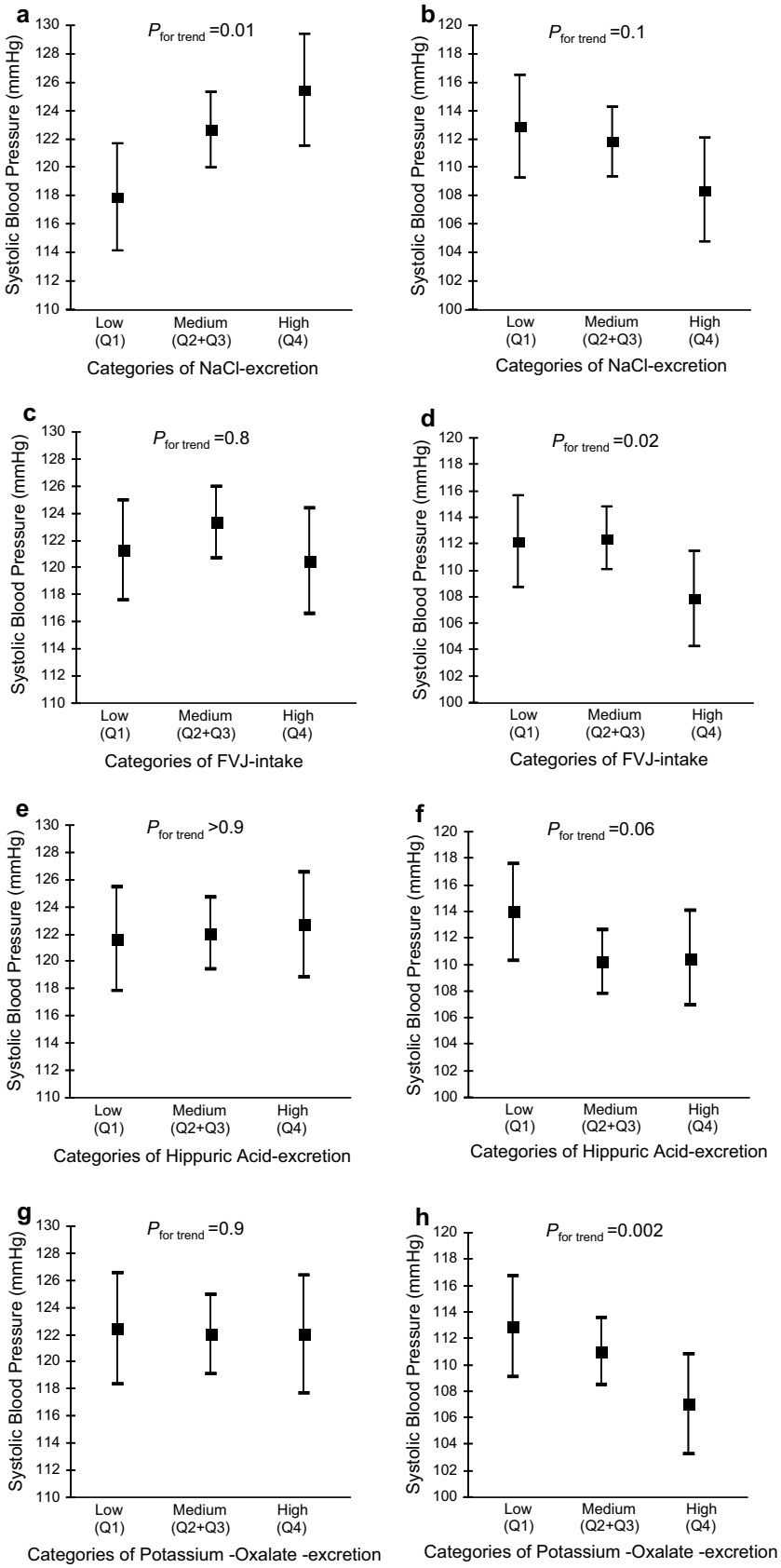


**Fig. 1** Adjusted (Model 2, Table 4) means (95 % CI) of young adult systolic blood pressure in categories of adolescent NaCl excretion (**a**, **b**), FVJ intake (**c**, **d**) and FV-related biomarkers (**e**, **f**, **g**, **h**). Data for males are shown in panels **a**, **c**, **e** and **g**, while data for females are shown in panels **b**, **d**, **f** and **h**. $P_{for\ trend}$ refers to *P* values obtained in the linear regression models with dietary predictors and adult blood pressure outcomes as continuous variables. Data for 108 males and 98 females, except for potassium–oxalate excretion, for which data were available in 97 males and 87 females. *Q* quartile

**Table 5** Results of the linear regression models on the association between NaCl excretion, FVJ intake and FV-related biomarkers with *diastolic BP* in 206 DONALD participants

| Outcome | Boys ($n = 108$) | | | Girls ($n = 98$) | | |
|---|---|---|---|---|---|---|
| Diastolic BP (mmHg) | β (95 % CI) | *P* | $R^2$ | β (95 % CI) | *P* | $R^2$ |
| *NaCl excretion (mmol/day)* | | | | | | |
| Model 1[a] | −0.02 (−0.08, 0.04) | 0.6 | 0.10 | 0.01 (−0.03, 0.06) | 0.6 | 0.12 |
| Model 2[b] | 0.02 (−0.05, 0.08) | 0.6 | 0.28 | 0.03 (−0.03, 0.08) | 0.3 | 0.15 |
| Model 3[c] | 0.02 (−0.05, 0.08) | 0.6 | 0.28 | 0.02 (−0.03, 0.08) | 0.4 | 0.15 |
| *FVJ intake (100 g/day)* | | | | | | |
| Model 1 | −0.10 (−0.76, 0.57) | 0.8 | 0.10 | 0.14 (−0.53, 0.82) | 0.7 | 0.12 |
| Model 2 | −0.08 (−0.73, 0.58) | 0.8 | 0.28 | 0.23 (−0.49, 0.96) | 0.5 | 0.15 |
| Model 3 | −0.08 (−0.73, 0.58) | 0.8 | 0.28 | 0.24 (−0.49, 0.97) | 0.5 | 0.15 |
| *Ln Hippuric acid (mmol/day)* | | | | | | |
| Model 1 | −3.32 (−8.52, 1.88) | 0.2 | 0.11 | −2.79 (−8.16, 2.59) | 0.3 | 0.13 |
| Model 2 | −2.82 (−7.94, 2.31) | 0.3 | 0.29 | −2.32 (−8.03, 3.39) | 0.4 | 0.15 |
| Model 3 | −2.83 (−7.98, 2.32) | 0.3 | 0.29 | −2.54 (−8.35, 3.26) | 0.4 | 0.15 |
| *Sum of standardized oxalate and potassium*[d] | | | | | | |
| Model 1 | −3.03 (−5.38, −0.68) | 0.01 | 0.18 | −0.34 (−2.78, 2.09) | 0.8 | 0.13 |
| Model 2 | −2.55 (−4.96, −0.13) | 0.04 | 0.35 | −0.48 (−3.34, 2.38) | 0.7 | 0.15 |
| Model 3 | −2.58 (−5.01, −0.16) | 0.04 | 0.35 | −0.49 (−3.37, 2.39) | 0.7 | 0.15 |

*BP* blood pressure, *FVJ* fruit and vegetables including 100% juices, *Ln* logarithmus naturalis, *NaCl* sodium chloride, *SDS* standard deviation score

[a] Adjusted for mean pubertal diastolic BP SDS and adult age

[b] Model 1 additionally adjusted for standardized energy intake, calcium intake (mg/day), birth weight, smoking in the household, maternal BP and for NaCl excretion in models with FV-related predictors or for FV intake in the model with NaCl as the predictor

[c] Model 3 (Mediator model): Model 2 additionally adjusted for adult BMI

[d] Data available for 97 boys and 87 girls

increase renal sodium excretion, thus diminishing BP increases on a high-salt diet [29]. Differences in the renin–angiotensin system between men and women may also be involved in a diverging renal sodium regulation and BP response to high sodium intakes [29]. Data on sex differences regarding the beneficial effect of a high FV consumption on BP are rare, but in a large ($n > 29{,}000$) Japanese cohort, a higher fruit intake, and especially a higher vegetable intake, was associated with a lower mortality from cardiovascular diseases in women only [30]. It is also possible that the observed sex differences in diet–BP associations may be partly attributable to different dietary behaviors of girls and boys, because females in our study population had a nonsignificantly ($P = 0.1$) higher FV intake per MJ as well as a significantly higher HA excretion per MJ ($P = 0.047$, data not shown).

In our present analysis, adjustment for BMI in young adulthood (Model 3; Tables 4, 5) did not attenuate the observed diet–BP associations. Moreover, results were basically unchanged when our BP models (Table 4 and 5) were adjusted for mean adolescent BMI SDS instead of BP SDS (data not shown). These findings indicate that associations of FVJ intake and salt consumption with BP in our study could not be explained by differences in body size and are in accordance with the prospective studies of Moore et al. [6, 7], in which adjustment for BMI at the time of the outcome measurement attenuated the diet–BP relations only slightly.

In the above-mentioned studies [6, 7], a higher dairy intake during childhood or adolescence was related to lower BP several years later. Data in adults suggest that not only dairy intake, but also dietary protein per se might be inversely related to BP, while diets rich in meat could be associated with higher BP levels compared with vegetarian diets [3]. However, in our analyses, we did not find any association between total adolescent meat, dairy or protein intake, estimated from dietary records or urinary nitrogen excretion, and young adult BP. Moreover, there was no close correlation between the intakes of meat, dairy and FVJ in our cohort and adjustment for meat, dairy or protein did not modify our results for FVJ and salt intake.

Several constituents of FV, alone or combined, might explain their beneficial effect on BP regulation. A higher intake of specific polyphenols, especially the subgroup of anthocyanins, of which dark-colored fruits and berries are major sources, was related to a lower hypertension

incidence in the pooled analysis of three prospective cohort studies [31]. This association can probably be explained by a nitric oxide-mediated vasodilatation on a high anthocyanin intake [31]. Urinary HA excretion has been proposed as a biomarker of total polyphenol consumption [21] and might therefore be closely related to the consumption of polyphenol-rich FV rather than FV in general in our study population. In our analysis, however, associations with systolic BP were weaker for HA compared with calculated FVJ intake and the combined potassium–oxalate biomarker, probably suggesting that polyphenols may not be the major explanatory components for the observed inverse FVJ–BP relation in our female study participants. FV also provide relatively high amounts of potassium, which might reduce BP via vasodilatation and increased renal sodium excretion [32], as well as magnesium and fiber, which have also been related to BP reductions [3]. Additionally, FV-rich diets are usually characterized by a low dietary acid load, which was associated with lower BP levels and a reduced hypertension incidence in two observational studies in adults [33, 34] and in our recent cross-sectional analysis in healthy children [35]. In a solely observational study like ours, the individual BP relevance of these different FV constituents is difficult to identify. Further limitations of the present analysis are the comparably small sample sizes in the sex-stratified analyses and the fact that only one measurement occasion, albeit with two separate readings, could be used to evaluate individual BP levels in young adulthood. The change in BP measurement method during the study period might have additionally influenced our findings, but almost all BP measurements in young adulthood were performed with the standard mercury sphygmomanometer. A simple sensitivity analysis including only those subjects who did not undergo random-zero device BP measurements during young adulthood yielded comparable results.

End-digit preferences (i.e., the fact that more BP recordings end with a zero than would be statistically expected) could also affect BP analyses based on auscultatory measurements, but this aspect might be more important in studies in which definite thresholds are used to classify individuals as hypertensive or not. Moreover, in our study, only minor evidence for a zero end-digit preference existed, with about 30 % (instead of expected 20 %) of the systolic and diastolic BP measurements in young adulthood ending with a zero.

Compared with German reference data, average BP levels were relatively low in our study population, with negative mean BP SDS in both boys and girls during adolescence. Moreover, in young adulthood, only 11 of our 206 participants (corresponding to 5.3 % of the study population) had a systolic BP $\geq$ 140 mmHg or a diastolic BP $\geq$ 90 mmHg, i.e., hypertensive BP values according to current criteria for adults [1, 2]. Because the influence of most dietary factors appears to be stronger in subjects with high BP [3], our study may underestimate the effect strengths of FV intake and salt consumption on future BP. We were also not able to specifically control for physical activity in our analyses, because a more detailed questionnaire on physical activity in DONALD has only been administered from 2004 on and thus was not available for a number of participants in adolescence. Nevertheless, considering mean pulse rate during puberty—as a measure of physical fitness—did not change our results for the investigated diet–BP associations.

Strengths of our study include its prospective design as well as the availability of repeated dietary, urinary and BP measurements during adolescence with parallel assessed anthropometric data. Estimation of dietary salt intake was based on excretion of sodium and chloride in 24-h urine samples, which is considered the "gold standard" for determining salt intake in population surveys [11]. Additionally, repeated detailed dietary records as well as two different urinary biomarkers with reasonable correlation to dietary intake data (see Table 1) were available for validation of the investigated FV–BP association. Finally, the DONALD Study design enabled us to control for several early life and socioeconomic characteristics in our analyses.

To conclude, our study provides original and observational evidence suggesting that a habitually higher salt intake during adolescence may contribute to higher systolic BP in young men, while a higher FVJ consumption during growth may be beneficially related to young adult systolic BP in females. Because young adult BP may relevantly influence later cardiovascular risk, the observed associations in this comparably small study population are worth to be confirmed and specified in further studies, particularly regarding possible mechanisms for potential sex differences.

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**Conflict of interest** The authors declare that they have no conflict of interest.

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