Genetic and environmental influences on sodium intake determined by using half-day urine samples: the Healthy Twin Study¹–³

Minjung Kho, Jung Eun Lee, Yun-Mi Song, Kayoung Lee, Kyunga Kim, Sarah Yang, Hyojeong Jung, and Joohong Sung

ABSTRACT
Background: Salt is essential in our diet, but excess intake is a well-established risk factor for hypertension. The presence and importance of genetic contributions to salt intake, however, are not well understood.

Objective: The aim of this study was to examine whether a genetic predisposition and an environmental influence exist for sodium intake and salt habit.

Design: In a twin-family cohort, half-day urine samples from 1204 individuals (133 pairs of monozygotic twins, 29 pairs of dizygotic twins, and 880 singletons) were collected to assess 24-h sodium intakes. Daily total sodium intake, sodium density per calorie (Na-D), and salt habit questions were analyzed with adjustment for other epidemiologic characteristics. We calculated heritability (h²) and intraclass correlations to examine the genetic and shared environmental contributions to total sodium intake traits.

Results: The average sodium intake was 208.4 ± 107.0 mmol/d. Men had a higher absolute sodium intake (242.6 ± 117.4 mmol/d), but Na-D did not differ by sex. Moderate genetic influences existed (h² = 0.31–0.34) for sodium intake and Na-D. We also found that sharing current residence rather than being a family member explained 22% of the variance in Na-D.


INTRODUCTION
Salt is essential to the existence of humans. Although evolutionarily humans and terrestrial animals may have adapted to a shortage of salt, the relatively recent phenomenon of excessive salt intake has become a major health risk, notably for hypertension and cardiovascular diseases (1–3). Globally, elevated blood pressure was estimated to be the most important health risk attributable to 7.5 million deaths (4). The inventory of adverse health effects from excessive salt intake is still growing: stomach cancer (5, 6), obesity (7–9), type 2 diabetes (10), kidney stones (11, 12), osteoporosis (13, 14), and asthma (15, 16), to name a few. The traditional Korean diet has been reported to contain high amounts of salt (12.4 g/d), ~2-fold higher than the WHO recommendation (17, 18). A study involving populations with high salt intakes will confer the advantage of a larger variation in exposure level.

Quantifying the amount of salt intake remains challenging, assessing sodium intakes through dietary questionnaires or records may be suboptimal (19), and estimating sodium intake from the urinary excretion of sodium is more accurate, particularly for recent salt intake (20). Generally, 24-h urine sodium excretion is regarded as the gold standard for salt intake assessment. However, low compliance with the method limits its use in epidemiologic studies, whereas collecting spot urine samples (21) may be acceptable in a large-scale population study. Sodium intake estimated from half-day urine (HU) collection samples is a fair replacement of the 24-h urine collection method and is feasible for epidemiologic studies (22–24). Salt taste reflects the preferred level of salt for a single portion and has been used as a proxy for the overall salt intake level in several studies (25). Although preference to salty food is a strong predictor of salt intake, it may not adequately indicate the total salt intake level because health-conscious people may intentionally lower their salt intake. Sodium density (Na-D; in mg/kcal)—sodium intake divided by total calorie intake—is another index of salt preference (3, 8, 26). We also measured diverse aspects of sodium intake, including salt-intake behavior assessed by questionnaires.

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Abbreviations used: Cal-Na, calorie-adjusted sodium intake; h², heritability; HU, half-day urine; ICC, intraclass correlation coefficient; Na-D, sodium density; T-Na, total sodium intake.

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Salt taste may be related to both environment and genetics, and understanding both genetic and behavioral predispositions toward salt intake would be of scientific and practical significance. Only a few studies, however, have investigated the role of a genetic predisposition to salt intake or salt preference, and previous studies have limitations as a result of their use of suboptimal measurements (27, 28). The aim of this study was to estimate the relative importance of genetics and environment on diverse aspects of sodium intake by using accurate sodium measures involving twin pairs with their families.

SUBJECTS AND METHODS

Participants

The Healthy Twin Study is a cohort of adult like-sex twin pairs aged ≥30 y and their first-degree family members who have been recruited since 2005. The participants underwent comprehensive health examinations and completed an extensive questionnaire survey. The initial recruitment process was done through mail, based on the National Twin and Family Registry, independent of their health status. Detailed protocols and general characteristics of the participants were previously described (29, 30).

The zygosity of twins was screened by a zygosity questionnaire that had a predictive power of 97.5% (31) and was further validated by 16 short tandem repeat markers (for more than two-thirds of the subjects). One of the inclusion criteria of the Healthy Twin Study was like-sex twins; thus, the number of dizygotic twins was relatively small in this study. Siblings, adjusted for age and sex, were combined with dizygotic twins as necessary. Familial relations were aggregated to calculate intraclass correlation (ICC) and heritability (h²) values. Self-reported family relationships were further examined by genome-wide single nucleotide polymorphism data by using Affymetrix GeneChip version 6.0. Any dubious family relation conflicting with the genetic information was deleted.

Participants were excluded if their urine samples did not satisfy the quality criteria (>8 h collection and the exact information on volume) or if they were currently being treated for hypertension or kidney disease. As a result, a total of 1204 participants were included in the analyses.

Measurements

HU samples were collected from all participants in the Healthy Twin Study. HU collection started at ~1900 on the day before their visit, after the subjects had completely voided and discarded their urine; the exact time was recorded. Each participant’s urine was collected in a bag until the next day’s visit for his or her health examination. In the morning, at ~0900 on site, any remaining urine was further voided and the time and the total volume were reported as final records. The amount of sodium in the urine samples was measured by ion-selective electrode potentiometry in one central laboratory, which was certified and had passed all quality-control regulations set forth by the government. We assumed that the sodium excretion level was a measure of recent dietary sodium intake throughout this study.

The 24-h sodium excretion level was estimated by using simple volume-time linear extrapolation on the HU samples. To validate this extrapolation, a pilot study was conducted to obtain the correlation coefficient between the measured and the estimated 24-h sodium excretions by applying the same linear extrapolation. In this pilot study, 44 healthy individuals (age 14–50 y, 26 males and 18 females) consuming their usual diet participated and provided half-day and 24-h urine samples, which were consecutively collected; 2 separate bags were given together with the same instruction to collect half-day and 24-h urine samples.

Because the salt intake of individuals can be determined by both salt taste and total diet amount, calorie-adjusted sodium intake (Cal-Na; adjustment of the sodium intake level for total calorie intake by using the residual model) and Na-D (mmol/kcal × 1000) were also estimated to examine behavioral aspects of sodium intake. Although these 2 measures have a similar meaning because total calories were considered, we included both to increase the compatibility with other studies using each measure. Residual sodium intake obtained by regressing sodium intake on total calorie intake was denoted as “Cal-Na,” whereas “Na-D” stood for sodium intake per total calorie intake directly divided by calories. In the Healthy Twin Study, dietary information was assessed by both a standardized food questionnaire and 3-d dietary records for all participants. In this study, the energy intake data calculated from the 3-d food records within a range of 500 to 5000 kcal/d were used as a proxy for short-term food intakes. The amount of dietary salt intake was also assessed by using the 3-d record data. Calorie and dietary salt intakes were calculated on the basis of the standardized food-composition database from the Korean Nutrition Society (CanPro 3.0) (32).

We estimated the salt habit of participants by using multiple questionnaires. They included 5 choices from “very salty” to “very bland” for the question “How salty is your daily diet?” and 3 choices from “I usually feel it salty” to “I usually feel it insipid” for the question “When you eat out, does your food taste salty?”, which was considered as the perception of salty taste when dining out. We compared those who answered “very salty” or “salty” with those who did not, and, for eating-out, those who answered “I usually feel it insipid” were compared with those who did not. To obtain data on the degree of sharing meals among participants, information about whether families and which family members were living together was collected through a questionnaire.

Statistical analyses

The comparisons of continuous variables and dichotomous variables by sex, income level, and education level were conducted by using t tests and chi-square tests, respectively. To calculate the P-trend in total calorie intake groups and age groups, a mixed linear model was used for continuous variables and a generalized linear mixed model was used for dichotomous variables; household effects were included as random effects. SAS software (version 9.3; SAS Inc) was used for these analyses.

To investigate the genetic contribution to total sodium intake (T-Na) level, Cal-Na, Na-D, and salt habit questions, we first calculated ICCs between monozygotic twins, dizygotic twins, siblings, and spouses and pooled the estimations based on genetic distance. ICC was defined as a proportion of covariance within a particular family relation over the total phenotypic variance, which was the sum of the within-group variance and residual variance. This analysis was performed by using the mixed model with SAS software after adjustment for age and sex for nontwins.
The h2 values of T-Na, Cal-Na, Na-D, and salt habit questions were estimated by using a standard quantitative genetic variance-components model implemented in the Sequential Oligogenic Linkage Analysis Routines (SOLAR) software package (http://solar.sibergenetics.org/version 4.2.7). Inverse normal transformations were performed to obtain a normal distribution of the sodium intake levels. Total phenotypic variation in sodium intake level, taking covariates into consideration, was divided into additive genetic (A), shared environments within a family living together (C), and residual errors (E). The h2 of sodium intake level was calculated as a proportion of phenotypic variance explained by additive genetic effects. Best-fitting models were selected based on the likelihood of the explanatory models.

RESULTS

Our validation study showed that the correlation coefficient between the measured and the estimated 24-h sodium excretion with the HU samples was 0.837 (n = 44; P < 0.0001; see Supplementary Figure 1 under “Supplemental data” in the online issue). However, concordance between sodium measures by dietary survey and those by urinary excretion was poor: the Pearson correlation coefficients between urinary sodium excretion and sodium intake from 3-d dietary records and that from food-frequency questionnaires were 0.13 and 0.03, respectively. The weighted kappa values of urinary sodium excretion with sodium intake from 3-d dietary records and that from food-frequency questionnaires were 0.13 and 0.06, respectively.

Of 3079 participants in the Healthy Twin Study, 1767 were excluded because they did not satisfy the quality criteria (>8-h urine collection and the exact information on volume). In addition, a total of 108 participants were excluded because they were being treated for hypertension or kidney disease at the time of the study. As a result, a total of 1204 individuals (133 pairs of monozygotic twins, 29 pairs of dizygotic twins, and 880 nontwin family members from 391 families) were included in this study (Figure 1). Of the 1204 participants, there were 828, 60, and 529 relation pairs of sibling, spouse, and parent-offspring in total, respectively.

The average T-Na value in this study was 208.4 ± 107.0 mmol/d (242.6 ± 117.4 mmol/d in men and 189.2 ± 95.5 mmol/d in women). The T-Na of men was ~1.3-fold higher than that of women (Table 1; P < 0.001). Men were more likely to have a higher total calorie intake than were women (1955.3 and 1636.2 kcal, respectively; P < 0.0001). After adjustment for total calorie intake, a significant difference between the sodium intakes of men and women remained (P < 0.001); however, the difference between men and women disappeared when Na-D (mmol/kcal × 1000) was compared. The T-Na, Cal-Na, and Na-D were all higher in those with a high total calorie intake than in those with a low calorie intake (Table 1; all P < 0.01). Na-D increased with age (P-overall trend <0.01). The younger age group was more likely to reply “very salty” or “salty” than was the older age group when asked “How salty is your daily diet?” (P-overall trend < 0.05). More men (26.9%) than women (19.7%) responded “very salty” or “salty” to the question “How salty is your daily diet?” (P < 0.01). Those with a higher education tended to have a higher Na-D and answer “I usually feel it insipid” to the question “When you eat out, does your food taste salty?” than did the lower education group (all P < 0.05). Those who answered that they had more salty taste for the salt behavior questions had significantly higher T-Na, Cal-Na, and Na-D values than did those who did not (all P < 0.05; see Supplementary Table 1 under “Supplemental data” in the online issue).

We found no statistically significant differences in T-Na, Cal-Na, and Na-D values or in the salt habit questions by income level. When we examined the T-Na, Cal-Na, and Na-D values across 5 regions in Korea, which have differences in culture and traditional diet, we found no significant differences according to region (see Supplementary Figure 2 under “Supplemental data” in the online issue).

The ICCs between family pairs are shown in Table 2. Correlations of T-Na, Cal-Na, and Na-D values were the highest among the monozygotic twin pairs (0.47, 0.49, and 0.41 in 133, 110, and 110 pairs, respectively) and the lowest among first-degree relative pairs (siblings combined with dizygotic twins: 0.09, 0.10, and 0.14 in 828, 589, and 589 pairs, respectively; parent-offspring: 0.07, 0.14, and 0.15 in 529, 410, and 410 pairs, respectively). Interestingly, the correlations between spouses (0.19, 0.26, and 0.38 in 60, 45, and 45 pairs, respectively) were lower compared with the monozygotic twins but higher compared with first-degree relatives. The correlation of the answers “very salty” or “salty” to the salt habit question “How salty is your daily diet?” was the highest between the monozygotic twin pairs (0.60 in 112 pairs), followed by spouses (0.37 in 54 pairs). The correlation of the answer “I usually feel it insipid” to “When you eat out, does your food taste salty?”, was the highest between spouses (0.56 in 46 pairs), followed by monozygotic twin pairs (0.39 in 97 pairs).

The estimated h2 of the sodium intake level is presented in Table 3. In our study, 2 models were fitted based on different combinations of components: 1) variance attributable to additive genetics (A) and others (E) (AE model) and 2) variance attributable to additive genetics (A), shared environment (C), and others (ACE model). The ACE model was the best-fitting model based on the likelihood in all the analyses. The h2 of T-Na level was 0.34 (0.22, 0.46), adjusted for age and sex. The Cal-Na and Na-D had slightly lower h2 estimates [0.32 (0.20, 0.44) and 0.31 (0.17, 0.45), respectively] than T-Na. The h2 estimates of the answers “very salty” or “salty” to the salt habit question “How salty is your daily diet?” and the answer “I usually feel it insipid” to “When you eat out, does your food taste salty?”,
TABLE 1
Baseline characteristics of participants in the Healthy Twin Study

<table>
<thead>
<tr>
<th>Age</th>
<th>24-h Sodium intake</th>
<th>Energy-adjusted sodium intake</th>
<th>Sodium density</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mmol/d</td>
<td>mmol/d</td>
<td>mmol/kcal × 1000</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Men</td>
<td>242.6 ± 117.4 [344]***</td>
<td>240.0 ± 113.5 [344]***</td>
<td>132.3 ± 73.2</td>
<td>350 (26.9)***, 312 (26.5)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>189.2 ± 95.5 [770]</td>
<td>192.1 ± 90.0 [609]</td>
<td>124.1 ± 72.2</td>
<td>624 (19.7), 561 (57.2)</td>
<td></td>
</tr>
<tr>
<td>Total energy intake</td>
<td>177.8 ± 92.0 [308]***</td>
<td>195.6 ± 91.7 [308]***</td>
<td>157.9 ± 85.0</td>
<td>305 (23.6), 269 (61.3)</td>
<td></td>
</tr>
<tr>
<td>1400-1800 kcal/d</td>
<td>203 ± 101.5 [315]</td>
<td>213.2 ± 101.3 [315]</td>
<td>127.7 ± 63.3</td>
<td>314 (22.6), 287 (57.5)</td>
<td></td>
</tr>
<tr>
<td>&gt;1800 kcal/d</td>
<td>223.6 ± 108.2 [330]</td>
<td>218.7 ± 109.6 [330]</td>
<td>97.7 ± 54.1</td>
<td>328 (19.8), 296 (57.4)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>206.2 ± 114.6 [135]</td>
<td>206.3 ± 110.6 [95]</td>
<td>124.5 ± 83.3</td>
<td>96 (34.4)<em><strong>, 87 (67.8)</strong></em></td>
<td></td>
</tr>
<tr>
<td>30-39 y</td>
<td>201.1 ± 104.0 [441]</td>
<td>202.9 ± 100.8 [369]</td>
<td>118.6 ± 66.4</td>
<td>374 (22.7), 352 (54.0)</td>
<td></td>
</tr>
<tr>
<td>40-49 y</td>
<td>206.3 ± 107.7 [283]</td>
<td>208.1 ± 102.1 [218]</td>
<td>128.7 ± 76.1</td>
<td>224 (19.2), 295 (54.9)</td>
<td></td>
</tr>
<tr>
<td>50-59 y</td>
<td>230.5 ± 112.7 [189]</td>
<td>227.8 ± 104.9 [142]</td>
<td>135.7 ± 75.9</td>
<td>145 (18.6), 127 (63.0)</td>
<td></td>
</tr>
<tr>
<td>≥60 y</td>
<td>208.1 ± 97.5 [156]</td>
<td>212.2 ± 92.0 [129]</td>
<td>141.0 ± 69.4</td>
<td>135 (21.5), 112 (71.4)</td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td>210.7 ± 110.1 [360]</td>
<td>206.1 ± 97.9 [285]</td>
<td>126.3 ± 69.6</td>
<td>690 (25.4), 612 (59.3)</td>
<td></td>
</tr>
<tr>
<td>≥350 US$</td>
<td>207.5 ± 105.7 [844]</td>
<td>217.2 ± 110.1 [668]</td>
<td>128.9 ± 79.3</td>
<td>284 (21.0), 261 (58.6)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>205.3 ± 107.6 [577]</td>
<td>213.2 ± 101.1 [466]</td>
<td>132.1 ± 73.8</td>
<td>508 (21.9), 433 (65.8)***</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>211.3 ± 106.5 [627]</td>
<td>205.4 ± 102.3 [487]</td>
<td>121.8 ± 71.1</td>
<td>466 (22.6), 440 (52.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Values were adjusted for age and sex.

1 Age: 25 years
2 n = 974
3 n = 873
4 **P < 0.01
5 ***P < 0.001

DISCUSSION

In this study, we measured various aspects of sodium intake: T-Na, Cal-Na, Na-D, and salt habit questions. Cal-Na and Na-D were the proxy measures of salt intake together with the salt habit questions. Measures of salt intake generally showed a similar

adjusted for age and sex, were 0.42 (0.18, 0.66) and 0.41 (0.23, 0.59), respectively. The effects of shared environment were significant for Na-D and answers to the salt habit questions [0.22 (0.04, 0.40), 0.40 (0.13, 0.67), and 0.42 (0.20, 0.64), respectively].

TABLE 2
Intraclss correlations of total sodium intake, calorie-adjusted sodium intake, sodium density, and salt habit questions within family pairs

<table>
<thead>
<tr>
<th></th>
<th>MZ (A + C)</th>
<th>DZ (1/2 A + C)</th>
<th>DZ + SIB (1/2 A + C)</th>
<th>PO (1/2 A + C)</th>
<th>Spouse (C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sodium intake</td>
<td>0.47 [133]</td>
<td>0.36 [29]</td>
<td>0.09 [828]</td>
<td>0.07 [529]</td>
<td>0.19 [60]</td>
</tr>
<tr>
<td>Calorie-adjusted sodium intake</td>
<td>0.49 [110]</td>
<td>0.45 [25]</td>
<td>0.10 [589]</td>
<td>0.14 [410]</td>
<td>0.26 [45]</td>
</tr>
<tr>
<td>Sodium density</td>
<td>0.41 [110]</td>
<td>0.26 [25]</td>
<td>0.14 [589]</td>
<td>0.15 [410]</td>
<td>0.38 [45]</td>
</tr>
<tr>
<td>Salt habit A</td>
<td>0.60 [112]</td>
<td>0.51 [25]</td>
<td>0.18 [488]</td>
<td>0.11 [435]</td>
<td>0.37 [54]</td>
</tr>
<tr>
<td>Salt habit B</td>
<td>0.39 [97]</td>
<td>0.34 [21]</td>
<td>0.31 [406]</td>
<td>0.31 [355]</td>
<td>0.56 [46]</td>
</tr>
</tbody>
</table>

1 Number of complete pairs in brackets. A, 100% additive genetic sharing; C, effects from shared environment contribute to ICC; DZ, dizygotic twins; ICC, intraclass correlation; MZ, monozygotic twins; PO, parent-offspring; SIB, siblings; salt habit A, answers “very salty” or “salty” to the question “How salty is your daily diet?”; salt habit B, answers “I usually feel it insipid” to the question “When you eat out, does your food taste salty?”; 1/2 A, 50% additive genetic sharing.

2 Values were adjusted for age and sex.
degree of ICC and genetic contributions; the h2 values for various measures of salt intake were very similar, ranging from 0.31 to 0.34. Salt habits were similar, but had slightly higher genetic components (h2 = 0.41–0.42) compared with sodium intake measures. The implication of this finding on sodium homeostasis is not clear in this study alone; whether elevated salt taste causes an increased sodium intake and sodium retention or upregulation in sodium metabolism requires elevation in salt taste. Our findings, however, suggest a genetic background underlying both the level of salt equilibrium and salt behavior and a possible interrelation between them.

A few studies have examined the genetic predisposition of salt intake level showing no evidence (28) or positive evidence based on questionnaires (27). One previous twin study of 24-h sodium excretion reported a slightly higher h2 of 0.43 (33); however, considering that additive genetics are hardly discriminated from nonadditive genetics in classic twin models, the slight inflation of h2 estimates can be interpreted as compatible.

We found the highest resemblance between monozygotic twin pairs, followed by dizygotic twins and spouses for Cal-Na and Na-D and the lowest correlation between siblings. The implication of the family-specific ICC measure is complex. Significant differences between the ICC of monozygotic twins and first-degree relatives support the presence of a moderate genetic influence. The presence of ICC between spouses, which was higher than the ICCs between siblings or between pooled first-degree relations, suggests that shared environment plays a role in sodium intake. In genetic models, the ACE model including both polygenic effects and shared environment outperformed the AE model with polygenic effects only. The ICC between spouses is attributed to nongenetic variance—either to shared environments or assortative mating. To our knowledge, no data about assortative mating. Furthermore, the significant difference in the resemblance of sodium intake between the dizygotic twins and siblings is noteworthy. Genetically, dizygotic twins are exactly the same as sibling, except that they shared intrauterine environments and more of relatively early-stage growth and development. It is not likely that residual age and sex effects among siblings account for the remarkable difference in the ICC estimates with dizygotic twins. On the other hand, the difference between the monozygotic twins and dizygotic twins was relatively small. This might imply possible influences from the early stage of development on salt taste. This possibility is also suggested by the “intrauterine origin of adult diseases” hypothesis, whereby upregulation of fetal stress hormone concentrations was shown to have long-term health consequences (37, 38). Alteration in salt appetite in animal models (39–41) and salt taste preference in humans (42–45) by intrauterine or prenatal environments have been reported.

The degree of sharing meals was not assessed in dietary surveys and is probably more difficult to measure than individual diet. The contributions of shared environments to Na-D and salt habit became stronger and meaningful when information about current cohabitation status was a unit of environmental sharing instead of being a family member was used, which were congruous to the higher ICCs between spouses. For Na-D, 54% of the total variance was explained by genetic and current cohabitation (Table 3), whereas 40% was explained when shared environment was based on conventional measures of household, ie, being a family member or not (see Supplementary Table 2 under “Supplemental data” in the online issue). The authors believed that these findings might suggest the importance of shared environment, including fetal-perinatal milieu and relatively recent experience of cohabitation even during adulthood.

The number of study subjects was smaller (n = 1204) than the original cohort (n = 3079), but the selection of the subjects was based on the completeness of biospecimens, which should be independent of sodium intake. We believe our findings will be compatible with those from the general population, because twins are not different in most traits (46); in this study, the average amount of salt intake was 12.2 g/d, similar to that of the general Korean population (12.4 g/d) (17). In our data, the total calorie intake was relatively lower than that of previous reports in Korea and western countries (17, 47), whereas Na-D (127.1 mmol/kcal × 1000 kcal) was higher than that of a western

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Best-fitting model</th>
<th>h2</th>
<th>c2</th>
<th>Variance due to final covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sodium intake</td>
<td>ACE</td>
<td>0.34 (0.22, 0.46)**</td>
<td>0.07 (= 0.09, 0.23)</td>
<td>0.06</td>
</tr>
<tr>
<td>Calorie-adjusted sodium</td>
<td>ACE</td>
<td>0.32 (0.20, 0.44)**</td>
<td>0.12 (= 0.06, 0.30)</td>
<td>0.05</td>
</tr>
<tr>
<td>Sodium density</td>
<td>ACE</td>
<td>0.31 (0.17, 0.45)**</td>
<td>0.22 (0.04, 0.40)*</td>
<td>0.02</td>
</tr>
<tr>
<td>Salt habit A</td>
<td>ACE</td>
<td>0.42 (0.18, 0.66)**</td>
<td>0.40 (0.13, 0.67)*</td>
<td>—</td>
</tr>
<tr>
<td>Salt habit B</td>
<td>ACE</td>
<td>0.41 (0.23, 0.59)**</td>
<td>0.42 (0.20, 0.64)*</td>
<td>—</td>
</tr>
</tbody>
</table>

1. All models were adjusted for age and sex. *P < 0.05, **P < 0.001. c2, proportion of phenotypic variance due to shared environmental effects; h2, heritability; salt habit A, answers “very salty” or “salty” to the question “How salty is your daily diet?”; salt habit B, answers “I usually feel it insipid” to the question “When you eat out, does your food taste salty?”
2. Model with additive genetic factors (A), shared environmental factors (C), and others (E).
3. Proportion of variance due to environmental effects based on sharing residence.
population (62.6–75.7 mmol/kcal × 1000). Our calorie measure was based on 3-d dietary recalls, which might have resulted in an underestimation of overall calorie intake and consequently inflation of Na-D. However, our finding for Na-D values agrees with that from a previous study in a Korean population (111.5 mmol/kcal × 1000 derived from an average sodium intake of 219.9 mmol/d and total calorie intake of 1972.0 kcal/d) (9).

We believe that using HU instead of 24-h samples did not materially change the findings, because they showed good correlation in our pilot study (r = 0.84; see Supplementary Figure 1 under “Supplemental data” in the online issue) and in a previous study (r = 0.86) (24). Based on the correlation with the 24-h collection method, findings from half-day samples should be more accurate than those from spot urine or dietary measures alone.

The authors believe that this study had several strengths. First, the inclusion of both twins and extended family members enabled us to discriminate shared environmental effects from genetic contribution with a better resolution, particularly in terms of environmental effects throughout the life course. Second, multiple measures of sodium intake were applied to provide a more comprehensive understanding of various aspects of sodium intake. Third, to our knowledge, our study was the first report of a formal h2 estimation focused on sodium intake with ICC measures across diverse family relationships. Finally, the relatively large variance and higher sodium intakes (average: 12.2 g/d) in Koreans (17, 48) along with sizeable numbers of participants allowed a statistical power to dissect genetic from environmental effects of sodium intake.

Some potential limitations of this study should be considered. The number of dizygotic twin pairs was relatively small because we recruited only like-sex twins in the Healthy Twin Study cohort. The comparison between dizygotic twins and siblings with respect to early-stage environment might have been unstable, mainly because of the limited number of dizygotic twin pairs. Because we lacked information on sharing meals, cohabitation information was used instead. Our study may not be fully generalizable to other ethnic groups because genetic background and diets affecting sodium intakes may vary.

In summary, we conclude that genetic predisposition plays an important role in both sodium intake level and salt habits. Our study warrants further genetic studies, such as a genome-wide association study, to elucidate the specific genetic sites associated with sodium intake and salt habits.

The authors’ responsibilities were as follows—MK, JS, and JEL: analyzed the data and drafted the manuscript; Y-MS, KL, SY, and HJ: collected and analyzed the data; and KK: analyzed the data. All authors read and approved the final manuscript. None of the authors had a conflict of interest.

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