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Heritability of high sugar consumption through drinks and the genetic correlation with substance use[1,2]

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ABSTRACT

Background: High sugar consumption contributes to the rising prevalence of obesity. Sugar can have rewarding effects that are similar to, but less strong than, the effects of addictive substances. People who consume large amounts of sugar also tend to use more addictive substances, but it is unclear whether this is due to shared genetic or environmental risk factors.

Objective: We examined whether there are genetic influences on the consumption of sugar-containing drinks and whether genetic factors can explain the association with substance use.

Design: The frequency of consumption of sugar-containing drinks (e.g., cola, soft drinks, and energy drinks) and addictive substances (nicotine, caffeine, alcohol, cannabis, and illicit drugs) was obtained for 8586 twins who were registered at the Netherlands Twin Register (women: 68.7%; mean ± SD age: 33.5 ± 15.3 y). Participants were categorized as high or low sugar consumers (>1 compared with ≤1 SD above daily consumption in grams) and as high or low substance users (≥2 compared with <2 substances). Through bivariate genetic modeling, genetic and environmental influences on sugar consumption, substance use, and their association were estimated.

Results: Genetic factors explained 48% of the variation in high sugar consumption, whereas unique environmental factors explained 52%. For high substance use, these values were 62% and 38%, respectively. There was a moderate phenotypic association between high sugar consumption and high substance use (r = 0.2), which was explained by genetic factors (59%) and unique environmental factors (41%).

Conclusions: The positive association between high sugar consumption and high substance use was partly due to unique environmental factors (e.g., social situations). Genetic factors were also of influence, suggesting that neuronal circuits underlying the development of addiction and obesity are related. Further research is needed to identify genes that influence sugar consumption and those that overlap with substance use. *Am J Clin Nutr* doi: 10.3945/ajcn.115.127324.

Keywords: addiction, genetics, substance use, sugar consumption, twin study

INTRODUCTION

High sugar consumption contributes to the rising prevalence of overweight and overweight-related disorders such as type 2 diabetes (1–3). A recent study that monitored the eating habits of Americans from the 1960s until 2011 showed that, while the consumption of fats dropped (from 45% to 34% of the total caloric intake), the consumption of carbohydrates, including sugars, increased (39–51%) (4). Sugar can be consumed through foods but also through beverages such as soft drinks or by adding it to coffee or tea. In Asian countries that are economically developing and, thus, transitioning to more Western eating habits, carbonated soft drinks, together with commercially baked goods, were the most important source of increased sugar consumption (5).

Sugar consumption has been linked to the use of addictive substances. In 1970, it was already observed that smokers consumed more sugar in total and in their coffee and tea than did never or former smokers (6). Moreover, individuals who were dependent on alcohol or drugs had a higher sweet preference than did nondependent individuals (7–9). These findings have led to the suggestion that neuronal circuits that are responsible for the development of addiction and obesity are related, although most of the evidence in support of this hypothesis has stemmed from animal research (10–12). Sugar consumption can promote the release of dopamine in the brain, which results in rewarding properties that are similar to but less strong than are elicited by substances such as nicotine or alcohol (13–15). An investigation as to whether sugar consumption and substance use share genetic or environmental risk factors may clarify the nature of their association.

For substance use, genetic factors play an important role with heritability estimates of 75% for nicotine dependence (16), 49% for alcohol use disorders (17), 51–59% for problematic cannabis use (18), 49% for high caffeine consumption (19), and 60–80% for illicit psychoactive drug use (20). To our knowledge, the

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[2] Supplemental Figure 1 and Supplemental Tables 1–5 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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heritability of sugar consumption has not been examined specifically. A sweet and high-carbohydrate food-liking pattern was 52% heritable (21), whereas the heritability of the liking of a sweet solution and the frequency of consumption of sweet foods were similar at 49–53% (22). The variation in liking and use frequency of sweet and fatty foods was explained by genetic factors for ~45% (23). Finally, soft drink consumption was explained by genetic factors for 26–30% (24). On the basis of these studies, one would expect genetic factors to explain a considerable part of individual differences in sugar consumption through drinks.

We examined the contribution of genetic factors to individual differences in the consumption of sugar-containing drinks and explored its association with the use of conventional addictive substances (nicotine, alcohol, cannabis, caffeine, and illicit drugs) in adult Dutch twins (n = 8586). By comparing the resemblance between monozygotic twins (who share ~100% of their genetic material) with that between dizygotic twins (who share ~50% of their segregating genes), genetic and environmental influences on both traits and their association were estimated.

METHODS

Study sample

All participants were adults who are registered at the NTR (Netherlands Twin Register)[7], which is an ongoing longitudinal study of twins and their family members (25). Data for the current study were obtained through the 10th NTR survey that was sent in 2013–2014. Permission was obtained from a medical ethical committee. The survey included questions on smoking behavior, alcohol use, cannabis use, and the use of illicit drugs such as ecstasy or cocaine. In addition, there were questions on the consumption of a comprehensive list of caffeinated and decaffeinated drinks, which allowed for measurements of caffeine and sugar through drinks. Questions were asked separately for drinks with sugar (such as regular soft drinks) and without sugar (such as diet soft drinks).

In total, data on the consumption of sugar-containing drinks and substance use were available for 8586 twins (mean ± SD age: 33.5 ± 15.3 y; women: 68.7%), including 2642 complete pairs and 3302 twins from incomplete pairs. Of this group, there were 1174 monozygotic male (MZM) twins, 724 dizygotic male (DZM) twins, 2984 monozygotic female (MZF) twins, 1596 dizygotic female (DZF) twins, and 2108 dizygotic opposite-sex (DOS) twins.

Measures

Sugar consumption

High consumption of sugar was measured with a dichotomous variable whereby 1 SD above the mean daily consumption of sugar in grams through sugar-containing drinks was chosen as a cutoff [0 = low sugar consumption (≤1 SD above the mean); 1 = high sugar consumption (>1 SD above the mean)]. This cutoff was determined for men and women separately because of sex differences in energy requirements. For each drink included in the survey, it was determined whether it was consumed daily, weekly, or never or almost never, and in the case of daily or weekly consumption, the number of servings were calculated. Daily sugar consumption through all drinks was calculated by weighting the number of consumed drinks by their sugar content. The sugar content was set at 15.4 g/glass (180 mL) of soft drink, 16.5 g/glass (180 mL) of fruit juice or other fruity (noncarbonated) drink, 28 g/can (250 mL) of energy drink, 18.8 g/bottle (250 mL) of sport drink, 30.8 g/mug (180 mL) of chocolate milk, 18.5 g/glass (180 mL) of yogurt drink, 7 g/glass (180 mL) of regular milk, 6 g/cup (125 mL) of coffee or tea with sugar, and 0 for all diet (soft) drinks or coffee and tea without sugar (26).

Substance use

High substance use was measured with a dichotomous variable that distinguished participants who used ≥2 substances from subjects who used maximally 1 substance (0 = <2 substances; 1 = ≥2 substances). For 3 substances, regular use was counted (smoking, cannabis, and illicit drugs), whereas for the remaining 2 substances, excessive use was counted given that most people used alcohol and caffeine at least regularly.

For smoking, the following 2 questions were asked: "Have you ever smoked?" (with answer categories of no, a few times just to try, and yes), and "How often do you smoke now?" (with answer categories of I do not smoke regularly, I have quit smoking, ≤1 time/wk, a few times per week, and ≥1 time/d). Subjects who answered yes to the first question and stated that they currently smoked ≥1 time/d were classified as daily smokers (0 = no or nondaily current smoking, 1 = daily current smoking). To assess cannabis use, participants were asked the following question: "Did you use cannabis in the past year?" (with answer categories of no, yes, occasionally, and yes, regularly). All participants who answered yes, regularly, were classified as regular cannabis users (0 = no or nonregular cannabis use; 1 = regular cannabis use). For illicit drug use, questions were asked about the use of ecstasy, cocaine, speed, ketamine, γ-hydroxybutter acid (GHB), hallucinogenic mushrooms, and opiates. For each type of drug, participants were asked whether they had used it in the past year, and if so, how many times. When the number of times that any of these drugs were used equaled or exceeded 12 times in the past year (monthly), a person was considered a regular user (0 = no or nonregular drug use; 1 = regular drug use). To distinguish individuals who showed signs of harmful alcohol consumption the Alcohol Use Disorders Identification Test was used. Scores that resulted from this 10-item questionnaire ranged from 0 to 40 (for each question ≤4 points can be counted) (27). Harmful alcohol consumption was detected with a cutoff ≥9 for men and ≥6 for women (28, 29) (0 = no or nonharmful alcohol use; 1 = harmful alcohol use). For caffeine intake, a dichotomous variable was created in which 1 SD above the mean daily consumption in milligrams was chosen as a cutoff to distinguish low from high caffeine consumers [0 = low caffeine use (≤1 SD above the mean); 1 = high caffeine use (>1 SD above the mean)]. The cutoff was determined for men and women separately because of sex differences in caffeine consumption (30). Mean daily consumption was calculated by summing the number of caffeinated

[7] Abbreviations used: A, additive genetic factors; C, common environmental factors; DOS, dizygotic opposite sex; DZF, dizygotic female; DZM, dizygotic male; E, unique environmental factors; EEA, equal environments assumption; MZF, monozygotic female; MZM, monozygotic male; NTR, Netherlands Twin Register.

drinks, which were weighted by the caffeine content (75 mg/cup of regular coffee, 65 mg/cup of espresso, 40 mg/cup of regular tea, 20 mg/cup of green tea, 18 mg/glass of cola, and 80 mg/can of energy drink) (31).

Statistical analyses

The classical twin model provides estimates of how much of the variation in a trait is due to additive genetic factors (A), common environmental factors (C) shared by family members, and unique environmental factors (E). These variables are identified through the different genetic relatedness of monozygotic and dizygotic twins. Monozygotic twins share ~100% of their genetic material, whereas dizygotic twins share ~50% of their segregating genes. A higher resemblance, which is often expressed in correlations, in sugar consumption for monozygotic twins than for dizygotic twins would be consistent with the hypothesis that the genome influences sugar consumption. If the correlation between dizygotic twins is greater than one-half the correlation between monozygotic twins, the common environment that the twins share (C) is of importance. The difference in sugar consumption between monozygotic twins must be due to E and also includes measurement error. The bivariate twin model estimates the influence of A, C, and E on sugar and substance use and also estimates how much of the association between sugar and substance use (cross-trait within-person correlation) is due to A, C, and E. To estimate how much of this association is due to genetic or environmental correlations, cross-trait, cross-twin correlations (sugar consumption in twin 1 with substance use in twin 2) are compared between monozygotic and dizygotic pairs. A higher cross-trait, cross-twin correlation in monozygotic twin pairs than in dizygotic twin pairs suggests that sugar consumption and substance use are associated because of correlated genetic influences. If for dizygotic twins, this correlation is greater than one-half that for monozygotic twins, there is an influence of C. When the cross-trait, cross-twin correlation in monozygotic twins is lower than the cross-trait, within-person correlation, an influence of E is implied. The patterns of correlations and the conclusions drawn from these are summarized in **Table 1**.

The influence of genetic and environmental factors was estimate with the use of structural equation modeling in OpenMx, a free and open source software package in R (version 2.3.1) (33). A liability threshold model was fitted to the data. This model assumed an underlying liability that resulted from genetic and environmental factors with a threshold that divides groups of individuals into high and low sugar consumers and high and low substance users. Thresholds depended on the prevalence of high sugar consumption and high substance use (32, 34) and were allowed to differ as a function of age (categories: <20, 20–24, 25–34, 35–44, 45–54, and ≥55 y) and sex.

Genetic and environmental influences on sugar consumption and substance use were estimated in 2 steps (**Table 2**). In step 1, a saturated model was fitted to estimate tetrachoric twin correlations, which give the resemblance between twins for the liability distribution in each zygosity by sex group (MZM, DZM, MZF, DZF, and DOS twin pairs). The effect of age on the thresholds (represented by β) was estimated separately for sugar and substance use in men and women. On this fully saturated model, we imposed several constraints (models 1–5). These constraints tested the significance of the effect of age, whether there were sex differences for sugar use and substance use, and whether the correlations within monozygotic and dizygotic twin pairs depended on the sex of the twins. In step 2, a bivariate ACE model was fitted. Constraints were imposed on each of the A, C, and E to test their significance (models 6–13). Likelihood-ratio tests assessed the fit of all submodels, which followed a chi-square distribution where the number of df were equal to the difference in the df of the 2 models. If a constraint did not significantly deteriorate the fit ($P > 0.05$), it was retained.

RESULTS

Descriptive statistics

Mean ± SD sugar consumption through sugar-containing drinks was 48.2 ± 36.4 g/d in men and 31.8 ± 28.0 g/d in women. Thus, sex-specific cutoffs to distinguish high sugar consumers (>1 SD above the mean) were 84.6 and 59.8 g/d, respectively. After the application of these cutoffs, the prevalence of high sugar consumption was 14.1% in men and 13.0% in women.

Current daily smokers were more likely to be men (11.8%) than women (10.3%; Pearson's chi-square $P < 0.05$), whereas

TABLE 1
Expected patterns of twin correlations (r) when there are additive genetic, common environmental, or unique environmental influences on a single trait (univariate) or on the association between 2 traits (bivariate)[1]

	Patterns of twin correlations	Fictional example
Univariate		
Additive genetic influence	rMZ > rDZ	rMZ = 0.8 > rDZ = 0.4; heritability is 80%[2]
Common environmental influence	rDZ > 0.5 rMZ	rMZ = 0.8 > rDZ = 0.6; heritability is 40%[2]
Unique environmental influence	rMZ < 1	1 − rMZ (= 0.8); contribution of E is 20%[2]
Bivariate		
Additive genetic influence	rCTCT-MZ > rCTCT-DZ	—
Common environmental influence	rCTCT-DZ > 0.5 rCTCT-MZ	—
Unique environmental influence	rCTCT-MZ < rCTWT	—

[1]Different patterns of twin correlations described in the table can occur at the same time, such that the variation in a trait or the association between 2 traits is due to additive genetic and/or common environmental and/or unique environmental factors. CTCT, cross-trait cross-twin correlation, CTWT, cross-trait within-twin correlation; DZ, dizygotic twin correlation; E, unique environmental factors; MZ, monozygotic twin correlation.

[2]Calculation of heritability was based on Falconer's formula (32).

TABLE 2
Structural equation models to explore A, C, and, E on sugar consumption, substance use, and their association (n = 8586)[1]

	Estimated variables	−2LL	df	Compared with	X^2	P
Step 1: saturated model						
1) Full saturated 5-group model	38	11,471.42	17,134	—	—	—
2) βs covariate dropped	34	11,606.01	17,138	1	134.59	<0.001
3) Thresholds and βs constrained across sex for sugar consumption	36	11,473.05	17,136	2	1.63	0.44
4) Thresholds and βs constrained across sex for substance use	35	11,505.09	17,137	3	32.05	<0.001
5) Correlations MZM = MZF + correlations DZM = DZF = DOS[2]	14	11,493.22	17,158	3	20.17	0.57
Step 2: ACE model						
6) Full ACE model	17	11,491.88	17,159	1	20.47	0.72
7) C for sugar consumption dropped	16	11,492.92	17,160	6	1.03	0.31
8) C for substance use dropped	15	11,492.92	17,161	7	0.0	1.0
9) C for association dropped[2]	14	11,494.75	17,162	8	1.84	0.18
10) A for sugar consumption dropped	13	11,573.88	17,163	9	79.13	<0.001
11) A for substance use dropped	13	11,556.84	17,163	9	62.09	<0.001
12) A for association dropped	13	11,502.26	17,163	9	7.51	0.01
13) E for association dropped	13	11,498.83	17,163	9	4.07	0.04

[1]In step 1, a full saturated model was fitted (model 1) after which certain constraints were applied in nested models (models 2–5). In step 2, a full ACE model was fitted (model 6) after which certain constraints were applied in nested models (models 7–13). The fit of nested models was determined with the use of likelihood ratio tests with the amount of df being equal to the difference in df of the 2 models. X^2 represents the difference in LL (−2LL) between the 2 compared models. When the P value of a nested model compared with the fuller model was <0.05, the constraint in question resulted in a significant deterioration of the fit, and it was not retained in the model. A threshold represents the prevalence of either substance or sugar use. β denotes the effect of age on the prevalence (threshold) of substance or sugar use. A, additive genetic factors; C, common environmental factors; DOS, dizygotic opposite sex twin pairs; DZF, dizygotic female twin pairs; DZM, dizygotic male twin pairs; E, unique environmental factors; MZF, monozygotic female twin pairs; MZM, monozygotic male twin pairs; LL, log likelihood.

[2]Best-fitting model.

24.2% of men were classified as harmful alcohol users compared with 18.4% of women ($P < 0.001$). There were not many regular users of cannabis (2.9% and 0.7%, respectively) or illicit drugs (1.5% and 0.6%, respectively), but here too, prevalences were higher for men ($P < 0.001$). The prevalence for high caffeine use on the basis of sex-specific cutoffs (>1 SD above the mean) was similar in men (14.4%) and women (15.7%). **Supplemental Figure 1** depicts the substances of choice for participants who used 1, 2, 3, or 4 of the above mentioned substances. When only 1 substance was used, the substance was most often alcohol for both men and women. In men and women who used 2 substances, the combination of smoking and alcohol was most common. The combination of smoking, alcohol, and caffeine was most frequently seen in subjects who used 3 substances. There were only 11 participants who used 4 substances (4 men and 7 women), and none of the participants used all 5 substances. The prevalence of high substance use (i.e., the use of ≥2 substances) was 10.9% in men and 8.0% in women ($P < 0.001$). More descriptive statistics are shown in **Supplemental Table 1**.

Saturated model fitting and twin correlations

Covariate age (reflected by β) had a significant effect on the prevalence of high sugar consumption and high substance use (reflected by thresholds) (Table 2, model 2). The modeled prevalence of high sugar consumption and high substance use across the different age groups is shown in **Supplemental Table 2**. As expected because of the sex-specific cutoffs, the prevalence of high sugar consumption could be constrained across sex (model 3). The prevalence of high substance use differed significantly between men and women (model 4). The best-fitting saturated model estimated a decrease in high sugar consumption over the age groups from 23.0% in the <20-y-olds to 9.0% in ≥55-y-olds. In men, high substance use decreased from 12.5% in the lowest age category (<20 y) to 10.6% in the highest age category (≥55 y), whereas in women, the prevalence increased from 5.2% to 10.0%. The correlations between MZM and MZF twin pairs and between DZM, DZF, and DOS twin pairs were not significantly different, thereby indicating no sex differences in twin resemblance (model 5).

Twin correlations are shown in **Table 3**. Compared with dizygotic twins, monozygotic twins were more similar in sugar consumption, which pointed to genetic influences. The same result was true for substance use. There was a significant but moderate correlation between high sugar consumption and high substance use in all twins (r = 0.2). The cross-trait, cross-twin correlation was higher for monozygotic twins (r = 0.12; 95% CI: 0.01, 0.22) than for dizygotic twins (r=0.08; 95% CI: −0.03, –0.19), which implied a genetic correlation between sugar use and substance use.

Genetic and environmental influences

Genetic and environmental influences were modeled in a bivariate ACE model. The path loadings of the best-fitting structural equation model are depicted in **Figure 1**. From these raw path loadings, the relative influence of A, C, and E on sugar consumption, substance use, and their association could be calculated (as explained in the Figure 1 legend). The variation in sugar consumption was due to both A (48%; 95% CI: 38%, 57%) and E (52%; 95% CI: 43%, 62%). For substance use, individual differences were mainly the result of A (62%; 95% CI: 52%, 71%) with the remainder being due to E (38%; 95% CI: 29%, 48%). The association between the 2 traits was explained by both A (59%; 95% CI: 18%, 99%) and E (41%; 95% CI: 1%, 82%).

TABLE 3
Twin correlations (95% CIs) from the best-fitting saturated model[1]

		Within-trait, cross-twin			
	n	Sugar consumption	Substance use	Cross-trait, within-twin	Cross-trait, cross-twin
Monozygotic	2672	0.46 (0.35, 0.56)	0.59 (0.48, 0.69)	0.21 (0.12, 0.29)	0.12 (0.01, 0.22)
Dizygotic	3272	0.30 (0.17, 0.43)	0.40 (0.26, 0.53)	0.23 (0.16, 0.30)	0.08 (−0.03, 0.19)

[1] *n* represents the total number of complete and incomplete twin pairs. Within trait, cross-twin denotes the correlation between sugar consumption in twin 1 and sugar consumption in twin 2 or substance use in twin 1 and substance use in twin 2. Cross-trait, within-twin denotes the correlation between sugar consumption and substance use within one twin. Cross-trait, cross-twin denotes the correlation between sugar consumption in twin 1 and substance use in twin 2.

The genetic correlation, which reflected to what degree genetic influences on sugar consumption predicted the genetic influences on substance use, was moderate at 0.24 (95% CI: 0.07, 0.40). The unique environmental correlation was similar at 0.20 (95% CI: 0.01, 0.40).

DISCUSSION

To our knowledge, this is the first study to investigate the heritability of sugar consumption and its genetic correlation with substance use in a large population-based sample of Dutch twins. Both traits were moderately to highly heritable and individuals who consumed large amounts of sugar were more likely to also use many addictive substances. This association was due to genetic and unique environmental factors, each of which explained ∼50% of the variation.

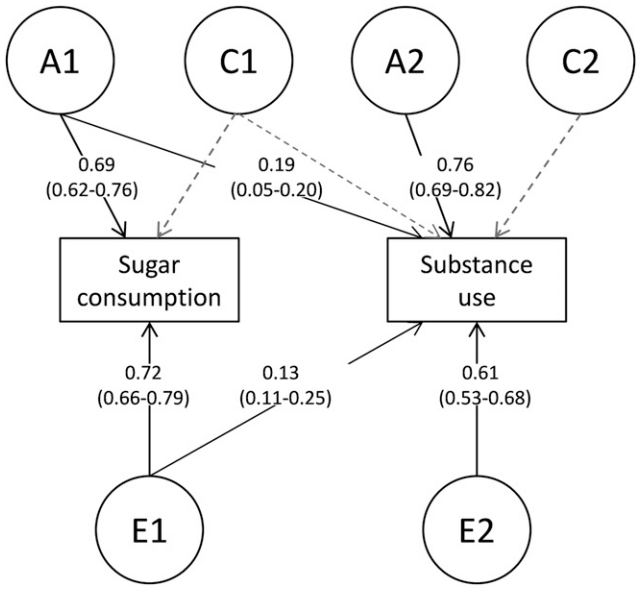

FIGURE 1 Bivariate twin model of high sugar consumption and high substance use. Raw path loadings (95% CIs) for A, C, and E are shown. Arrows extending from A1, C1, and E1 to sugar consumption and from A2, C2, and E2 to substance use represent path loadings on individual traits. Factors that are shared by both traits are represented by arrows extending from A1, C1, and E1 to substance use. Arrows with dashed lines represent path loadings that were not significant and, therefore, were dropped from the model. To arrive at the relative factor of each of the factors, path loadings that are shown in this figure were squared. As such, the total variance of sugar consumption was 1 ($0.69^2 + 0.72^2$) with the amount of variance explained by A being 0.48 (0.69^2) and by E being 0.52 (0.72^2). For substance use, the amount of variance explained by A was 0.62 ($0.76^2 + 0.19^2$) and by E was 0.38 ($0.61^2 + 0.13^2$). The cross-trait, within-twin correlation of 0.22 [derived after equating monozygotic (0.21) and dizygotic (0.23) from Table 3] was explained by A for 0.59 [(0.69 × 0.19) ÷ 0.22] and by E for 0.41 [(0.72 × 0.13) ÷ 0.22]. A, additive genetic factors; C, common environmental factors; E, unique environmental factors.

For the consumption of sugar through drinks, we showed a heritability estimate of 48%. This value is in accordance with heritability estimates for traits that are related to the liking or frequency of use of sweet foods (45–53%) (21–23). A previous study that estimated the heritability of the consumption of soft drinks showed slightly lower heritability estimates (26–30%) (24). Overall, the evidence points to a moderate genetic influence on nutritional intake, including the consumption of palatable nutrients such as sugar. The consumption of sugar triggers the brain's reward system by promoting the release of neurotransmitters such as dopamine (13). It is plausible that a (genetically determined) variation in the functioning of dopamine receptors influences the rewarding effects of sugar and, thereby, its consumption. Interestingly, the common environment shared by twins was not important for the dissimilarity or similarity in high sugar consumption. Previous twin studies also showed little or no common environmental influence (21–24). The results suggest that (early) family life and upbringing have no major effect on sugar consumption in adulthood. This proposition seems contradictory to evidence that parents' attitudes and norms toward soft drinks predict children's soft drink consumption (35, 36) and that parents create environments that promote either healthy or unhealthy nutritional intake (37). It could be that parents' attitudes and their creation of certain environments are genetically driven, and parent-offspring similarity is the result of their genetic relatedness. Alternatively, common environmental influences may decrease when transitioning from childhood to adulthood. Such a decrease was also shown for substance use (38), and it could explain why we did not find an influence of C on sugar consumption in our adult sample. Worldwide, more and more sugar is being consumed because of the increased availability and affordability of sugar-rich drinks and foods (3, 4). Although it may seem odd that such an environmentally driven trait is heritable, it is because of this increased availability that genetic influences are given the chance to be expressed. When faced with easy access to sugar-rich products, some individuals will be genetically predisposed to consume large amounts, whereas other individuals are not (39).

The moderate association between sugar consumption and substance use was largely due to genetic factors (59%; 95% CI: 18%, 99%). The wide CIs and, thus, high level of uncertainty in this estimate were likely due to the modest cross-trait, cross-twin correlations and warrant some caution in their interpretation. Despite this limitation, our results from a bivariate twin model are

in agreement with previous findings from experimental and animal studies. For example, it has been suggested that there are common genetic markers (including dopamine receptor genes) for alcohol dependence and obesity (7, 40). For substances other than alcohol, evidence on genes shared with sugar consumption or obesity has been less clear. In a recent genome-wide association study of >300,000 individuals, 97 genetic variants associated with BMI were identified (41). These variants included those located in the brain-derived neurotrophic factor gene, which is also known for its association with smoking. One of these variants (rs6265) has been linked to both smoking initiation (42) and coffee consumption (43). In addition, a genetic variant in the $\alpha 5$, $\alpha 3$, and $\beta 4$ nicotinic acetylcholine receptor gene cluster associated with the number of cigarettes smoked per day, predicted increased BMI and waist and hip circumferences in nonsmokers (44, 45). This gene may play a role in mechanisms that mediate the response to rewarding stimuli in general, including natural rewards such as food. Besides genetics, sugar consumption and substance use were associated because of unique environmental factors (41%; 95% CI: 1%, 82%). This result implies that there are environments that influence both sugar consumption and substance use. These environments may include social situations such as going out to drink and eat or spending time with friends. Previous studies have shown that, in young adults, the consumption of soft drinks and sweet pastries (46) and substance use (47) were influenced by peers in social situations.

The classical twin model rests on certain assumptions. One of these assumptions is the equal environments assumption (EEA). The EEA states that monozygotic twins experience the same similarity in environment as do dizygotic twins. If monozygotic twins would be exposed to more similar environments than dizygotic twins are, this does not necessarily result in monozygotic-dizygotic differences in phenotypic similarity. The validity of the EEA has been supported for substance use (20, 48) and other traits (49). A limitation to the classical twin model is that gene-environment interaction and gene-environment correlation are not taken into account. Under gene-environment interaction, the effect of the environment depends on the genotype or vice versa, whereas under gene-environment correlation, a person's genotype is associated with his or her exposure to particular environments. An interaction between A and E would inflate the E estimate, and a correlation between A and E is part of the variance attributable to the A estimate (50). Our A and E estimates for both substance use and sugar consumption concur well with a large body of previous literature. We analyzed sugar consumption as a dichotomous trait (high compared with low) instead of as a continuous trait (grams of sugar per day). Such dichotomization could have affected our results by a loss of statistical power. To explore if this was the case, we repeated the analyses with sugar included as a continuous measure. Results were very similar (**Supplemental Tables 3–5**), but because of the severe (right) skewness of the measure of sugar consumption, the model fit was poor.

We focused on high sugar consumption because it may reflect a person's ability or inability to resist rewarding stimuli. BMI, which is a measure of adiposity, was not taken into account. BMI may increase because of high sugar consumption through soft drinks, but it also depends heavily on food intake and physical activity and exercise. In our sample, sugar consumption through drinks was not associated with (higher) BMI and, thus, was not corrected for in our analyses.

We showed a high mean daily consumption of sugar in Dutch adult men (48.2 g) and women (31.8 g). Although these estimates included drinks only, they exceeded the total maximum intake of 25 g/d as recently recommended by the WHO (51).

In conclusion, with the current study, we show the importance of genetic factors for an individual's intake of sugar-containing drinks. Some individuals seem less able to resist the temptations of drinks that are high in sugar, possibly because the individuals are more perceptive to the taste or because they experience more rewarding effects. The association between sugar use and substance use was partly genetic in nature, and a possible explanation is that this association is due to a general lack of ability to resist rewarding stimuli. A next step would be to identify the specific genes that influence sugar consumption and the genes that overlap with other substance use. Because the common or family environment was of little importance for individual differences in sugar consumption, individual-based preventive measures to reduce sugar consumption may be more suited than are measures that are family-based.

The authors' responsibilities were as follows—JLT and JMV: were responsible for designing and conducting the research (data collection) and wrote the manuscript; DIB: supervised the data collection; DIB, LL, and GW: assisted with the writing and interpretation of the findings; LL: was responsible for the data cleaning and checks; and all authors: reviewed the content of the manuscript and approved the final version of the manuscript. None of the authors reported a conflict of interest related to the study.

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