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Rural Environments Reduce the Genetic Influence on Adolescent Substance Use and Rule-Breaking Behavior

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Abstract

Background—There is increasing evidence that certain environmental factors can modify genetic effects. This is an important area of investigation, for such work will help guide the development of new intervention programs. In this paper, we address whether rural environments moderate the genetic influence on adolescent substance use and rule-breaking behavior (i.e., externalizing psychopathology).

Method—Over 1200 Minnesotan 17-year-old twins were classified as either urban or rural. Externalizing was operationalized as the use and abuse of alcohol and drugs along with symptomatology of Conduct, Oppositional Defiant, and Antisocial Personality Disorders. Biometric factor modeling estimated whether the relative contribution of genetic and shared environmental factors varied from urban to rural settings.

Results—In urban environments, externalizing behavior was substantially influenced by genetic factors, while in rural environments, shared environmental factors explained most of the variance. This was apparent at both the factor and individual-variable level, and reached statistical significance for the male sample.

Conclusions—These findings suggest a gene-environment interaction in the development of male adolescents' problem behaviors, including substance use. There was a nonsignificant trend in the same direction for the females. The results fit within an expanding literature demonstrating both the contextual nature of the heritability statistic and how certain environments may constrain the expression of genetic tendencies.

Introduction

Adolescence is often regarded as a time of defiance, rule breaking, and drug and alcohol experimentation. But in truth there is great variability in how this period of life is experienced. Some adolescents become mired in deviant behavior and then ensared by its consequences while others sail through these years without so much as sampling a cigarette. What accounts for these considerable individual differences?

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Declaration of Interest

None.

The behaviors that seem to worry parents most, such as an unwillingness to conform to rules and expectations, a general lack of behavioral constraint, and compulsive substance use, are typically referred to as externalizing behaviors. These behaviors tend to hang together such that if an adolescent does one, they are likely to do another (Krueger, 1999; Krueger *et al.* 1998). In fact, they predict each other. For example, early trouble with the police predicts adult alcohol problems just as well as does early alcohol experimentation (McGue & Iacono, 2005). This co-occurrence is largely a consequence of them having the same genetic root. Disinhibited, antisocial behavior and substance use seem to be variable expressions of a common, general vulnerability (Hicks *et al.* 2004), and a vulnerability that is highly heritable (Kendler *et al.* 2003; Krueger *et al.* 2002; Young *et al.* 2000). Most of the genetic risk for each, individual externalizing disorder is then explained by this general, latent risk factor.

Thus, genes appear to play a significant role in determining who is most predisposed to this clustering of behaviors. Yet genes are, of course, only one part of the equation. Research consistently shows important but largely unknown shared environmental influences on the individual disorders (e.g., Han *et al.* 1999; Jacobson *et al.* 2002) as well as nonshared environmental influences on both the disorders and the general externalizing factor (e.g., Krueger *et al.* 2002; Young *et al.* 2000). Biometric analyses were, however, not necessary to know that such behaviors are sensitive to environmental conditions. The historically low rates of both substance use and rule breaking within communities such as the Amish demonstrate the essential role played by community and cultural norms.

An underexploited strength of twin studies is their ability to identify such non-genetic factors. One inventive innovative? method postulates that genetic influences on a phenotype become attenuated whenever external factors limit personal choice, for personal choice is believed to be a reflection of innate characteristics and personality (Heath *et al.* 1985). As a result, a trait that is heritable at the population level may not be heritable when measured only under conditions of limited choice. Alternatively, certain environments may elicit genetically influenced behaviors by providing a greater range of opportunities for their expression. By using twins to obtain heritability estimates across two or more sets of circumstances, researchers can thus learn about the strength, and effects, of particular social pressures.

For example, educational attainment's heritability rises as societies become more egalitarian and educational opportunities more widespread (e.g., Heath *et al.* 1985). That is, when social standing no longer restricts access, education level increasingly comes to reflect innate ability. Even more striking is the finding that while measured IQ is quite heritable at the population level, conditions of extreme poverty can negate this effect (Turkheimer *et al.* 2003). Under such strong environmental pressures, genes no longer play an important role in determining individual differences in children's IQ. This demonstrates that even highly heritable traits may be modified by external factors such as poverty and its accompanying deprivation.

These statistical interactions are generally referred to as gene-environment interactions, as the effect of the genes is dependent upon the environmental condition. It is, however, not

necessarily clear *a priori* which environments will constrain the genetic influence on a particular behavior and which will allow for its more full expression. Precocious menarche has been shown to reduce the heritability of conduct problems (Burt *et al.* 2006), low socioeconomic status to reduce the heritability of illegal activities (Tuvblad *et al.* 2006), and family dysfunction to reduce the heritability of females' smoking (Kendler *et al.* 2004). One can reason *post hoc* that these environments limit personal choice or, as another theorist has put it, that environments like this provide so much of a "social push" (Raine, 2002), encouraging problematic behavior, that the importance of genetic factors diminish in comparison. But it is not clear that all these results could have been predicted.

Kendler *et al.* (2004), in fact, predicted the opposite. Their presupposition was that heritability would *increase* in the presence of an adversity such as family dysfunction, a hypothesis backed by both the diathesis-stress model of mental disorders and by some earlier research. For instance, marriage and religiosity could be conceptualized as stress buffering and, for women, being single rather than in a marriage-like relationship magnifies the impact of inherited tendencies toward both depression (Heath *et al.* 1998) and alcohol consumption (Heath *et al.* 1989). For males, receiving a non-religious rather than religious upbringing amplifies the genetic influences on the personality trait of disinhibition (Boomsma *et al.* 1999). Likewise, the molecular-genetic interaction research has consistently supported the diathesis-stress model, whereby genetic vulnerabilities are most often expressed under stressful circumstances (e.g., Caspi *et al.* 2003, 2005; Eley *et al.* 2004; Kahn *et al.* 2003).

There is therefore, at present, no one formula that adequately captures how nature and nurture interact to produce complex behaviors. As mentioned, low socioeconomic status sometimes constrains genetic effects, as seen in the reduced heritability of adaptive traits like intelligence (e.g., Turkheimer *et al.* 2003) and also non-adaptive traits like delinquency (Tuvblad *et al.* 2005). Other times, this same stress encourages the expression of a genetic susceptibility, as seen in the increased heritability of chronic illness within the lower socioeconomic statuses (Johnson & Krueger, 2005). Clearly, much remains to be learned about the dynamic nature of the heritability statistic and how group-specific environmental pressures moderate genetic effects for particular phenotypes.

In this paper, we examine one potentially constraining environment, that of rural Minnesotan communities. We hypothesize that genetic predisposition will be less important in shaping individual differences in externalizing behavior in these sparsely populated areas; rather, family- or community-level influences (i.e., shared environmental influences) will take on more importance. Conversely, urban environments, with their wider variety of social niches, will allow for a more complete expression of genetically influenced traits. Whether someone's genes nudge them toward substance use and rule breaking, or abstinence and obedience, there will be more opportunities to express these genetic tendencies in an urban setting. Note that these same results would also be expected under the diathesis-stress model, for there is some suggestion that urban environments are more stressful and that this stress can elicit psychological disorders (e.g., Paykel *et al.* 2000). We are not pitting these two theories (constraining/eliciting versus diathesis-stress) against each other; we believe they both have explanatory power. Rather, we propose a particular hypothesis, backed by

both theories, while acknowledging that prior gene-environment interaction research in the behavioral sciences suggests caution when advancing any particular prediction.

We also have reason to believe that rural settings can modify the genetic effects on externalizing psychopathology because Rose *et al.* (2001) have demonstrated that the etiological influences on one externalizing behavior, drinking frequency, varies by regional residency. For both males and females, living in rural rather than urban Finland reduced the genetic influence on adolescent drinking frequency. Because alcohol misuse is a central component of the externalizing spectrum, it seems likely that urban-rural environments will interact with genetic risk for the entire latent factor. Here, we include a broad array of markers of disinhibition to ask whether a gene-environment interaction previously observed at the individual-variable level extends to the entire spectrum of related disorders. That is, are individual differences in adolescents' externalizing behaviors, behaviors which are immensely costly to both families and communities, influenced by where their parents have chosen to raise them?

Method

Participants

The 608 same-sex twin pairs (male: 184 monozygotic (MZ), 97 dizygotic (DZ); female: 213 MZ, 114 DZ) were born in the state of Minnesota between 1972 and 1979 and, at the time of their assessment (average age 17.47; range 16.55 – 18.52; SD = 0.46), continued to reside there. Seventeen is an age at which adolescents have begun to express the phenotypes of interest but still remain in the family environment. See Iacono *et al.* 1999, for additional information about the Minnesota Twin Family Study's design and sample.

Measures

Urban-Rural Classification—We used the U.S. census Rural-Urban Commuting Area (RUCA) system to classify the adolescents as urban or rural. Census 2000 data was used, as over 94% of the sample was assessed subsequent to the gathering of the Census 1990 data. Classification was based on their school zip code; these data were available and considered appropriate given the salience of the school environment to adolescent development. The RUCA system uses measures of urbanization, population density, and daily commuting patterns. There are 4 general population classifications: urban (> 49,999), large town (10,000 to 49,999), small town (2,500 to 9,999), and isolated rural (< 2,500). For our analyses, “rural” individuals go to school in towns of less than 10,000 and towns in which the primary commuting pattern is within that town or to a town of equally small size. Or they go to school in an area that is classified as isolated rural and there is no primary flow to a larger area. The remainder was classified as “urban.”

Zip-code areas receive a higher classification than would be expected by population alone whenever the primary commuting pattern is >30% to a town or city of greater size (e.g., a small town is classified as “urban” when there is sufficient commuting to a nearby large town). Approximately 9% of our sample received a higher classification in this manner. Zip-code areas with only 5–30% of the primarily commuting going to a nearby area are similarly

re-classified; however, in our sample, < 0.5% were classified based on such low levels of commuting. This classification system created a 60.5% urban, 39.5% rural division and assured that our rural group was very rural. Its fairly substantial size reflects Minnesota's largely agricultural landscape.

Externalizing Behaviors—We used the Diagnostic Interview for Children and Adolescents – Revised (DICA-R; Reich & Welner, 1988) to separately interview the twins and their mothers regarding the twins' Conduct Disorder (CD) and Oppositional Defiant Disorder (ODD) symptomatology. The DICA-R addresses lifetime disorders under DSM-III-R, the current diagnostic system when these data were collected. Nine criterion-A ODD symptoms and 12 criterion-A CD symptoms were assessed (the forced sexual activity symptom was omitted). We did not enforce the DSM-III-R stipulation that ODD symptoms not be assigned in the presence of a CD diagnosis. Adult Antisocial Behavior (AAB) was similarly assessed, except mothers did not report. AAB is the post-age-15 portion of the Antisocial Personality Disorder criteria; we relaxed the DSM requirement that only adults be assessed for personality disorders.

A team of doctoral students reviewed each file, considered both the twin's and mother's report, and assigned symptoms for each diagnosis. When the described behavior fell short of our severity or frequency criteria, but was nonetheless judged significant, that symptom was assigned at the subthreshold level. In the symptom-count scales used in the analyses, these were weighted half (0.5) of those judged fully present.

The adolescents reported on their alcohol (ALC) and drug (DRUG) use via the Substance Abuse Module (Robins *et al.* 1987) of the Composite International Diagnostic Interview (Robins, *et al.* 1988). For ALC, we used DSM-III-R Alcohol Dependence symptoms plus 9 items assessing non-criterion behaviors, ranging from simply using alcohol to consuming 20+ drinks on a single occasion, because employing only psychiatric criteria with this community-based, adolescent sample produced a restricted range and highly skewed distribution. Previous research supports the validity of this alcohol-problems continuum (Krueger *et al.* 2004). DRUG was simply a tally of the classes of substances tried from: tobacco, alcohol, marijuana, amphetamines, tranquilizers, Quaaludes/barbiturates, cocaine, heroin/opiates, PCP/psychedelics, and inhalants.

Statistical Analyses

We examined externalizing behaviors separately and as a factor construct. Support for our contention that they may appropriately be conceptualized as a single, broad risk factor comes from several sources. First, they are commonly comorbid, and this appears to be due to genetic overlap among them (Krueger *et al.* 2002; Young *et al.* 2000). Second, their familial transmission appears to be general, meaning that what is passed from parent to child is a vulnerability to a spectrum of disorders rather than a disorder-specific risk (Hicks *et al.* 2004). Finally, they predict each other (McGue & Iacono, 2005).

Data were analyzed using SPSS (11.0.1, Chicago, IL), SAS (Littell *et al.* 1996), and Mx (Neale *et al.* 2002). SAS was used for the hierarchical linear models, which took the clustered nature of the twin sample into account. Mx, a structural-equation modeling

program, was used for the biometric analyses. Mx uses maximum-likelihood techniques that maximize fit between the model and the data, thus providing parameter estimates that offer the smallest discrepancies from the data. We modeled the means using raw data. Initially, we fit a five-variable Cholesky model (Neale & Cardon, 1992), which allowed us to estimate simultaneously the genetic and environmental contributions to each variable. Next, we fit a single factor (or common-pathway) model in which each variable's variance was partitioned into that which is common to them all (i.e., attributable to the factor) and that which is specific to each.

In the base factor model, all parameters were free to vary both by gender and across the urban/rural division. The fit of this model was then compared to a number of more restrictive models that constrained parameters to be equal across the gender and urban/rural groups. Model fit was evaluated by taking the difference in minus twice the log-likelihood values ($-2\ln L$), which is distributed as a chi-square random variable under the null hypothesis of the more restrictive model. Akaike's Information Criterion (AIC; Akaike, 1987) was also used to compare the fit of alternative models. AIC is a fit index conventionally used in behavioral-genetic analyses. It is the model's chi-square minus twice its degrees of freedom; it thus considers both parsimony and goodness of fit. Since a general aim of model fitting is to explain the data as parsimoniously as possible, the model with the smallest AIC is generally considered best.

Results

As would be expected with a population-based sample, the symptom counts and substance-use measures were all positively skewed. Thus, to better approximate normality, they were log transformed for all analyses. Hierarchical linear modeling determined the effects of gender and residency on externalizing while simultaneously controlling for the non-independence of the twins. In both urban and rural environments, males demonstrated significantly more symptoms of CD [$F(1,366) = 86.61, p < .0001$ urban; $F(1,238) = 59.37, p < .0001$ rural], AAB [$F(1,365) = 23.27, p < .0001$ urban; $F(1,238) = 21.85, p < .0001$ rural], and ALC [$F(1,366) = 3.96, p < .05$ urban; $F(1,238) = 4.35, p < .05$ rural]. Within gender, there was a trend toward more externalizing behavior in urban areas. However, the only variable to reach statistical significance was the males' ODD, with more symptomatology exhibited in urban than in rural settings ($p < .05$). There were no gender-by-residency interactions; all F values were less than 0.65 and all p values greater than .40.

Table 1 presents the intraclass twin correlations. The larger differences in correlation size between MZ and DZ twins in urban environments, as opposed to rural environments, implies that the factors influencing externalizing behavior vary by environment, with genetic influences taking on more importance in urban settings. This impression was then confirmed through formal biometric modeling. We fit a general multivariate model in which no constraints were placed on the genetic and environmental parameter estimates (i.e., a Cholesky; [$\chi^2(260) = 306.99, p < .05$, AIC = -213.01 when compared to the fully saturated]). Constraining the model parameters to be equal across gender resulted in a significant increase in chi-square [$\chi^2(90) = 184.45, p < .001$, AIC = 4.45]. Constraining the model parameters to be equal across urban-rural produced an equivocal set of findings, as

the chi-square was significant [$\chi^2(90) = 124.98, p < .01$], but the AIC was negative [AIC = -55.02]. Given the existence of significant gender differences we consequently sought to clarify the nature of any urbanicity effect by testing for it separately in the male and female samples. In males, we found consistent evidence of an urbanicity effect [$\chi^2(XXX) = XXX.X, p < .05, AIC = -XXX$], but in females the urbanicity effect was non-significant [$\chi^2(XXX) = XXX.X, p < .05, AIC = -XXX$]. Consequently, estimates for the proportion of variance in the 5 variables attributable to additive genetic (a^2), shared or common environmental (c^2), and nonshared or unique (e^2) environmental influences are presented separately for males and females in Table 2. With ODD as the only exception, genetic influences are relatively more important, and shared environmental influences relatively less important, in urban than in rural settings.

The 5 variables were then used as indicators of a latent, externalizing factor. Relative to the fully saturated model, the factor model fit reasonably well [$\chi^2(352) = 585.38, p < .001, AIC = -118.62$]. Non-standardized, or raw, parameter estimates were compared. The model-fitting results are presented in Table 3 for the entire sample and then separately by gender. Initially, all parameter estimates were allowed to vary by urban-rural residency (as well as by gender; the base factor model, or Model 1). Constraining both the factor loadings and the residual variance estimates to be equal across urban/rural environments produced an improvement in fit as measured by a negative AIC of -19.39 (Model 2). This suggests that the same externalizing construct is being measured in the two environments. Of models 2a through 2d, the best-fitting model as measured by AIC was 2c in which the nonshared (E) factor variance was constrained equal across urban and rural environments but the genetic (A) and shared environmental (C) factor variance estimates were allowed to vary by environmental circumstance. This suggests a gene-environment interaction by regional residency, as A and C factors are differentially contributing to the latent externalizing factor in the two environments. This is an overall regional effect for the full sample.

The male sample alone also demonstrates a gene-environment interaction. This is seen in Model M2c having the lowest AIC value. Also, while the factor loadings and residual variance estimates could be constrained equal across urban-rural environments without sacrificing fit, the estimates for the A, C, and E variance that is common to the factor could not then also be constrained equal across environments without producing a significant decrement in fit [$\chi^2(3) = 11.84, p < .01, AIC = 5.84$].

Figure 1 presents the best-fitting male model in which the factor's genetic and shared environmental variance estimates were allowed to differ by environment. Please note that the raw parameter estimates for the factor loadings, residual variances, and nonshared environmental factor variance (E) were all constrained equal across environments, although the standardized estimates for the E factor variance give the impression that it varies slightly by residency. Standardized estimates for the A, C, and E factor variances are all presented in boxes above the nonstandardized estimates. For males, there was a clear and significant moderating influence of the environment. In urban environments, genetic factors accounted for 64% of the factor's variance and shared environmental influences for 25% of the factor's variance. In rural environments, genetic influences dropped to 0% and shared environmental influences increased to 86%.

For the female sample alone, the gene-environment interaction model was not the best fitting model. The lowest AIC value accompanies a model in which the factor variance estimates were held constant across urban-rural, and a comparison of models F2 and F2d show that these additional constraints do not cause a significant reduction in fit [$\chi^2(3) = 3.49$, *ns*, $AIC = -2.51$]. Nevertheless, there was a trend in the direction of an interaction. When the variance contributions to the externalizing factor were allowed to vary across environments, in urban settings genetic factors accounted for 35% of the factor's variance (95% CI: .08–.73) and shared environmental influences for 50% of the factor's variance (95% CI: .11–.75). In rural settings the same estimates were 5% (95% CI: .00–.44) and 76% (95% CI: .37–.87), respectively. Note that the 95% confidence interval for the genetic contribution contains zero, suggesting that different etiological factors are contributing to females' externalizing behaviors in the two environments.

Discussion

We had hypothesized a gene-environment interaction in the development of adolescent externalizing psychopathology. Specifically, we thought externalizing behavior would be more heritable in urban environments where greater personal choice allows for a more complete expression of genetically influenced individual differences. The male sample supported our hypothesis. For our female sample, there was a nonsignificant trend in the same direction. Although the biometric factor modeling did not confirm a statistically significant interaction, both the females' factor variance estimates and the estimates from the modeling of the individual variables were consistent in suggesting that females' externalizing is more heritable in urban settings.

These findings fit with an emergent literature suggesting that certain environments may restrict the expression of particular genetic tendencies. Even in the face of high heritability estimates, many psychologists had been unwilling to relinquish their belief that the environment plays a tremendously important role in development. Now, as evidence such as ours for gene-environment interactions accumulates, it seems possible that these “nurture” proponents will be vindicated.

Our results highlight the contextual nature of the heritability statistic: heritability is not a fixed quality of a trait, but is instead quite sensitive to environmental conditions. For males in urban environments, heritable factors are primarily responsible for individual differences in substance use and rule-breaking behavior, explaining 64% of the variance. But for males in rural environments, it is shared environmental factors that are most influential, explaining 86% of the variance. Thus, the generally substantial heritability of externalizing behavior (e.g., Iacono *et al.* 1999; Kendler *et al.* 2003; Krueger *et al.* 2002; Rhee & Waldman, 2002) was not evident for male adolescents raised in towns of less than 10,000 that were isolated from areas of greater population density.

While rural environments constrained the genetic effects on externalizing, they did not constrain the overall behavioral expression. The level of externalizing behavior appeared greater in urban settings, but this difference only reached statistical significance for one disorder, ODD, and only in males. This should not be surprising, for contemporary studies

generally suggest that adolescent substance use is equally, if not more, prevalent in rural than in urban settings (e.g., CASA, 2000; Cronk & Sarvela, 1997; Levine & Coupey, 2003). Moreover, while juvenile delinquency has historically been associated with urban areas (e.g., Shaw & McKay, 1969), we could find no modern, American replication. Rather, an urban-rural difference in conduct disorder/delinquency was either not detected (Offord *et al.* 1987), or showed up only for females, only under parents' (not teachers') report (Zahner *et al.* 1993), and thus was not a robust effect.

It is not unprecedented to have found a gene-environment interaction in the absence of an environmental main effect. Rose and colleagues (2001) found that regional residency moderated adolescent alcohol use, but they did not find an urban-rural difference in the abstinence rates, or a mean regional difference in drinking frequency among the non-abstinent. Others, similarly, have found interactions without environmental main effects (Eley *et al.* 2004; Kahn *et al.* 2003; Koopmans *et al.* 1999; O'Connor *et al.* 2003; Ozkaragoz & Noble, 2000; Silberg *et al.* 2001; Wahlberg *et al.* 1997). Not only do these studies demonstrate the prevalence of this phenomenon, but they serve as valuable reminders that without knowledge of the interaction, key environmental variables could go unrecognized.

There is also precedence for an interactive effect reaching statistical significance for one gender but not the other (e.g., Boomsma *et al.* 1999; Grabe *et al.* 2005; Tuvblad *et al.* 2005). Several papers examining environments' constraining influences on genetic effects have shown this. Moreover, to the extent that environmental or social pressures vary by gender, this might actually be anticipated. To illustrate, secular changes, which weakened the social taboo surrounding women's smoking, led to a significant increase in the heritability of tobacco use for women in recent years (Kendler *et al.* 2000). This effect was not seen for men over the same time period, presumably because the social disapproval surrounding men's smoking was always less pronounced. Similarly, while a religious upbringing suppressed the heritability of alcohol-use initiation for both males and females, the disparity in heritability across the two environments only reached statistical significance for the female sample (Koopmans *et al.* 1999). Other environmental changes seemed to reduce the constraining influences only for males. For instance, societal changes in Norway resulted in males' but not females' educational attainment becoming more heritable in recent years (Heath *et al.* 1985). Therefore, not only is there a power issue when attempting to replicate an interaction across gender, but any time social pressures might limit one gender more than the other, non-replication could be expected. In our sample, rural environments appear slightly less genetically constraining for females than for males, especially when it comes to the non-substance-related behaviors (see Table 2). Simultaneously, urban environments are somewhat less eliciting of genetic tendencies for females than males, creating a smaller heritability differential and thus a lack of a significant interaction in the female sample.

The present study has a number of strengths, including our use of diagnostic criteria and our application of a factor model. A growing body of research suggests that there is value in thinking beyond single behavioral variables, in conceptualizing certain types of behaviors and disorders as interrelated (e.g., Krueger, 1999). Another advantage to our work is that our externalizing measures, while not based on direct observations, were obtained from in-person interviews by trained staff of both the parent and the child. These interviews were

later reviewed by a separate team of doctoral students in clinical psychology who assigned the behavioral symptoms. Yet while our sample was representative of Minnesota at the time it was ascertained, an evident limitation is its lack of racial and ethnic diversity. This restricts the generalizability of our results, as does the relatively few number of subjects living in abject poverty (Iacono *et al.* 1999). Whether the findings hold for other racial and ethnic groups, and whether they hold for urban areas characterized by concentrations of extreme poverty, is left for future researchers to determine. We also acknowledge that the studied behaviors may not be completely comparable across males and females, for externalizing behavior is more rarely expressed in females (e.g., Romano *et al.* 2001), and the lower rates of behavioral expression could have contributed to our lack of a significant interactive effect. A further limitation is that any interaction, unless disordinal, will depend on measurement scale. It is thus possible that there are nonlinear transformations of our variables that would eliminate the evidence in support of the existence of an interaction (Eaves, 2006). Nevertheless, the robustness of our findings across multiple measures (see Table 1 and Table 2) gives us confidence in the reliability of our results. One final critique would be to ask whether families that choose to live in rural environments differ, genetically, from those that choose to reside in urban areas. While it is true that if such a gene-environment correlation existed it would affect the interpretation of our results, the lack of an environmental main effect in our sample argues against its existence.

Our results provide evidence for a specific, identifiable environmental effect on externalizing behavior. Rural environments appeared to dampen the expression of genetic differences for externalizing, replacing them with familial differences. These findings underscore the importance of refraining from assuming that population-level results will extend to all subpopulations. It must not be forgotten that traits that are highly heritable in one situation may be much less so when measured in another population or setting. Perhaps community norms are stronger in small towns. Or perhaps, for rural parents who choose to do so, it is easier to monitor and thus control their adolescents' activities. These are important areas of investigation that, unfortunately, cannot be directly tested with the current dataset. In the future, it will be of interest for researchers to investigate exactly what the operative environments might be. What is it about very rural, Midwest America that allows families and communities more influence over their children? In the meantime, when looking for ways to increase influence over adolescents' substance use or rule-breaking behavior, any variable that varies by urban-rural residency would be a good place to start.

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Figure 1. Biometric Factor Model of Males' Externalizing Psychopathology

Note: CD = Conduct Disorder, ODD = Oppositional Defiant Disorder, AAB = Adult Antisocial Behavior, ALC = alcohol use, and DRUG = substance use. The figure presents the urban (U) and rural (R) estimates, with 95% confidence intervals, for the standardized genetic (A), shared environmental (C), and nonshared environmental (E) contributions to the factor's variance. For males, the A, C, and E influences on the factor's variance differ significantly by region, indicating a gene-environment interaction. Also standardized for presentation are the factor loadings and residual variance estimates (i.e., the residual A, C, and E variances plus the square of that variable's factor loading will sum to 1.0). Residual variance is any variance that is not explained by the factor but remains specific, or residual, to one of the 5 variables.

Table 1

Intraclass Correlations for the 5 Externalizing Variables

Variable	Urban		Rural	
	r_{MZ}	r_{DZ}	r_{MZ}	r_{DZ}
Males				
CD	.55	.44	.44	.45
ODD	.64	.45	.45	.36
AAB	.56	.19	.37	.26
ALC	.70	.45	.63	.69
DRUG	.76	.48	.66	.53
Females				
CD	.62	.29	.57	.37
ODD	.57	.40	.73	.45
AAB	.51	.13	.24	.35
ALC	.65	.54	.63	.71
DRUG	.74	.47	.67	.73

Note: CD = Conduct Disorder symptom count, ODD = Oppositional Defiant Disorder symptom count, AAB = Adult Antisocial Behavior symptom count, ALC = alcohol use, and DRUG = substance use. Sample sizes for the males are: urban MZs ($N=230-232$), urban DZs ($N=130$), rural MZs ($N=136$), rural DZs ($N=64$). Sample sizes for the females are: urban MZs ($N=228-232$), urban DZs ($N=140-142$), rural MZs ($N=194$), rural DZs ($N=86$).

Table 2

Parameter Estimates and 95% Confidence Intervals for Additive Genetic (a^2), Shared Environmental (c^2), and Nonshared Environmental (e^2) Components of Variance

Variable	Urban			Rural		
	a^2	c^2	e^2	a^2	c^2	e^2
Males						
CD	.24 (.03 – .52)	.34 (.08 – .54)	.42 (.32 – .54)	.05 (.00 – .50)	.42 (.03 – .59)	.53 (.38 – .71)
ODD	.39 (.10 – .64)	.28 (.05 – .52)	.34 (.25 – .45)	.29 (.03 – .58)	.23 (.01 – .48)	.48 (.34 – .67)
AAB	.51 (.24 – .65)	.05 (.00 – .29)	.44 (.33 – .57)	.02 (.00 – .24)	.35 (.17 – .50)	.63 (.46 – .78)
ALC	.49 (.25 – .71)	.22 (.03 – .45)	.29 (.22 – .38)	.03 (.00 – .21)	.65 (.46 – .76)	.32 (.23 – .44)
DRUG	.57 (.31 – .79)	.21 (.01 – .46)	.22 (.16 – .29)	.04 (.00 – .35)	.62 (.31 – .74)	.34 (.24 – .47)
Females						
CD	.51 (.20 – .68)	.10 (.00 – .38)	.39 (.30 – .51)	.37 (.07 – .63)	.22 (.01 – .50)	.40 (.30 – .54)
ODD	.31 (.04 – .63)	.26 (.00 – .52)	.43 (.33 – .55)	.47 (.16 – .71)	.26 (.04 – .55)	.27 (.19 – .37)
AAB	.34 (.11 – .53)	.13 (.01 – .33)	.52 (.40 – .67)	.15 (.00 – .42)	.20 (.02 – .40)	.65 (.50 – .82)
ALC	.19 (.02 – .47)	.48 (.20 – .65)	.34 (.26 – .43)	.03 (.00 – .30)	.64 (.39 – .74)	.33 (.24 – .43)
DRUG	.32 (.07 – .60)	.40 (.13 – .63)	.28 (.21 – .37)	.02 (.00 – .30)	.69 (.42 – .77)	.29 (.21 – .39)

Note: CD = Conduct Disorder symptom count, ODD = Oppositional Defiant Disorder symptom count, AAB = Adult Antisocial Behavior symptom count, ALC = alcohol use, and DRUG = substance use.

Biometric Factor Model-Fitting Results for Urban versus Rural Residency (presented for the overall sample and then separately by sex)

Table 3

Model	Males and Females Combined				
	-2lnL	df	χ^2 (df)	p value	AIC
1. Base factor model: all parameters free to vary	-384.2	5899	---	---	---
2. Factor loadings & residual variances constrained U=R	-327.6	5937	56.6 (38)	$p<.05$	-19.4
2a. and A factor variance constrained U=R	-315.2	5939	68.9 (40)	$p<.005$	-11.1
2b. and C factor variance constrained U=R	-322.7	5939	61.4 (40)	$p<.05$	-18.6
2c. and E factor variance constrained U=R	-325.6	5939	58.6 (40)	$p<.05$	-21.4
2d. and ACE factor variance constrained U=R	-312.2	5943	71.9 (44)	$p<.005$	-16.1

Model	Male Sample Only				
	-2lnL	df	χ^2 (df)	p value	AIC
M1. Base factor model: all parameters free to vary	75.2	2723	---	---	---
M2. Factor loadings & residual variances constrained U=R	92.4	2742	17.2 (19)	ns	-20.8
M2a. and A factor variance constrained U=R	103.1	2743	27.9 (20)	ns	-12.1
M2b. and C factor variance constrained U=R	97.0	2743	21.8 (20)	ns	-18.2
M2c. and E factor variance constrained U=R	94.3	2743	19.1 (20)	ns	-20.9
M2d. and ACE factor variance constrained U=R	104.2	2745	29.0 (22)	ns	-15.0

Model	Female Sample Only				
	-2lnL	df	χ^2 (df)	p value	AIC
F1. Base factor model: all parameters free to vary	-459.4	3176	---	---	---
F2. Factor loadings & residual variances constrained U=R	-419.9	3195	39.4 (19)	$p<.005$	1.4
F2a. and A factor variance constrained U=R	-418.3	3196	41.1 (20)	$p<.005$	1.1
F2b. and C factor variance constrained U=R	-419.7	3196	39.6 (20)	$p<.01$	-0.4
F2c. and E factor variance constrained U=R	-419.9	3196	39.5 (20)	$p<.01$	-0.5
F2d. and ACE factor variance constrained U=R	-416.5	3198	42.9 (22)	$p<.005$	-1.1

Note: U = Urban, R = Rural. The best-fitting model is Model 2c for the overall sample, Model M2c for the male sample alone, and Model F2d for the female sample alone. AIC values are calculated relative to the base factor model.