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Index of the Transmissible Common Liability to Addiction: Heritability and Prospective Associations with Substance Abuse and Related Outcomes

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Abstract

Background—Substance use disorders (SUDs) are highly comorbid and exhibit a relatively late onset. As such, many behaviors and personality traits present prior to the initiation of substance use can be used to predict later SUDs. The transmissible liability index (TLI) is a quantitative measure of such behaviors that indexes the common liability to SUDs. We examined the predictive utility and heritability of the TLI in a large community twin sample.

Methods—Using the Minnesota Twin Family Study (N = 2510), we estimated TLI scores from mother, child, and teacher reports of symptom and personality measures assessed at age 11. We then estimated the genetic and environmental contributions to the association between TLI scores at age 11 and composite measures of substance abuse and behavioral disinhibition (antisocial behavior) at age 17.

Results—For both male and female twins, TLI scores were highly heritable (.76) and exhibited moderate associations with adolescent substance abuse (r = .29) and behavioral disinhibition (r = .40). Genetic factors accounted for the association between TLI scores and the adolescent outcomes.

Conclusions—Findings support the utility of the TLI as a measure of the inherited, common liability to SUDs.

Keywords

Substance use disorders; antisocial behavior; transmissible liability index; genetic; twins; longitudinal

1. Introduction

Substance use disorders (SUDs) are among the most prevalent and costly of all mental health disorders (Harwood et al., 1998; Kessler et al., 2005). These disorders are responsible for substantial distress to the individuals that suffer from them as well as to their family members while also wreaking great economic costs to society in terms of increased demands on the health care and criminal justice systems. To better prevent, intervene, and mitigate the consequences of SUDs it is essential to better understand the etiological processes underlying the development of these disorders.

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A key finding regarding SUDs is that while there are substance-specific risk factors, much of the liability underlying SUDs is the same across different drug classes (alcohol, nicotine, illicit drugs), especially for early onset substance use and abuse that emerges in late adolescence and early adulthood (Iacono et al., 2008). This common liability is inferred based on findings that heavy substance users tend to use multiple substances (alcohol, nicotine, and different illicit drugs) (Bachman et al., 1997) as well as the high rates of comorbidity (i.e., meeting criteria for more than one disorder) among SUDs (Kessler et al., 2005). Additionally, SUDs are strongly associated with antisocial behavior and disinhibited personality traits such as impulsivity, sensation seeking, rebelliousness, and aggression (Krueger, 1999; Krueger and Markon, 2006). Twin studies have demonstrated that much of the comorbidity among SUDs is due to common genetic risk factors (Agrawal et al., 2004; Kendler et al., 2003a, 2007; True et al., 1999). Further, multiple twin studies have shown that the co-occurrence among SUDs, antisocial behavior, and disinhibited personality traits is best accounted for by a broad, highly heritable liability dimension, often referred to as externalizing or behavioral disinhibition (Kendler et al., 2003b; Krueger et al., 2002; Young et al., 2001). The heritability estimate of the externalizing factor is approximately 0.80, and this general genetic risk accounts for most of the heritable risk in specific disorders. Family studies have further demonstrated that risk for SUDs and antisocial behavior is transmitted in the form of this broad liability dimension. That is, rather than risk for a specific disorder, parents pass on a general risk to all disorders in the externalizing spectrum to their offspring (Hicks et al., 2004).

While there is evidence for specific genetic and non-genetic risk factors for individual SUDs (Kendler et al., 2003a, 2003b, 2007), a prudent scientific approach is to first understand the common liability processes and then begin to delineate substance specific risk factors that result in dependence to specific substances (Vanyukov et al., 2003a). As such, one should first identify the developmental precursors of this common liability to SUDs that are present prior to initiation of substance use, in order to distinguish the causes and effects of substance abuse. Especially strong predictors of early substance use and abuse include childhood disruptive disorders such as attention deficit/hyperactivity disorder (ADHD), conduct disorder (CD), and oppositional defiant disorder (ODD) (Armstrong and Costello, 2002; Elkins et al., 2007; Kim-Cohen et al., 2003; King et al., 2004). Similar to SUDs and antisocial behavior in adulthood, these disorders exhibit high rates of comorbidity, and this comorbidity is heavily influenced by common genetic risk factors (Dick et al., 2005; Nadder et al., 2002). Additionally, the link between parental SUDs and antisocial behavior and their offspring's childhood disruptive disorders is best accounted for by the transmission of a general externalizing factor, suggesting childhood disruptive disorders lie on the same liability dimension and are developmental precursors of SUDs (Bornovalova et al., 2010).

Having a quantitative index of this common liability to SUDs in childhood would provide substantial benefit to the study of development and etiology as well as guides for prevention and intervention. Recently, investigators at the Center for Education and Drug Abuse Research (CEDAR) have undertaken this task by utilizing their longitudinal study of high risk families (Vanyukov et al., 2003b). The CEDAR sample includes several hundred families with a male offspring 10 to 12 years (female offspring are now also recruited), with half of the families including a father with a drug use disorder. Their goal was to construct a transmissible liability index (TLI), that is, a measure of risk factors that are transmitted or shared between parents and offspring. Candidate items assessed child characteristics that discriminated between offspring with affected and nonaffected parents, the inference being that these items are indicators of the liability to SUDs. A final item set was identified by the iterative application of several psychometric techniques (exploratory and confirmatory factor analysis, item response theory) to measures included in the extensive intake assessment including child, parent, and teacher reports. The item content of the TLI

primarily relates to symptoms of childhood disruptive disorders and how easily the child adapts to and maintains a routine in daily activities (e.g., sleep and meal times) (Vanyukov et al., 2009). TLI scores have been shown to predict SUDs in adolescence and adulthood for European American offspring, but not African American offspring (Kirisci et al., 2009; Vanyukov et al., 2009). Additionally, a pilot twin study estimated a high heritability (0.80) in male twins, but a modest heritability for female twins (Vanyukove et al., 2009).

We sought to replicate and extend research on the validity of the TLI developed by CEDAR investigators using comparable data from the Minnesota Twin Family Study (MTFS), a longitudinal study of twins and their families (Iacono et al., 2006). The replication aspects entailed using the same or similar items to calculate TLI scores (though some items were not available in the MTFS assessment), to estimate the heritability of TLI scores, and to determine how well TLI scores predicted substance use and abuse in late adolescence. The extension aspects of the study included: (1) using a community rather than a high risk sample, (2) slightly different assessment procedures for TLI items and scores, (3) inclusion of a large female sample, (4) dimensional outcome measures of both substance abuse and behavioral disinhibition (i.e., antisocial behavior and disinhibited personality traits), and (5) estimating the genetic and environmental contributions to link between TLI scores in childhood and the adolescent substance abuse and behavioral disinhibition outcome measures. Despite slight differences in assessment and scoring procedures between the MTFS and CEDAR versions of the TLI, we anticipated TLI scores would predict adolescent substance use and abuse in a community sample for both male and female twins and exhibit high heritability. Also, consistent with the theory of a broad and highly heritable common liability, we hypothesized that genetic factors would account for the link between age 11 TLI scores and age 17 outcomes.

2. Methods

2.1.Sample

Participants were members of 1255 same-sex twin pairs participating in the MTFS. Families were identified using public birth records of twins born in Minnesota between 1977 and 1984, and from 1988 to 1994, and recruited into the study the year the twins turned 11 years old. Twins are then invited to take part in follow-up assessments every 3–4 years. For twins born in the earlier target birth years (1977–1984), families were recruited from the general community with only minimal exclusionary criteria such as no physical or mental handicap that would preclude participation in the day long assessment and the requirement that the family lived a day's drive of the University of Minnesota laboratories (a full description of the goals and methods of the recruitment method for this part of the study have been described previously elsewhere) (Iacono et al., 1999; Keyes et al., 2009). For twins born in the later target birth years (1988–1994), families were recruited using a procedure designed to ensure elevated levels of childhood disruptive disorders in the sample. Of this latter subset, half of the families were screened by interviewing the mother and only retained if at least one twin exhibited elevated symptoms of CD or ADHD. The other half of this subset was recruited using the same methods as described above. Results did not differ across twins ascertained using the different sampling strategies. Zygosity was determined by the agreement of a standard zygosity questionnaire completed by parents, evaluation of physical similarity by MTFS staff, and an algorithm assessing the twin similarity on ponderal and cephalic indices and fingerprint ridge counts The gender and zygosity breakdown for the sample are as follows: 394 monozygotic (MZ) male twin pairs, 221 dizygotic (DZ) male pairs, 391 MZ female pairs, and 249 DZ female pairs. Consistent with the demographics of Minnesota during the target birth years, 96% of twins are of European American ancestry.

2.2. Assessment

At age 11, twins participate in a multi-informant, multi-method assessment that covers several childhood disorders including attention deficit disorder (ADD), ADHD, CD, ODD, and major depressive disorder (MDD). *DSM-III-R* criteria (American Psychiatric Association, 1987) were used, as this was the current diagnostic system when the study began. *DSM-III* criteria were used for ADD (American Psychiatric Association, 1980). Both mothers and twins reported on symptoms. Trained staff interviewed members of each twin pair separately and concurrently. Symptoms were assessed using the Diagnostic Interview for Children and Adolescents Revised (DICA-R; Welner et al., 1987). Mothers reported on the presence of symptoms in their children using the parent version of the DICA-R. All interviews were reviewed in a case conference by at least two graduate students in the clinical psychology program at the University of Minnesota. The diagnosticians were required to reach consensus prior to assigning any symptoms taking into account all relevant information and referring to audio tapes of the interview when necessary. Diagnostic reliability kappas for the disorders ranged from .71 for ODD to .89 for MDD. In addition to the child and parent interviews, ratings from up to 4 teachers were obtained regarding various dimensions of the twin's behavior including items that assessed criteria for childhood disruptive disorders. Minnesota has a policy of placing members of a twin pair in different classrooms whenever possible which should minimize potential rater bias for the teacher ratings.

At age 17, twins are invited to participate in a second follow-up assessment. At this assessment, the Substance Abuse Module of the Composite International Diagnostic Interview (Robins et al., 1987) is used to assess nicotine, alcohol, and illicit drug use as well as symptoms of abuse and dependence. Kappa reliabilities are > .91 for all SUDs. Participants are also interviewed to assess symptoms of adult antisocial behavior (the adult criteria for antisocial personality disorder), and complete other self-report questionnaires and interviews that assess antisocial behavior and disinhibited personality traits. Further details regarding the specific measures of substance use and antisocial behavior used in the analyses are provided below.

2.3. TLI

The TLI is a quantitative measure of the latent or underlying liability to develop SUDs. The CEDAR TLI includes 45-items identified based on their ability to differentiate among a sample of young male offspring (age 10–12) in terms of whether their parent had a history of drug use disorder (Vanyukov et al., 2003b). Items were identified from a variety of interview and questionnaire data and include child, mother, and teacher reports. CEDAR TLI scores have been shown to predict drug use disorders in young adulthood (Kirisci et al., 2009; Vanyukov et al., 2009).

The diagnostic and psychometric measures used in the MTFS assessment were reviewed to identify items of similar content to those that compose the CEDAR TLI. The measures of greatest similarity were a subset of symptoms from the diagnostic criteria for ADHD, ADD, CD, ODD, and MDD, as well as items from the teacher rating form. The symptoms and items from the teacher rating form are provided in Table 1. Symptoms were rated as absent (0), present at a subthreshold level (1), and present at full level (2) (ratings are done separately for mother and child reports). Determining whether a symptom criterion was met and at what level of severity requires substantial time and information, and typically entails asking multiple questions including probes for frequency and duration. Diagnosticians then review this information and refer to normative standards developed by the study prior to making a final rating. Symptom ratings were then averaged across the mother and child reports. Teachers made ratings of how characteristic each behavior was of the child on a 4-

point scale (0 = not at all, 1 = just a little, 2 = pretty much, 3 = very much). If more than one teacher provided ratings for a twin, the mean rating for an item was used in the analysis. In the CEDAR sample, TLI scores have been calculated using item parameters derived from item response theory analyses (Vanyukov et al., 2003b). For simplicity, however, TLI scores in the current analysis were simply calculated as the mean z-score across the items.

2.4. Adolescent Substance Abuse and Behavioral Disinhibition

TLI scores calculated at age 11 were correlated with outcome measures of overall substance use and abuse and behavioral disinhibition collected at the age 17 assessment (M = 17.7 years, SD = 0.8 years). Three measures of each major substance class (nicotine, alcohol, illicit drug) were used to calculate a substance abuse composite. For nicotine, the measures were frequency of nicotine use (average number of days per month), average number of cigarettes smoked per day, and symptoms of *DSM-III-R* nicotine dependence. For alcohol, the measures were average number of drinks per occasion, maximum number of drinks consumed in 24 hours, and symptoms of *DSM-III-R* alcohol abuse and dependence. For illicit drugs the measures were number of different drug classes tried (marijuana, amphetamines, cocaine, barbiturates, tranquilizers, heroin, opiates, PCP, inhalants, and gas), number of lifetime marijuana uses, and *DSM-III-R* abuse and dependence symptoms for the substance the participant used the most. The mean z-score across the 9 measures was used as the substance abuse composite score.

The behavioral disinhibition composite included indices of antisocial behavior and disinhibited personality traits. These measures included symptoms of adult antisocial behavior; scores on the Delinquent Behavior Inventory, a 36-item self-report measure inquiring about the commission of various antisocial acts (α = .95; Taylor et al., 1999); scores on the Behavioral Disinhibition scale, a 12-item inventory derived from the Socialization scale of the California Psychological Inventory (α = .67; Taylor et al., 1999); a tally of life events associated with behavioral disinhibition including ever being suspended or expelled from school, contact with the police other than for traffic violations, and early initiation of sexual intercourse (0 = 18 years or older, 0.5 = 15–17 years, 1 = < 15 years). Any symptoms or questionnaire items that related specifically to substance use or abuse were omitted from the calculation of the scale scores. The mean z-score of the four measures was used for the behavioral disinhibition composite score. As the MTFS is an ongoing longitudinal study, outcome data was available for 1743 (69.4%) and 1711 (68.2%) participants for the substance abuse and behavioral disinhibition composites, respectively. To examine any bias due to attrition, we compared twins from the earlier birth years (1977–1984) who had versus had not participated in the age 17 assessment (89.8% retention rate) on TLI scores. The difference was modest (Cohen's d = .17, higher for twins who did not participate in the follow-up assessment) and non-significant, suggesting our results were not affected by the modest rate of attrition.

2.5. Biometric Analyses

Standard biometric models (Neale and Cardon, 1992) were used to examine the influence of additive genetic (A), shared environmental (C), and non-shared environmental (E) influences on the TLI. These models were also used to examine the extent to which the association between TLI scores and the adolescent substance abuse and behavioral disinhibition composites was due to genetic and environmental factors. The additive genetic component refers to the effect of individual genes summed over loci. An MZ correlation greater than that of the DZ correlation indicates additive genetic influences contribute to trait variance. Shared environmental effects refer to environmental factors that contribute to twin similarity on a trait. Shared environmental effects are inferred if the DZ correlation is greater than ½ the MZ correlation. Non-shared environment refer to environmental influences that

contribute to differences between members of a twin pair. Non-shared environmental influences are present if the MZ correlation is less than 1.0. Measurement error is also included in the estimate of non-shared environmental variance. The univariate twin model can be extended to the bivariate case, wherein it is possible to estimate the ACE contributions to the covariance between two traits. These models also allow for calculating the genetic correlation (an index of the amount of heritable variance that is shared between two traits) and the environmental correlations (a measure of the amount of environmental variance that is shared between two traits). All biometric analyses were conducted in the computer program *Mx* (Neale et al., 2002) and fit to the raw data using full information maximum likelihood that allows for missing data and produces a loglikelihood that indexes model fit. Sex differences were examined by constraining the heritability to be the same across males and females. The significance of gender effects was evaluated via a loglikelihood ratio test (distributed as a χ^2) between the constrained and unconstrained models. Similar procedures were followed to test for sex differences in the genetic correlation between TLI scores and the substance abuse and behavioral disinhibition outcomes.

3. Results

Table 2 provides the twin correlations and univariate ACE estimates for the TLI separately for boys and girls. As there were no significant gender differences in the heritability of any of the measures, we also report results after constraining the parameters to be the same across gender. TLI scores exhibited uniformly high MZ correlations and relatively low DZ correlations. As such, the heritability estimate for the TLI was very high for both boys and girls with no significant shared environmental contributions and moderate non-shared environmental effects. For the adolescent substance abuse and behavioral disinhibition composites, the MZ correlations were all high while the DZ correlations were moderate to high. Behavioral disinhibition scores exhibited high heritability with virtually no shared environmental contribution and moderate nonshared environmental effects. Substance abuse scores also exhibited moderate to high heritability as well as moderate and statistically significant shared and nonshared environmental effects.

Table 3 provides the correlations between TLI scores at age 11 and the adolescent substance abuse and behavioral disinhibition outcomes at age 17. TLI scores and the adolescent outcomes exhibited moderate phenotypic and moderate to high genetic correlations (i.e., a moderate amount of the heritable variance in TLI scores overlapped with the heritable variance of the adolescent outcomes). Effects were slightly greater for behavioral disinhibition relative to the substance abuse composite. The nonshared environmental correlations were non-significant and close to zero (because the TLI did not exhibit shared environmental variance, shared environmental effects could not contribute to the covariance with the adolescent outcomes). The phenotypic correlation between TLI scores and the adolescent outcomes was almost entirely due to genetic effects (92–98%). All correlations were similar for male and female twins with no significant gender differences.

4. Discussion

We employed a large community sample of male and female twins to replicate and extend evidence for the validity of the TLI as a measure of the common liability to SUDs. Despite using a different sampling strategy and slightly different assessment procedures than was used by CEDAR, TLI scores in the MTFS exhibited moderate phenotypic associations with adolescent substance abuse and the related construct of behavioral disinhibition. We extended this finding by showing that the predictive utility of TLI scores was comparable for male and female participants. This is particularly noteworthy, because the CEDAR TLI

item set was derived using a male only sample (Vanyukov et al., 2003b). We also found that TLI scores were highly heritable for both male and female twins using much larger samples than the previous pilot twin study of TLI scores (Vanyukov et al., 2009). Finally, consistent with the theory of a highly heritable common liability for SUDs (Bornovalova et al., 2010; Vanyukov et al., 2003b), we showed that genetic factors alone accounted for the association between childhood TLI scores and the adolescent substance abuse and behavioral disinhibition outcome measures.

While our findings are impressive regarding the consistency with theory and generlizabiilty of the TLI, some limitations should be noted. First, not all of the items identified in the original CEDAR item set were well represented in TLI scores for MTFS participants. In particular, item content related to how well the child is able to adapt to and maintain a routine in daily activities was represented by only a single item (i.e., moves a lot during sleep). Potentially, better coverage of this content would have resulted in greater effect sizes between TLI scores and the adolescent outcomes. Additionally, the MTFS sample is not racially or ethnically diverse. Therefore, we could not examine whether TLI scores exhibited comparable validity across racial and ethnic groups; an important point for future research as TLI scores failed to predict later substance abuse for African American participants in the CEDAR sample (Vanyukov et al., 2009). Finally, while the associations between TLI scores and adolescent substance abuse and behavioral disinhibition were robust, the effect sizes were of moderate magnitude. Clearly, many other factors contribute to substance use and abuse in late adolescence.

Despite these limitations, our findings provide strong support for the notion of using a pre-morbid liability index to investigate the etiology of SUDs (Bornovalova et al., 2010; Vanyukov et al., 2003b). The primary advantage of such a measure is that it avoids potential confounds associated with access and exposure to substances that are inherent in “post-morbid” measures of SUDs. Therefore, such a measure may provide a more sensitive index of the heritable liability to SUDs. Based on the item content, the liability underlying the common risk for SUDs might be described as a disinhibited behavioral style evidenced by antisocial behavior, difficulty regulating behavioral patterns and emotional reactions, and failure to consider consequences and modify behavior accordingly. While clearly a key risk factor, this behavioral disinhibition liability is not isomorphic with SUDs (i.e., substance abuse has distinctive features unrelated to disinhibition), and so a focus on measures of behavioral disinhibition per se provides a comprehensive rather than redundant strategy to investigating genetic and non-genetic etiological factors underlying substance abuse (i.e., such measures may focus on behaviors that are more direct expressions of the underlying genetic risk). A limitation of the TLI approach, however, is the use of parental status as the criterion to identify items as this taps only the liability that can be linked to the parent-offspring phenotypic transmission, and so incompletely reflects the total genetic liability (i.e., offspring receive only one-half their genes from each parent, and parent-child resemblance is limited to additive genetic effects while total genetic risk includes additive and non-additive genetic effects). An important direction for future research will be to employ prospective data to derive an index of pre-morbid liability on the basis of item utility to differentiate individuals on their actual SUD outcomes—rather than family history of SUDs—as this strategy is likely to yield greater effect sizes. Such a pre-morbid liability index could also be very useful in delineating developmental processes of gene-environment interplay in the emergence of SUDs, including mechanisms of environmental exposure (G-E correlation) and sensitivity (G × E interaction) (Johnson, 2007).

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Table 1

Minnesota Twin Family Study Transmissible Liability Index Items

Item Content	Informant and Response Format
Often lies Other than lying to your parents, did you often lie or make up stories to get out of trouble? Did you often tell lies for no reason at all? How often do you tell lies?	Mean rating of mother and child 0 = Absent 1 = Present at subthreshold 2 = Present at full threshold
Stolen without confrontation of a victim more than once Have you ever stolen anything from someone without their knowing it? Have you ever taken money from your parents without asking? **IF YES**, What did you steal? How much was it worth?	
Often truant Have you ever skipped school?	
Deliberately destroyed others' property Have you ever wrecked someone else's property on purpose? For example, breaking windows of a building, scratching a car, throwing rocks at cars, writing graffiti on a building, breaking other kids' toys or things? How many times?	
Often actively defies or refuses adult requests or rules Has there ever been a time when you often just refused to do things that your parents, teachers, or other adults asked you to do? What sorts of things?	
Often deliberately annoys other people Has there ever been a time when people said that you often did things on purpose to annoy or bug them? For example, grabbing another kid's hat, making funny noises, arguing with people, playing practical jokes, teasing people, making fun of them or calling them names.	
Often interrupts or intrudes on others Did your teacher or other people ever complain you interrupted them or butted into conversations, games, or other things that they were doing?	
Often blurts out answers to questions before they have been completed Did the teacher or your parents ever say that you started answering questions before they finished asking them?	
Difficulty waiting turn in games or group situations Did you ever have a hard time waiting your turn when you were playing with other children or waiting in line?	
Often engages in physically dangerous activities without considering possible consequences; not for the purpose of thrill seeking Did people ever get upset with you for doing dangerous things, like running out into the street without looking? How about climbing on things that are dangerous or climbing on something you might fall off of? Did you do these things without thinking about them, or did you plan them to get some excitement?	
Acts before thinking Have you ever gotten in trouble, maybe even hurt, because you often rushed into doing things without thinking about what would happen later? Do you think about things before you do them, or do you usually just do or say things without thinking about them first?	
Calls out in class Have you ever gotten in trouble at school because you spoke out when you were supposed to be quiet?	
Moves during sleep Are you a restless sleeper? Do you move around a lot in your sleep? When you wake up in the morning, are your sheets and blankets usually messed up? Do you fall out of bed a lot?	
Suicidal ideation During this period (when you were depressed), did you think about death or dying? During this period (when you were depressed), did you wish that you were dead or think about killing yourself? During this period (when you were depressed), did you have a plan about how you were going to kill yourself? Have you ever tried to kill yourself?	
Teacher Rating Often engages in physically dangerous activities without considering possible consequences (not for the purpose of thrill-seeking), e.g., runs into street without looking	Mean rating across teachers 0 = Not at all 1 = Just a little 2 = Pretty Much 3 = Very much

Item Content	Informant and Response Format
Has difficulty waiting turn in games or group activities	
Often blurts out answers to questions before they have been completed	
Often interrupts or intrudes on others, e.g., butts into other children's games	
Often acts before thinking	
Frequently calls out in class	
Is excitable, impulsive	

Note. The example items are worded for the child version. Items for the mother report are rephrased to refer to the twins' behavior.

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Table 2

Twin Correlations and Univariate Estimates of Additive Genetic (A), Shared Environment (C), and Nonshared Environmental (E) Variance Components (95% Confidence Intervals).

Variable	MZ	DZ	A	C	E
TLI age 11					
Boys	.78	.42	.69 (.49, .81)	.08 (.00, .28)	.23 (.19, .26)
Girls	.69	.17	.72 (.66, .76)	.00 (.00, .04)	.28 (.24, .33)
No sex differences	.76	.33	.76 (.70, .79)	.00 (.00, .06)	.24 (.21, .27)
Substance Abuse age 17					
Boys	.80	.53	.59 (.39, .82)	.21 (.00, .41)	.20 (.16, .24)
Girls	.72	.58	.50 (.32, .71)	.26 (.06, .43)	.24 (.19, .29)
No sex differences	.77	.55	.54 (.40, .70)	.25 (.09, .38)	.21 (.18, .24)
Behavioral Disinhibition age 17					
Boys	.77	.41	.74 (.49, .81)	.03 (.00, .27)	.23 (.19, .28)
Girls	.70	.44	.77 (.57, .81)	.00 (.00, .18)	.23 (.19, .29)
No sex differences	.75	.42	.75 (.58, .80)	.02 (.00, .18)	.23 (.20, .27)

Table 3

Phenotypic, Genetic, and Environmental Correlations (95% Confidence Intervals) between TLI scores at Age 11 and Substance Abuse and Behavioral Disinhibition at Age 17.

	TLI Scores at age 11			
Age 17 outcome measures	**r_P**	**r_G**	**r_E**	**% covariance due to A**
Substance Abuse				
Boys	.28 (.20, .36)	.36 (.25, .48)	.08 (−.05, .20)	92
Girls	.30 (.22, .38)	.45 (.30, .60)	.05 (−.09, .19)	94
No sex difference	.29 (.23, .34)	.39 (.30, .48)	.07 (−.02, .16)	92
Behavioral Disinhibition				
Boys	.42 (.35, .48)	.56 (.45, .70)	.01 (−.11, .14)	99
Girls	.34 (.25, .41)	.43 (.31, .55)	.06 (−.08, .20)	94
No sex difference	.40 (.34, .44)	.52 (.44, .61)	.03 (−.07, .12)	98

Note. r_P= phenotypic correlation; r_G= genotypic correlation; r_E= environmental correlation; A = additive genetic variance.