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Heritability of Smoking, Alcohol Use, and Psychological Characteristics Among Adolescent Twins in Qingdao, China

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Abstract

Background—Previous studies of genetic and environmental influences on adolescent substance use have been limited to Western samples.

Methods—This study assesses genetic and environmental contributions to cigarette smoking, alcohol use, and psychological variables (depression, anxiety, aggression, hostility) among 602 pairs of adolescent twins, 11 to 19 years old, in Qingdao, China.

Results—Heritable influences were more pronounced for alcohol use than cigarette smoking. In univariate analyses, no heritable effects were found for depression or aggression, and modest heritability was found for anxiety. Hostility was relatively more heritable in girls than boys. Bivariate associations between substance use and psychological measures could be attributed to a combination of common genetic and environmental factors.

Conclusions—Among Chinese adolescents, experimentation with tobacco is familial, and experimentation with alcohol is heritable. The genetic and environmental architecture of hostility differs by gender. Consistency of univariate results with Western adolescent samples appears limited to the alcohol use measures.

Keywords

child health; family medicine; adolescent health; public health; smoking/tobacco/drug abuse; health informatics; health management; health education; health promotion; medical statistics

Studies of adults have shown clear genetic contributions to tobacco and alcohol use.^{1–7} In adolescents, the heritable components of substance use become increasingly expressed over the transition from childhood to adulthood.⁸ Initiation of substance use appears to be more strongly influenced by environmental factors, whereas progression to higher levels of dependence is more strongly influenced by genetic factors.^{9,10}

Although several studies have examined the genetic and environmental influences on adolescent tobacco and alcohol use in Western cultures such as the United States,^{11–13} Australia,¹⁴ Finland,^{10,15,16} and the Netherlands,¹⁷ this research has not been replicated across different cultural contexts such as Asia. The cultural context of behavioral genetics research is important because social-environmental factors can influence the expression of genetic tendencies. Genetic influences on adolescent substance use can be moderated by social-environmental factors, including parental monitoring,¹⁸ parental strictness and closeness,¹⁹ religion,²⁰ or rural versus urban environments.²¹ Estimates of relative heritability and environmental influences on behavior are specific to a given population at a given time.²²

The frequency of some genetic variants associated with substance use varies across populations. For example, Asian populations have a higher population prevalence of genetic variants that control the rate of metabolism of nicotine²³ and alcohol.²⁴ Therefore, one might expect the genetic contributions to substance use to vary across population groups.

This study examined the heritability of tobacco use, alcohol use, and related psychological factors among 602 pairs of adolescent twins in Qingdao, China. We hypothesized that genetic and environmental factors would contribute to substance use and psychological characteristics, and that the covariation between substance use and psychological characteristics would have a heritable component.

Method

Recruitment

Participants were recruited from the Qingdao Twin Registry (QTR),²⁵ a part of the Chinese National Twin Registry.²⁶ The QTR has been registering twins since 2000 through medical records, schools, and a media outreach campaign.^{25,27} Newborn twins are identified through Qingdao's immunization registry. The QTR includes approximately 74% of all twins living in Qingdao.²⁵

This study focused on adolescent twins. Parents of twins 11 to 19 years of age were contacted by mail and/or telephone and invited to participate in the study, which included surveys and a health screening. Data collection occurred on weekends at the Qingdao Center for Disease Control and Prevention (QCDC).

Survey Procedure

The research staff obtained written informed consent from the parents and verbal assent from the twins. The consent procedure was approved by institutional review boards at the University of Southern California and the QCDC. The twins completed paper-and-pencil

surveys in an auditorium. They were instructed to skip any questions they did not wish to answer and to stop completing the survey at any time if they felt uncomfortable.

Measures

Survey measures were obtained from published, validated surveys, including the Youth Risk Behavior Surveillance Survey,²⁸ the California Youth Tobacco Survey,²⁹ and the China Seven Cities Study.³⁰ Most of the measures had already been translated, backtranslated, and validated in previous studies.^{25,30–34} A team of bilingual researchers, public health experts, and graduate students (most of whom had grown up in China and immigrated to the United States as young adults) translated and verified each question. One team member translated each question from English to Chinese, another member translated the Chinese version back to English, and the whole team resolved any discrepancies. Staff members at the QCDC also evaluated each question for local idioms and reading level.

Tobacco and alcohol use—Tobacco measures included, “Have you ever tried cigarette smoking, even a few puffs?” and “During the past 30 days, on how many days did you smoke cigarettes?” Alcohol measures included, “During your life, on how many days have you had at least 1 drink of alcohol?” and “During the past 30 days, on how many days did you have at least 1 drink of alcohol?” One drink of alcohol was defined as “1 big glass of beer or 2 small glasses = 240 mL; 1 glass of red, yellow, or white wine = 120 mL (roughly 0.5 Jing), or 1 shot of liquor = 30 mL (roughly 1.5 Liang).” Because the distributions of the categorical items were skewed, they were recoded to 0 = 0 days or 1 = 1 or more days.

Depression, anxiety, and aggression and hostility—Depression was assessed with the Center for Epidemiologic Studies Depression (CES-D) Scale,³⁵ a 20-item scale that has been validated in China.^{32,36} Anxiety was assessed with the Zung Anxiety Scale,³⁷ a 20-item scale that has been validated in China.³¹ Aggression and hostility were assessed with 8-item subscales of the Buss and Perry³⁸ aggression questionnaire. In a previous study of 1388 Chinese 10th graders (unpublished data), our Chinese translations of the Buss and Perry aggression and hostility subscales each correlated ($r = 0.42$) with a 4-item version of the Buss and Durkee³⁹ hostility measure. Non-normal depression and anxiety measures were square-root transformed, and aggression and hostility measures were log transformed.

Demographic characteristics—They included zygosity, age, and gender. Zygosity was determined from blood samples by simultaneous detection of multiple short tandem repeat loci.⁴⁰ The probability of monozygosity determined by identity of all markers in the Chinese National Twin Registry is estimated to be .996.

Data Analysis

Means and frequencies were computed in SAS 9.1⁴¹ to describe demographic, substance use, and psychological characteristics. Using data from monozygotic (MZ) and dizygotic (DZ) twin pairs reared together, total phenotypic variance can be decomposed into genetic and environmental components. By comparing the degree to which MZ co-twins are similar for a given trait, relative to DZ co-twins, and using maximum likelihood statistical methods, the proportion of the total phenotypic variance can be attributed to the additive effects of

genes or heritability (A), which contribute to twin similarity, to shared environmental effects in common to co-twins (C), which also contribute to twin similarity, and to nonshared environmental effects or experiences unique to each twin that contribute to twin dissimilarity, which also includes measurement error variance (E). If C is not a significant influence, the contribution of nonadditive genetic effects (D) such as interaction of alleles of the same gene (dominance) or of different genes (epistasis) can also be modeled. The C and D variance components are confounded and cannot be modeled simultaneously.

Modeling of twin data involves identification of the best model that fits the data by comparing the goodness of fit of alternative models. Model fit was evaluated using the -2 log likelihood statistic and principles of model parsimony as indicated by the Akaike Information Criterion. The fit of the full 3-component “ACE” or “ADE” model was tested first. Next, the significance of the A and C (or D) parameters was tested by equating these parameters to zero and testing the fit of the reduced model relative to the fit of the 3-component model using the likelihood ratio χ^2 difference test. A significance test ($P < .05$) suggests that the reduced model fits the data worse than the full model, favoring the fit of the full model.

Because of the low prevalence of cigarette smoking and alcohol use in the girls in this sample, sex differences were not addressed for substance use. For the psychological variables, quantitative sex differences in genetic and environmental factors were tested. More general models where A, C (or D), and E parameters were freely estimated for boys and girls were compared with models where the parameters were equated across sex, using the likelihood ratio χ^2 difference test.

For smoking and drinking variables, univariate biometric models were fit to 2-group (MZ and DZ groups) raw data combined across sex, adjusting for sex and age. For the psychological measures, univariate models were fit to 5-group raw data (MZ same sex female [MZF] and male [MZM] pairs, DZ same sex female [DZF] and male pairs [DZM], and DZ opposite sex pairs [DZO]), and age was used as a covariate. Biometric modeling was conducted with Mx software.⁴²

Bivariate correlated factor models quantified the relative contribution of genetic and environmental influences to the covariance of substance use and psychological measures. (ie, genetic and environmental correlations). A correlation of 1 would suggest complete overlap in genetic or environmental influences, a 0 correlation would suggest independent influences for each phenotype, and a correlation between 0 and 1 would suggest partial genetic or environmental overlap. Bivariate models were fit to 2-group raw data combined across sex, adjusting for sex and age. Raw data for the psychological measures were dichotomized per median split.

Results

Table 1 shows the demographic, substance use, and psychological characteristics of the 602 twin pairs. The respondents' mean age was 12.8 years (standard deviation = 1.7 years). The

sample was 52% male. There were 170 (28.2%) MZF, 151 (25.1%) MZM, 81 (13.5%) DZF, 81 (13.5%) DZM, and 119 (19.8%) DZO pairs.

The prevalences of lifetime tobacco and alcohol use were 9.2% and 14.4%, respectively. The prevalences of past-month tobacco and alcohol use were 6.3% and 10.0%, respectively, similar to other studies of Chinese adolescents.³⁰ The prevalence of lifetime and past-month tobacco and alcohol use was higher among boys than among girls (χ^2 tests, all $P < .01$). There were no sex differences in depression and anxiety scores. Boys scored higher than girls on the aggression and hostility measures (mixed linear models, both $P < .01$).

Table 2 shows the best-fitting univariate models for each substance use and psychological measure. Individual variability in lifetime smoking was influenced by moderate genetic effects (27.9%) and relatively greater shared environmental effects (33.7%). The lower bound of the 95% confidence intervals of both estimates includes 0 because either variance component could be dropped from the model without significant deterioration of model fit. However, dropping both components together resulted in significant deterioration of model fit, suggesting that familial influences (ie, the joint effect of genetic and shared environmental factors) are important for lifetime smoking. Variability in past-month smoking was not significantly heritable and was influenced by substantial shared environmental effects (63.9%).

Variability in lifetime and past-month alcohol use was attributed to sizeable additive genetic effects (67.6% and 55.4%, respectively), with the remaining variance largely attributable to individual-specific environmental factors. The estimate for shared environmental influences for past-month alcohol use was 0; however, because either A or C (but not both) could be dropped from the model without significant deterioration of model fit, both components were freely estimated.

For depression, anxiety, and aggression, it was possible to equate genetic and environmental parameters across sex, indicating no quantitative sex differences. There was a small heritable component for anxiety (9.9%), but for all 3 measures, the majority of the variance was attributable to shared and nonshared environmental factors. Variance component estimates could not be equated across sex for hostility. Hostility was influenced by both heritable (17.6%) and shared environmental factors (14.0%) in girls, whereas in boys, there was a relatively smaller heritable contribution (0%) relative to shared environmental contribution (31.3%). For both girls and boys, either A or C, but not both components, could be dropped from the model without deterioration of model fit.

Each substance use measure was significantly related to each psychological measure (χ^2 tests, all $P < .01$; data not shown). Variance component estimates for the best-fitting bivariate genetic models appear in Tables 3 to 6. The relative contribution of genetic and environmental factors in each phenotype differs somewhat from that in univariate analysis because accounting for the covariance between 2 measures alters the relative contribution of genetic and environmental factors in residual phenotype-specific variance. This was particularly true for anxiety, which was weakly heritable in univariate analysis but strongly heritable in bivariate analyses.

Many of the bivariate analyses could not distinguish between additive genetic and shared environmental effects because either A or C components (but not both together) could be dropped without significant deterioration of model fit. Therefore, both components were freely estimated. Furthermore, in many of the models, the genetic and environmental correlations could be equated to either 0 or 1 without deterioration of model fit, and in such cases, the correlation coefficients were freely estimated. The inability to resolve the relative contribution of genetic and shared environmental influences or correlation estimates is evidenced by the large confidence intervals around point estimates, which often include 0 at their lower bound. Cases where variance components or correlation coefficients could be equated to 0 are indicated as “ns” (not significant) in Tables 3 to 6. When a correlation coefficient could be equated to 1, the numeral 1 is shown without confidence intervals.

Bivariate results of the relationship between lifetime smoking and each psychological measure are shown in Table 3. The results suggest that covariation in lifetime smoking and depression can be attributed to complete overlap in genetic influences, whereas shared environmental and nonshared environmental influences were phenotype specific. In the analysis of lifetime smoking and anxiety, the tendency of correlation effects was toward a modest overlap in genetic influences and a large overlap in shared environmental influences; nonshared environmental influences were not significantly correlated. In the analysis of the relationship between lifetime smoking and aggression, the tendencies of correlation effects were toward large genetic overlap and small shared environmental overlap; nonshared environmental effects were phenotype specific. Covariation between lifetime smoking and hostility could be attributed to modest overlap in genetic and shared environmental factors and statistically significant overlap in nonshared environmental factors ($r_e = 0.56$).

Bivariate results for past-month smoking and each psychological measure appear in Table 4. No significant heritable influences were found for past-month smoking and depression or aggression measures. Shared environmental influences for past-month smoking and depression were entirely in common and significantly overlapped between past-month smoking and aggression ($r_e = 0.61$). In contrast, past-month smoking and anxiety had entirely overlapping genetic effects and tendency for completely overlapping shared environmental effects as well. The tendency for correlation effects for past-month smoking and hostility was toward large overlap in genetic effects and smaller overlap in shared environmental factors; nonshared environmental factors were also significantly correlated ($r_e = 0.37$).

Table 5 shows bivariate results for lifetime alcohol use and psychological characteristics. Substantial overlap in genetic factors was seen for lifetime alcohol use and depression, and overlap in both genetic and shared environmental factors was seen between lifetime alcohol use and aggression or hostility. Covariation in lifetime alcohol use and aggression was also, in part, attributable to a significant correlation in nonshared environmental factors ($r_e = 0.37$). There was no evidence for a significant contribution of shared environmental effects of lifetime alcohol use and anxiety, and there was evidence for small significant overlap in genetic ($r_a = 0.30$) and non-shared environmental effects ($r_e = 0.32$).

Bivariate relationships of past-month alcohol use and psychological variables are shown in Table 6. There was complete overlap in heritable effects for past-month alcohol use and depression and a tendency for large overlap in shared environmental influences as well; nonshared environmental factors were phenotypic specific. No evidence for shared environmental contribution was seen in the analysis of past-month alcohol use and anxiety. There was substantial overlap in genetic influences ($r_a = 0.66$), but the incomplete overlap also suggests phenotype-specific heritability. The tendency of correlation effects for past-month alcohol use and aggression was for moderate genetic overlap and large shared environmental overlap; nonshared environmental influences were significantly correlated ($r_e = 0.53$). Covariation of past-month alcohol use and hostility tended to show substantial overlap in genetic and shared environmental factors and a significant nonshared environmental correlation ($r_e = 0.34$).

Discussion

To our knowledge, this is the first study to investigate the heritability of tobacco smoking, alcohol use, and related psychological measures among adolescent twins in China. Environmental factors shared between co-twins substantially contributed to variation in lifetime and past-month cigarette smoking. Further research is necessary to identify these shared environmental factors; previous studies of Chinese adolescents have implicated parents' smoking, availability of cigarettes at home, parents' rules about smoking, and family functioning as correlates of adolescent smoking.^{33,34,43}

The low prevalence of smoking in our sample indicates that most of the adolescents who smoked were in early stages of smoking experimentation rather than in the stage of regular smoking and nicotine dependence. Greater influence of shared environment compared with genetic effects has been shown for early stages of smoking behavior among adolescent twins of Western origin.^{9,10} There was some evidence for heritable influences on lifetime smoking but no evidence for heritable influences for past-month smoking. Although this appears counterintuitive, perhaps this low level of smoking is determined by family and individual-specific environmental factors such as availability of cigarettes, opportunities to smoke, parental restrictions, and peer norms. In the early stages of experimentation, smoking is sporadic and may be predominantly environmentally determined.

Alcohol use was significantly heritable, and shared environmental effects were not important contributors to alcohol use. This is consistent with some studies of adolescent twins of Western origin^{19,44} but inconsistent with others.^{11,45} This may indicate gene–environment interactions; for example, perhaps genetic influences on adolescent alcohol use are expressed more strongly under adverse family conditions, such as low parental support.^{19,44}

The relative contributions of genetic and environmental factors to smoking and alcohol measures were quite different. Cigarette smoking may be a more normative behavior (at least in boys) in this age group, which could obscure heritable influences. In China, cigarettes are given as gifts, and although their sale is restricted to adults, they are given to adolescent boys on special occasions. It is considered impolite to refuse a cigarette offer;

therefore, some boys may have smoked in response to social pressure rather than a genetic predisposition. Alcohol consumption, in contrast, could index a more deviant phenotype that is expressed because of strong(er) genetic influences. In China, alcohol use during social occasions is normative among adult men but is not socially acceptable among women and youth.⁴⁶

The expression of a genetic predisposition to experiment with substance use can be constrained by environmental barriers such as lack of access. Historically, China has not restricted adolescents' purchase of alcohol, and alcohol has been readily available to youth in stores.⁴⁷ A ban on alcohol sales to minors went into effect on January 1, 2006, several months before this survey was conducted.⁴⁸ The strictness of enforcement of the ban is not known, and some of the alcohol use reported in this survey could have occurred before the ban. Tobacco sales to minors younger than 18 have been banned in China since 1999.⁴⁹ Perhaps environmental barriers are more effective in suppressing adolescents' genetic tendencies to smoke than to drink alcohol.

Twin similarity for depression, anxiety, and aggression, and for hostility in boys is largely because of environmental factors shared by co-twins. These factors could include the home environment (family conflict, lack of emotional support, parent psychopathology or substance use, unstable employment or housing); peer influences (peers' substance use, peer social norms); or the school environment (pressure to get good grades).

In contrast to our results, most Western studies of adolescents have found significant genetic influences on depression, anxiety, aggression, and hostility,^{50–52} although other studies have found only environmental influences.^{53,54} It is not obvious why this study did not find larger genetic contributions to psychological characteristics. Genetic tendencies toward psychopathology may be expressed only under certain environmental circumstances and would be uncovered in analyses that explicitly test for gene–environment interactions. It is possible that the degree of psychological problems in this sample is not strongly heritable and that genetic variation would be observed at more severe levels of psychopathology or after adjusting for environmental covariates. For example, in bivariate analyses, heritable influences were indeed observed for depression, anxiety, and aggression. Such results suggest heterogeneity in total phenotypic variance where the relative contribution of genetic and environmental factors could differ across levels of psychopathology and associated comorbidity. For example, it is possible that only very high levels of depressive symptoms are explained by genetic factors and that in the present analyses, these genetic factors are observed in conjunction with substance use.

The bivariate relationships may appear redundant and general but represent an important first step in understanding causal factors in the covariation between substance use and psychological variables in Chinese adolescents. For example, the overlap in genetic risk between lifetime smoking and depressive symptoms or aggression suggests that Chinese adolescents who are depressed or aggressive may be at increased risk for ever smoking by virtue of shared genetic risk of these psychological constructs with ever smoking. In contrast, overlap in genetic factors for lifetime smoking and anxiety or hostility is lower and perhaps suggests that adolescents who fit these psychological constructs may be at lower

genetic risk for ever smoking but once they have initiated smoking, they may be at higher genetic risk for continuing to smoke as evidenced by high genetic correlations between past-month smoking and anxiety or hostility.

Limitations

These results are based on self-reports. The twins may have misreported their substance use, and biochemical validation was not performed. However, because this study focused on low-frequency behaviors that could have occurred months or years before the survey, biochemical validation would not have improved the accuracy of the results. The prevalence of regular (eg, daily, weekly) substance use was too low to include in the analyses; therefore, we were limited to measures of lifetime and past-month use.

When available, survey measures that had been validated in Chinese samples were used. However, validated measures did not exist for all constructs, so some measures were translated from English measures. Although the measures had been translated, backtranslated, and pilot tested with Chinese youth, perhaps they are invalid or their connotations differ across cultural contexts. Research is needed to validate age-appropriate psychological measures in China.

The sample represented a large age range (11–19 years) when significant physical and social changes occur. Expression of genetic and environmental influences on substance use and psychological characteristics may change during this developmental period. Unfortunately, this study lacked statistical power to stratify the analyses by age. Future studies could recruit large samples of twins with smaller age ranges and follow them longitudinally to examine the genetic and environmental contributions to stability and change in their substance use behavior and psycho-pathology.⁵⁵

Implications

Despite these limitations, this study provides new information about relative contributions of genes and environments to substance use and psychological characteristics among Chinese adolescents. This information could be useful for health education programs for the prevention and treatment of substance use and psychopathology. Because adolescent smoking appears to be heavily influenced by shared environmental factors such as the family environment, it may be useful to inform parents about the importance of restricting their children's access to cigarettes and establishing family rules against children smoking. It is also critically important to establish strong enforcement of the recently implemented regulations against tobacco and alcohol purchases by minors in China. Preventing or delaying excessive tobacco and alcohol use among future generations of Chinese adolescents could lead to widespread improvements in health outcomes.^{56–58}

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References

1. Carmelli D, Swan GE, Robinette D, Fabsitz RR. Heritability of substance use in the NAS-NRC Twin Registry. *Acta Genet Med Gemellol.* 1990; 39:91–98. [PubMed: 2392895]
2. Heath AC, Meyer J, Jardine R, Martin NG. The inheritance of alcohol consumption patterns in a general population twin sample: determinants of consumption frequency and quantity consumed. *J Stud Alcohol.* 1991; 52:425–433. [PubMed: 1943097]
3. Heath AC, Bucholz KK, Madden PA, et al. Genetic and environmental contributions to alcohol dependence risk in a national twin sample: consistency of findings in women and men. *Psychol Med.* 1997; 27:1381–1396. [PubMed: 9403910]
4. Lessov-Schlaggar CN, Pang Z, Swan GE, et al. Heritability of cigarette smoking and alcohol use in Chinese male twins: the Qingdao twin registry. *Int J Epidemiol.* 2006; 35:1278–1285. [PubMed: 16847025]
5. Li MD. The genetics of nicotine dependence. *Curr Psychiatry Rep.* 2006; 8:158–164. [PubMed: 16539894]
6. Madden PA, Pedersen NL, Kaprio J, Koskenvuo MJ, Martin NG. The epidemiology and genetics of smoking initiation and persistence: crosscultural comparisons of twin study results. *Twin Res.* 2004; 7:82–97. [PubMed: 15053857]
7. Maes HH, Sullivan PF, Bulik CM, et al. A twin study of genetic and environmental influences on tobacco initiation, regular tobacco use and nicotine dependence. *Psychol Med.* 2004; 34:1251–1261. [PubMed: 15697051]
8. Bergen SE, Gardner CO, Kendler KS. Age-related changes in heritability of behavioral phenotypes over adolescence and young adulthood: a meta-analysis. *Twin Res Hum Genet.* 2007; 10:423–433. [PubMed: 17564500]
9. Haberstick BC, Timberlake D, Ehringer MA, et al. Genes, time to first cigarette and nicotine dependence in a general population sample of young adults. *Addiction.* 2007; 102:655–665. [PubMed: 17309537]
10. Pagan JL, Rose RJ, Viken RJ, Pulkkinen L, Kaprio J, Dick DM. Genetic and environmental influences on stages of alcohol use across adolescence and into young adulthood. *Behav Genet.* 2006; 36:483–497. [PubMed: 16586152]
11. Han C, McGue MK, Iacono WG. Lifetime tobacco, alcohol and other substance use in adolescent Minnesota twins: univariate and multivariate behavioral genetic analyses. *Addiction.* 1999; 94:981–993. [PubMed: 10707437]
12. McGue M, Elkins IJ, Iacono WG. Genetic and environmental influences on adolescent substance use and abuse. *Am J Med Genet.* 2000; 96:671–677. [PubMed: 11054776]
13. Maes HH, Neale MC, Kendler KS, Martin NG, Heath AC, Eaves LJ. Genetic and cultural transmission of smoking initiation: an extended twin kinship model. *Behav Genet.* 2006; 36:795–808. [PubMed: 16810566]
14. Hopper JL, White VM, Macaskill GT, Hill DJ, Clifford CA. Alcohol use, smoking habits, and the Adult Eysenck Personality Questionnaire in adolescent Australian twins. *Acta Genet Med Gemellol.* 1992; 41:311–324. [PubMed: 1342137]
15. Rose RJ, Dick DM, Viken RJ, Pulkkinen L, Kaprio J. Drinking or abstaining at age 14? A genetic epidemiological study. *Alcohol Clin Exp Res.* 2001; 25:1594–1604. [PubMed: 11707634]
16. Viken RJ, Kaprio J, Koskenvuo M, Rose RJ. Longitudinal analyses of the determinants of drinking and of drinking to intoxication in adolescent twins. *Behav Genet.* 1999; 29:455–461. [PubMed: 10857250]
17. Koopmans JR, Slutske WS, van Baal GC, Boomsma DI. The influence of religion on alcohol use initiation: evidence for genotype X environment interaction. *Behav Genet.* 1999; 29:445–453. [PubMed: 10857249]
18. Dick DM, Viken R, Purcell S, Kaprio J, Pulkkinen L, Rose RJ. Parental monitoring moderates the importance of genetic and environmental influences on adolescent smoking. *J Abnorm Psychol.* 2007; 116:213–218. [PubMed: 17324032]

19. Miles DR, Silberg JL, Pickens RW, Eaves LJ. Familial influences on alcohol use in adolescent female twins: testing for genetic and environmental interactions. *J Stud Alcohol*. 2005; 66:445–451. [PubMed: 16240551]
20. Timberlake DS, Rhee SH, Haberstick BC, et al. The moderating effects of religiosity on the genetic and environmental determinants of smoking initiation. *Nicotine Tob Res*. 2006; 8:123–133. [PubMed: 16497606]
21. Legrand LN, Keyes M, McGue M, Iacono WG, Krueger RF. Rural environments reduce the genetic influence on adolescent substance use and rule-breaking behavior. *Psychol Med*. In press.
22. Turner, JR.; Cardon, LR.; Hewitt, JK. *Behavior Genetic Approaches in Behavioral Medicine*. New York, NY: Plenum; 1995.
23. Mwenifumbo JC, Myers MG, Wall TL, Lin SK, Sellers EM, Tyndale RF. Ethnic variation in CYP2A6*7, CYP2A6*8 and CYP2A6*10 as assessed with a novel haplotyping method. *Pharmacogenet Genomics*. 2005; 15:189–192. [PubMed: 15861044]
24. Thomasson HR, Edenberg HJ, Crabb DW, et al. Alcohol and aldehyde dehydrogenase genotypes and alcoholism in Chinese men. *Am J Hum Genet*. 1991; 48:677–681. [PubMed: 2014795]
25. Pang Z, Ning F, Unger J, et al. The Qingdao Twin Registry: a focus on chronic disease research. *Twin Res Hum Genet*. 2006; 9:758–762. [PubMed: 17254404]
26. Li L, Gao W, Lv J, et al. Current status of the Chinese National Twin Registry. *Twin Res Hum Genet*. 2006; 9:747–752. [PubMed: 17254402]
27. Pang Z, Bo T, Wang S, Peng X, Zhang W, Zhai Y. Analysis on recruitment of monodizymus in Qingdao. *Chin J Public Health*. 2003; 19:62–63.
28. Brener ND, Kann L, Kinchen SA, et al. Methodology of the youth risk behavior surveillance system. *MMWR Recomm Rep*. 2004; 53(RR-12):1–13. [PubMed: 15385915]
29. Gilpin, EA.; White, MM.; Berry, CC. *Methods Used for Final Report, Tobacco Control Successes in California: A Focus on Young People, Results From the California Tobacco Surveys, 1990–2002*. La Jolla, CA: University of California, San Diego; 2004. Technical Report on Analytic Methods and Approaches Used in the 2002 California Tobacco Survey Analysis. 3
30. Johnson CA, Palmer PH, Chou C, et al. Tobacco use among youth and adults in Mainland China: the China Seven Cities Study. *Public Health*. 2006; 120:1156–1169. [PubMed: 17007895]
31. Wang ZY. Chinese version of Zung's self-rating anxiety scale. *Shanghai Arch Psychiatry*. 1984; 2:73–74.
32. Cheung CK, Bagley C. Validating an American scale in Hong Kong: the Center for Epidemiological Studies Depression Scale (CES-D). *J Psychol*. 1998; 132:169–186. [PubMed: 9529665]
33. Shakib S, Zheng H, Johnson CA, et al. Family characteristics and smoking among urban and rural adolescents living in China. *Prev Med*. 2005; 40:83–91. [PubMed: 15530584]
34. Trinidad DR, Chou CP, Unger JB, Johnson CA, Li Y. Family harmony as a protective factor against adolescent tobacco and alcohol use in Wuhan, China. *Subst Use Misuse*. 2003; 38:1159–1171. [PubMed: 12901453]
35. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977; 1:385–401.
36. Yen S, Robins CJ, Lin N. A cross-cultural comparison of depressive symptom manifestation: China and the United States. *J Consult Clin Psychol*. 2000; 68:993–999. [PubMed: 11142551]
37. Zung WWK. A rating instrument for anxiety disorders. *Psychosomatics*. 1971; 12:371–379. [PubMed: 5172928]
38. Buss A, Perry M. The Aggression Questionnaire. *J Pers Soc Psychol*. 1992; 63:452–459. [PubMed: 1403624]
39. Buss AH, Durkee A. An inventory for assessing different kinds of hostility. *J Consult Psychol*. 1957; 21:343–348. [PubMed: 13463189]
40. Lv J, Zhan S, Qin Y, et al. The twin zygoty determination in epidemiological study. *Beijing Da Xue Xue Bao*. 2003; 35:212–214.
41. SAS Institute. *SAS/STAT User's Guide Version 9*. Cary, NC: SAS Institute; 2004.

42. Neale, MC.; Boker, SM.; Xie, G.; Maes, HH. Mx: Statistical Modeling. 6. Richmond, VA: Department of Psychiatry, Virginia Commonwealth University; 2002.
43. Wen X, Chen W, Muscat JE, et al. Modifiable family and school environmental factors associated with smoking status among adolescents in Guangzhou, China. *Prev Med*. 2007; 45:189–197. [PubMed: 17433427]
44. Penninkilampi-Kerola V, Kaprio J, Moilanen I, Rose RJ. Co-twin dependence modifies heritability of abstinence and alcohol use: a population-based study of Finnish twins. *Twin Res Hum Genet*. 2005; 8:232–244. [PubMed: 15989750]
45. Rhee SH, Hewitt JK, Young SE, Corley RP, Crowley TJ, Stallings MC. Genetic and environmental influences on substance initiation, use, and problem use in adolescents. *Arch Gen Psychiatry*. 2003; 60:1256–1264. [PubMed: 14662558]
46. Cochrane J, Chen H, Conigrave KM, Hao W. Alcohol use in China. *Alcohol Alcohol*. 2003; 38:537–542. [PubMed: 14633640]
47. Hao W. Alcohol policy and the public good: a Chinese view. *Addiction*. 1995; 90:1448–1450. [PubMed: 8528026]
48. People's Daily Online. [Accessed January 4, 2008] China bans alcohol sale to minors. http://english.people.com.cn/200601/11/eng20060111_234625.html. Updated January 11, 2006
49. Asia Times Online. [Accessed January 4, 2008] China ratifies int'l treaty on tobacco. <http://www.atimes.com/atimes/China/GI01Ad04.html>. Published 2005
50. Gelhorn H, Stallings M, Young S, et al. Common and specific genetic influences on aggressive and nonaggressive conduct disorder domains. *J Am Acad Child Adolesc Psychiatry*. 2006; 45:570–577. [PubMed: 16670651]
51. Glowinski AL, Madden PA, Bucholz KK, Lynskey MT, Heath AC. Genetic epidemiology of self-reported lifetime DSM-IV major depressive disorder in a population-based twin sample of female adolescents. *J Child Psychol Psychiatry*. 2003; 44:988–996. [PubMed: 14531581]
52. Silberg J, Pickles A, Rutter M, et al. The influence of genetic factors and life stress on depression among adolescent girls. *Arch Gen Psychiatry*. 1999; 56:225–232. [PubMed: 10078499]
53. Legrand LN, McGue M, Iacono WG. A twin study of state and trait anxiety in childhood and adolescence. *J Child Psychol Psychiatry*. 1999; 40:953–958. [PubMed: 10509889]
54. Thapar A, McGuffin P. Are anxiety symptoms in childhood heritable? *J Child Psychol Psychiatry*. 1995; 36:439–447. [PubMed: 7782407]
55. Nes RB, Roysamb E, Reichborn-Kjennerud T, Harris JR, Tambs K. Symptoms of anxiety and depression in young adults: genetic and environmental influences on stability and change. *Twin Res Hum Genet*. 2007; 10:450–461. [PubMed: 17564503]
56. Chen PL, Huang W, Chuang YL, et al. Exposure to and attitudes regarding secondhand smoke among secondary students in Taiwan. *Asia Pac J Public Health*. 2009; 21:259–267. [PubMed: 19443882]
57. Zheng P, Fu Y, Lu Y, Ji M, Hovell MF, Fu H. Community smoking behavior in Changqiao, Shanghai. *Asia Pac J Public Health*. 2008; 20:94–101. [PubMed: 19124303]
58. Li HZ, Sun W, Cheng F, Wang X, Liu W, Wang A. Cigarette smoking status and smoking cessation counseling of Chinese physicians in Wuhan, Hubei Province. *Asia Pac J Public Health*. 2008; 20:183–192. [PubMed: 19124312]

Table 1

Sample Characteristics Prevalence or Means

Characteristics	Girls	n	Boys	n	All	N	Range
Age	12.8 (1.7)	620	12.9 (1.8)	581	12.8 (1.7)	1201	11–19
Zygosity (percentage monozygotic)	54.8	621	51.8	583	53.3	1204	
Ever smoker	5.3 ^a	607	13.4	569	9.2	1176	
Past-month smoker	3.0 ^a	609	9.8	974	6.3	1183	
Ever alcohol user	11.1 ^a	614	17.9	577	14.4	1191	
Past-month alcohol user	6.8 ^a	614	13.3	577	10.0	1191	
Depression	10.3 (8.2)	615	11.5 (8.6)	572	10.9 (8.4)	1187	0–56
Anxiety	15.5 (6.9)	615	16.1 (7.2)	575	15.8 (7.1)	1190	0–48
Aggression	10.8 ^a (5.5)	617	13.3 (6.3)	573	12.0 (6.0)	1190	3–39
Hostility	13.4 ^a (4.8)	617	14.4 (5.8)	575	13.9 (5.3)	1192	8–39

^a Significant sex differences, $P < .01$.

Table 2Univariate Estimates (95% Confidence Interval) of Genetic and Environmental Influences^a

	A	C	E
Substance use			
Lifetime smoking ^b	27.9 (0, 78.9)	33.7 (0, 70.4)	38.4 (20.5, 62.1)
Past-month smoking	ns	63.9 (43.5, 79.0)	36.1 (21.0, 56.6)
Lifetime alcohol use	67.6 (50.6, 80.6)	ns	32.4 (19.4, 49.4)
Past-month alcohol use ^b	55.4 (0, 73.3)	0 (0, 50.3)	44.6 (26.7, 67.3)
Psychological variables			
Depression	ns	38.5 (17.5, 42.8)	61.5 (57.2, 66.0)
Anxiety ^b	9.9 (0, 38.2)	36.9 (11.7, 50.4)	53.2 (45.7, 61.7)
Aggression	ns	34.8 (27.5, 41.7)	65.2 (58.3, 72.5)
Hostility (girls) ^b	17.6 (0, 40.6)	14.0 (0, 37.1)	68.4 (56.7, 81.6)
Hostility (boys) ^b	0 (0, 34.3)	31.3 (0.9, 42.2)	68.7 (57.6, 80.6)

^a A, C, and E are additive genetic, shared environmental, and nonshared environmental influences; estimates are age adjusted.^b Either A or C but not both could be dropped from the model.

Abbreviation: ns, not significant.

Table 3

Bivariate Estimates (95% Confidence Interval) of Genetic and Environmental Influences on Lifetime Smoking and Psychological Variables^a

Pairs of Phenotypes	A	C	E
Lifetime smoking ^b	27.7 (4.7, 76.5)	31.9 (0, 59.0)	40.4 (22.5, 61.2)
Depression ^b	20.4 (3.2, 58.3)	40.2 (7.4, 58.2)	39.4 (28.3, 51.0)
Genetic–environmental correlations	1	0	0
Lifetime smoking ^b	20.7 (0, 75.3)	40.1 (0, 70.9)	39.2 (21.2, 61.7)
Anxiety ^b	52.7 (14.2, 71.8)	9.5 (0, 41.4)	37.8 (27.0, 50.9)
Genetic–environmental correlations	0.24 (0.003, 1.0) ^c	1.0 (0, 1.0) ^c	0
Lifetime smoking ^b	34.3 (0, 79.8)	29.6 (0, 65.9)	36.0 (19.5, 57.2)
Aggression ^b	13.8 (0, 52.0)	31.1 (0, 49.1)	55.2 (42.3, 68.1)
Genetic–environmental correlations	1.0 (0, 1.0) ^c	0 (0, 1.0) ^c	0
Lifetime smoking ^b	28.9 (0, 79.1)	32.6 (0, 69.7)	38.5 (20.5, 62.6)
Hostility ^b	20.0 (0, 60.0)	28.3 (0, 53.2)	51.7 (38.5, 66.2)
Genetic–environmental correlations	0.34 (0, 1.0) ^c	0.28 (0, 1.0) ^c	0.56 (0.25, 0.82)

^a Estimates are age-adjusted.

^b Either A or C, but not both, could be dropped from the model.

^c Genetic–environmental correlation could be equated to 0 or 1; correlations that could be equated to 0 or 1 are shown without confidence intervals.

Table 4

Bivariate Estimates (95% Confidence Interval) of Genetic and Environmental Influences on Past-Month Smoking and Psychological Variables^a

Pairs of Phenotypes	A	C	E
Past-month smoking	ns	58.9 (41.1, 73.2)	41.4 (25.4, 58.9)
Depression	ns	55.2 (45.0, 64.5)	44.8 (35.5, 55.0)
Genetic–environmental correlations	n/a	1	0
Past-month smoking ^b	19.0 (0.2, 68.3)	49.4 (1.4, 74.2)	31.6 (17.5, 50.3)
Anxiety ^b	48.4 (14.1, 70.8)	13.5 (0, 41.6)	38.1 (27.2, 51.1)
Genetic–environmental correlations	1	1.0 (1.0, 1.0)	0
Past-month smoking	ns	64.1 (44.0, 79.1)	35.9 (20.9, 56.0)
Aggression	ns	40.9 (29.1, 51.7)	59.1 (48.3, 70.9)
Genetic–environmental correlations	n/a	0.61 (0.34, 0.87)	0
Past-month smoking ^b	4.11 (0, 71.5)	58.6 (0, 77.5)	37.3 (20.1, 58.2)
Hostility ^b	19.0 (0, 59.5)	29.0 (0, 53.3)	52.1 (38.8, 66.5)
Genetic–environmental correlations	1.0 (1.0, 1.0) ^c	0.27 (0, 1.0) ^c	0.37 (0.04, 0.66)

^a Estimates are age-adjusted.

^b Either A or C, but not both, could be dropped from the model.

^c Genetic–environmental correlation could be equated to 0 or 1; correlations that could be equated to 0 or 1 are shown without confidence intervals.

Abbreviation: ns, not significant; n/a, not applicable.

Table 5

Bivariate Estimates (95% Confidence Interval) of Genetic and Environmental Influences on Lifetime Alcohol Use and Psychological Variables^a

Pairs of Phenotypes	A	C	E
Lifetime alcohol use ^b	68.2 (12.6, 80.9)	0 (0, 0)	31.8 (19.1, 51.0)
Depression ^b	18.6 (3.5, 59.1)	42.9 (7.7, 59.9)	38.5 (27.1, 50.5)
Genetic–environmental correlations	.72 (0.31, 1.0) ^c	0	0
Lifetime alcohol use	68.2 (51.4, 81.0)	ns	31.8 (19.0, 48.6)
Anxiety	63.3 (51.0, 73.8)	ns	36.7 (26.3, 49.0)
Genetic–environmental correlations	0.30 (0.09, 0.51)	n/a	0.32 (0, 0.64)
Lifetime alcohol use ^b	64.5 (8.9, 80.3)	3.2 (0, 49.5)	32.3 (19.3, 50.5)
Aggression ^b	7.9 (0, 52.5)	34.7 (0, 50.3)	57.4 (43.3, 69.9)
Genetic–environmental correlations	1.0 (1.0, 1.0) ^c	0.96 (0, 1.0) ^c	0.37 (0.08, 0.64)
Lifetime alcohol use ^b	67.9 (16.4, 80.7)	0 (0, 44.3)	32.2 (19.3, 48.9)
Hostility ^b	19.2 (1.13, 59.5)	29.1 (0, 48.2)	51.8 (38.7, 64.2)
Genetic–environmental correlations	0.93 (0.22, 1.0) ^c	1.0 (0, 1.0) ^c	0

^a Estimates are age-adjusted.

^b Either A or C, but not both, could be dropped from the model.

^c Genetic–environmental correlation could be equated to 0 or 1; correlations that could be equated to 0 or 1 are shown without confidence intervals.

Abbreviation: ns, not significant; n/a, not applicable.

Table 6

Bivariate Estimates (95% Confidence Interval) of Genetic and Environmental Influences on Past-Month Alcohol Use and Psychological Variables^a

Pairs of Phenotypes	A	C	E
Past-month alcohol use ^b	58.1 (18.4, 74.7)	0 (0, 8.1)	41.9 (25.4, 62.1)
Depression ^b	27.2 (6.4, 43.8)	36.2 (20.8, 55.4)	36.6 (27.2, 47.5)
Genetic–environmental correlations	1	1.0 (0, 1.0) ^c	0
Past-month alcohol use	57.2 (36.0, 74.2)	ns	42.8 (25.8, 64.1)
Anxiety	63.2 (51.0, 73.6)	ns	36.8 (26.4, 49.1)
Genetic–environmental correlations	0.66 (0.46, 0.88)	n/a	0
Past-month alcohol use ^b	52.2 (0.5, 73.7)	4.8 (0, 47.3)	43.0 (25.6, 65.0)
Aggression ^b	6.5 (0, 52.2)	35.9 (0, 51.6)	57.6 (43.2, 70.7)
Genetic–environmental correlations	0.41 (0, 1.0) ^c	1.0 (1.0, 1.0) ^c	0.53 (0.21, 0.80)
Past-month alcohol use ^b	56.1 (5.8, 73.7)	0 (0, 43.3)	43.9 (26.4, 65.8)
Hostility ^b	14.8 (0, 57.3)	32.8 (0, 50.0)	52.5 (39.2, 65.2)
Genetic–environmental correlations	0.88 (0, 1.0) ^c	0.74 (0, 1.0) ^c	0.34 (0.05, 0.60)

^a Estimates are age-adjusted.

^b Either A or C, but not both, could be dropped from the model.

^c Genetic–environmental correlation could be equated to 0 or 1.

Abbreviation: ns, not significant; n/a, not applicable.