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Modeling the Association between Sexual Maturation, Transmissible Risk, and Peer Relationships During Childhood and Adolescence on Development of Substance Use Disorder in Young Adulthood

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Abstract

Background—This prospective study investigated pubertal timing and transmissible risk in relation to affiliation with deviant peers on the development of substance use disorder (SUD).

Methods—Participants were boys (N = 500) ascertained through proband fathers with (N = 250) and without (N = 250) DSM-III-R lifetime diagnosis of SUD who were prospectively tracked from age 10–12 to 22. Transmissible liability index (TLI), Tanner stage, peer delinquency, and substance use were measured at ages 10–12 and 16. SUD diagnosis during early adulthood was determined.

Results—Structural equation modeling revealed two pathways in which transmissible risk and sexual maturation influenced development of SUD. In the first pathway, transmissible risk was correlated with and prospectively predicted affiliation with deviant peers and substance use presaging SUD. In the second pathway, advanced sexual maturation positively predicted affiliation with deviant peers and substance use, which in turn predicted SUD. However, transmissible risk was not associated with pubertal development.

Conclusions—These findings indicate that advanced sexual maturation and transmissible risk constitute unrelated facets of SUD liability; however, both factors bias development toward SUD via affiliation with deviant peers.

Scientific Significance—Youth with advanced sexual maturation and/or transmissible risk for SUD are at higher risk for developing SUD. Additional research is needed to determine if addressing these risk factors will contribute to advancements in SUD prevention.

INTRODUCTION

Findings from family and twin studies provide strong evidence for a genetic contribution to the etiology of substance use disorder (SUD)^{1–4}. Many environmental factors spanning peers, neighborhood and family environment also impact on SUD risk^{3,5–7}. However, little

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is known about the interaction of heritable liability (e.g., vulnerability to SUD transmitted across familial generations) and developmentally salient risk factors on progression to SUD.

One potentially important developmental factor amplifying risk for SUD is pubertal maturation. Earlier maturation, albeit within the non-pathological range, is associated with increased risk for substance use^{8–12} and SUD^{10,13,14}. Moreover, sexual maturation at a younger age heightens the propensity to affiliate with norm-violating peers^{15–17}, which in turn portends substance use^{18–20} and SUD²¹. Considering that pubertal maturation is influenced by genetics^{22,23}, the question is raised as to whether heritable liability for SUD is manifest, at least in part, as advanced sexual development.

Heritable liability, originally described by Falconer²⁴, refers to intergenerational continuity of susceptibility to disease development, taking into account predisposing heritable and environmental influences. Recent research by Vanyukov and colleagues^{25–29} demonstrates that heritable liability to SUD can be quantified as a complement of psychological characteristics comprising a unidimensional trait underlying intergenerational continuity for SUD. The trait, termed the *Transmissible Liability Index* (TLI), distinguishes offspring of SUD+ from SUD– fathers²⁵ and predicts SUD outcome²⁸. Approximately 85% of the variance on this trait is genetic as determined by twin studies³⁰. Accordingly, using the TLI affords the opportunity to ascertain whether advanced sexual maturation, relative to chronological age, is related to heritable liability for SUD. Both the TLI²¹ and advanced sexual maturation^{15,16} predict affiliation with deviant peers, presaging SUD³¹. Thus, it is theorized that advanced pubertal maturation mediated by heritable liability for SUD and associated with deviant peer affiliation predicts SUD. As shown in Figure 1, this prospective investigation draws together three factors, namely transmissible liability, pubertal development and affiliation with deviant peers into a unifying model of SUD etiology.

METHOD

Participants

Male participants (N = 500) were ascertained through proband fathers who either qualified for SUD consequent to using illegal drug(s) or had no Axis I adult psychiatric disorder. About 25% of the fathers with SUD were recruited from treatment centers, social service agencies and psychiatric clinics. The remaining portion was obtained through public service announcements, newspaper and radio advertisements and notices posted in public locations. In addition, a marketing firm assisted in identifying qualified families. Multiple recruitment strategies were employed owing to the low prevalence of men who have a biological son in the required age range and a current or previous spouse willing to participate in this long-term prospective investigation. The men without SUD were recruited using the same procedures except that none were accrued from treatment facilities. Exclusion criteria for the fathers included an IQ lower than 80, English not spoken as the first language, and poor health or severe chronic disability that would compromise validity of responses.

Procedure

Written informed consent was obtained prior to initiating the research protocol using the procedure approved by the University of Pittsburgh Institutional Review Board. Baseline study was conducted when the participants were 10–12 years of age (N=500). Follow-up evaluations were conducted around ages 16 (N = 404), 19 (N = 364), and 22 (N = 282). Family socioeconomic status (SES) was measured using the Hollingshead's Four-Factor Index of Social Status³². Exclusion criteria for the sons included inability to comprehend English, history of neurological injury, life threatening disease, psychosis, IQ below 80

measured by the Wechsler Intelligence Scale for Children III, and a positive breath alcohol or urine drug test.

Of the 460 age-eligible participants, 80.8% completed assessment on the outcome variable of SUD during young adulthood. Attrition (defined as failure to complete a visit) at the age 16 visit was due to inability to locate the participant (3.8% of all participants), participant refusal (15.2%), and death (0.2%). At the age 22 assessment, 8.6% of the sample could not be located, 29.7% refused to participate, and 0.9% were deceased.

Table 1 summarizes the characteristics of the sample, including comparisons of the participants who attrited at age 22 to those who were evaluated at age 22. There were no significant differences in the predictor variables (TLI, pubertal stage, peer delinquency) between retained and attrited participants at age 10–12, nor on the rates of Attention Deficit Hyperactivity Disorder, Oppositional Defiant Disorder or Conduct Disorder (measured using structured interview). There were no baseline differences between attrited and retained participants on most demographic characteristics, including grade in school, ethnicity and percentage of participants with married parents. However, the attrited participants had a lower full scale IQ ($p < .001$) and lower family SES compared to retained participants ($p = .05$). Participants who attrited between ages 16 and 22 had lower TLI scores ($p = .05$) but did not differ according to pubertal stage, peer delinquency scale score and substance use.

Measures

Transmissible Liability (age 10–12, 16)—The rationale²⁷ and the method²⁵ used to derive the Transmissible Liability Index (TLI) have been described in detail elsewhere. Briefly, the TLI was developed in several stages. First, constructs were derived and validated using exploratory and confirmatory factor analysis to characterize processes that have been frequently implicated to be related to SUD risk. Examples of constructs include aggression, hyperactivity, impulsivity, norm-violating behavior, sleep patterns, and cognitive flexibility. Next, the constructs that discriminated sons of SUD+/SUD– fathers were retained and the items comprising the constructs were submitted to second order exploratory factor analysis followed by confirmatory factor analysis. Lastly, item response theory (IRT) analysis was conducted on the final set of items which comprised the continuous latent trait of TLI to determine the threshold and discrimination parameter of each item and to estimate TLI score. The TLI was created as a latent variable; however, testing and validation of the TLI allow us to consider the TLI as a manifest variable. The TLI has predictive, discriminative and concurrent validity^{26,28}. Internal reliability was .93 at ages 10–12 and .95 at age 16.

Delinquent Peer Affiliation (age 10–12, 16)—The self-administered 15-item Peer Delinquency Scale documents involvement with friends who engage in negatively sanctioned and illegal behavior³³. Previous research has shown that this scale is a significant predictor of SUD³⁴. It has also been shown that the score on this scale mediates the relation between testosterone level during adolescence and SUD in young adulthood¹⁴ as well as mediates the relation between TLI score and SUD. Hence, it is an excellent measure for clarifying the relation between sexual maturation and transmissible risk on development of SUD. Internal consistency is .90.

Pubertal Stage (age 10–12, 16)—A trained nurse determined Tanner stage using standard examination procedures^{35–37}. The measured variables were quantity, quality and distribution of pubic hair. Tanner stage was rated on a five point scale.

Substance Use (age 10–12, 16)—Substance use frequency was measured by section 1A of the revised Drug Use Screening Inventory (DUSI-R)^{38,39}. Participants responded to the question: *Ordinarily, how many times each month have you used each of the drugs listed, in the last year?* The participants endorsed one of five categories (0 times; 1–2 times; 3–9 times; 10–20 times; more than 20 times) for 20 types or classes of substances. The scores are summed across all substances to yield the measured variable.

Substance Use Disorder—The fathers were administered the Structured Clinical Interview for DSM-III-R (SCID)^{40–42} to determine whether they satisfied ascertainment criterion (lifetime SUD due to illegal drug use, or no Axis I adult psychiatric disorder). DSM-III-R criteria were used because this study began in 1990 prior to advent of the DSM-IV. The diagnostic formulation was conducted by a committee consisting of a psychiatrist certified in addiction psychiatry and another psychiatrist or a psychologist.

Diagnosis of SUD in the participants was determined using structured interviews and DSM-IV criteria. The Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS)⁴³ was administered at each visit up to age 18 after which the SCID was utilized. The dependent variable was SUD diagnosis (abuse or dependence) pertaining to consumption of alcohol and/or illicit drugs. The most frequent SUD diagnoses involved alcohol (31%) and cannabis (32%). Overall, 41% of the sample qualified for a lifetime SUD diagnosis; this high rate is consistent with the high risk family paradigm.

Statistical Analysis

Structural equation modeling (SEM) with dichotomous outcome was conducted to model the associations of transmissible liability, pubertal maturation, and deviant peer affiliation at age 10–12 and 16 on development of SUD between 17 to 22, controlling for substance use breadth and frequency. Model parameters, estimated using Mplus⁴⁴, use the weighted least square method with diagonal weight matrix with robust standard errors. Four indices of model fit were used: χ^2 goodness-of-fit index, root mean square error approximation (RMSEA), comparative fit index (CFI), and Tucker-Lewis index. RMSEA values greater than .08 reflect poor model-data fit, values between .05 – .08 indicate acceptable fit, and values less than .05 reflect good fit⁴⁵. For the CFI and Tucker-Lewis index, values greater than .90 and .95 indicate good model data fit⁴⁶. Mediated paths between TLI score, Tanner stage, and SUD outcome were tested using the method described by Sobel⁴⁷. All of the variables used in the path analysis were manifest variables. Incomplete data sets were handled by MPlus using maximum likelihood estimation without imputation⁴⁴. This is a full-information method that simultaneously utilizes all of the available data and retains all cases, and is a highly robust method for handling missing data due to attrition^{48,49}. Post-hoc bivariate Pearson correlation was computed using SPSS version 19 (SPSS Inc., Chicago IL).

RESULTS

Figure 2 depicts the standardized coefficients in the path analysis. Overall model data fit was excellent: $\chi^2 = 4.984$, $df = 5$, $p = .418$; RMSEA < .001, CFI = .99, Tucker-Lewis Index = .99. Table 2 contains the standardized coefficients, z-score, and significance values for the significant paths.

The TLI at age 10–12 correlated with peer delinquency and substance use at age 10–12, and positively predicted peer delinquency, substance use, and transmissible liability at age 16. Pubertal stage at age 10–12 correlated with peer delinquency at age 10–12, and also predicted peer delinquency, substance use and pubertal stage at age 16. Both TLI and pubertal stage at age 16 predicted SUD outcome between ages 17 – 22. However, the TLI did not correlate with pubertal stage, nor did these variables predict each other between ages

10–12 and 16. Moreover, the TLI did not mediate the relation between pubertal stage and SUD.

Peer delinquency at age 10–12 positively predicted TLI, peer delinquency and substance use at age 16. Peer delinquency at 10–12 years of age also directly predicted SUD by adulthood. However, at age 16, peer delinquency in the tested model did not directly predict SUD, although it correlated with TLI, pubertal stage, and substance use which in turn predicted SUD. *Post-hoc* bivariate correlation analysis, conducted to further explore the absence of a correlation between peer delinquency at age 16 and SUD in the full model, revealed a moderate to strong correlation between peer delinquency and SUD outcome ($r = .514$, $p < .001$).

Substance use correlated with TLI and peer delinquency at age 10–12 but not pubertal stage. Substance use at age 10–12 positively predicted peer delinquency and substance use at age 16. In addition, substance use at age 10–12 directly predicted SUD by age 22.

DISCUSSION

This longitudinal study demonstrated that transmissible risk for SUD and advanced pubertal maturation in late childhood bias development toward SUD via separate, albeit converging pathways. In one path, transmissible liability prospectively predicted deviant peer affiliation and substance use during mid-adolescence leading to SUD. In a second path, sexual maturation positively predicted peer deviancy and substance use, which in turn predicted SUD by adulthood. Thus, transmissible liability and sexual maturation, although not associated, predicted affiliation with deviant peers and substance use portending SUD.

SUD in early adulthood was directly predicted by both substance use and peer deviancy at age 10–12. SUD was also predicted by transmissible liability, pubertal stage, and substance use at age 16. However, peer deviancy at age 16 did not predict SUD in the tested model. One possible reason for the absence of this prediction is high within-model correlation of peer delinquency and substance use. Notably, bivariate correlation analysis confirmed an association between peer deviancy at age 16 and SUD. In total, these findings correspond to other investigations suggesting an association between peer deviancy and development of SUD^{31,50}.

Although transmissible risk was not correlated with pubertal stage, both variables predicted peer deviancy and substance use in adolescence and SUD by young adulthood. These findings complement the results of previous studies linking early pubertal maturation with increased substance use^{8–11,51}, particularly when friends are reported as substance users¹⁰. Advanced sexual maturation may impact on SUD risk via several mechanisms, including premature exposure to adult roles and behaviors^{17,51–54} and earlier entry into adolescence¹⁰, a critical developmental period associated with high rates of drug and alcohol experimentation^{55–57}. In youth with advanced pubertal maturation, exposure to developmentally advanced situations may occur prior to the maturation of self-regulation capacities integral to decision making and impulse control^{58,59} that are necessary for resisting the influence of deviant peers^{60,61}. The observation that peer deviancy was a proximal factor emanating from both transmissible risk and pubertal maturation suggests that affiliation with socially deviant peers could result from both social selection (e.g., youths with high transmissible risk find similarly dysregulated friends who are prone to deviancy) and peer contagion (e.g., physically advanced youth are more susceptible to adverse influence of older peers).

Considering that transmissible risk and pubertal maturation were not associated, and that both factors biased development toward affiliation with socially deviant peers, it remains to be determined how social selection and contagion conjointly operate to potentiate SUD risk. From the practical standpoint, preventing access of high risk youth to peers who do not adhere to societal norms and laws would appear to be an important intervention for parents, schools, and SUD treatment programs⁶². Parent management training involving parental supervision, positive reinforcement, consistent discipline styles and increased monitoring of children reduces both substance use⁶³ and the opportunity to affiliate with deviant peers⁶⁴. Preventing peer contagion, however, is more challenging^{65,66} considering that youths are exposed to risk-enhancing peers in school as well as in unsupervised recreational and social settings⁶⁷. Notably, interventions directed at reducing peer contagion have largely been unsuccessful^{62,66}, underscoring the need to develop strategies to reduce the negative influence of risk-promoting friends. Recently, it has been shown that deviant socialization during childhood development mediates the association between transmissible liability to SUD and SUD outcome²¹. This suggests inculcating resistance to negative peers may be essential for preventing problematic substance use in high risk youth. To this end, the TLI affords the opportunity to monitor SUD risk throughout development so that vulnerable youths can receive preventative interventions that facilitate resistance to the negative influence of socially non-normative peers. Age-specific versions of the TLI have recently been validated using a ten minute web-based computer adaptive test (CAT)⁶⁸, and research at CEDAR is ongoing to develop a measure of heritable liability in pre-school age children. Additional research is needed, however, to determine whether additional benefit is provided by conjointly monitoring pubertal status.

Limitations

Several limitations of this study are noted. Although attrition is expected in longitudinal studies, it is important to ascertain whether attrition biased the results. In the present study, there were no differences between retained participants and attrited participants on most measured variables. Full scale IQ was lower in the attrited participants, although both groups scored in the normal range. The attrited participants also had lower family SES at the time of baseline evaluation ($p = .05$) and higher TLI scores at age 16 ($p = .05$). Considering that both family SES characteristics and TLI may be related to increased risk for SUD^{28,69}, these findings suggest that the attrited participants may have a higher risk for SUD. However, the finding that excellent model-data fit was obtained on the putatively less severe segment of the sample lends confidence to the results demonstrating important influences of transmissible risk and peer affiliation as intermediary factors linking sexual maturation timing and development of SUD.

The participants are sons who whose fathers were recruited using a standard high-risk family design, and thus the participants themselves were not randomly accrued from the general population. An advantage of the high-risk family paradigm is maximizing signal detection, namely the “risk factors” that portend adverse outcome⁷⁰. As such, the results should be viewed within this etiological paradigm and replication in a random sample of youth is warranted. Additionally, this study measured Tanner Stage at two time-points (age 10–12 and 16). Rate of change during the progression through puberty was not measured because the aim of this study pertained to documenting advanced pubertal stage relative chronological age and not rate of maturation. Lastly, it is recognized that other variables which may amplify risk for SUD were not included in this investigation as they were not part of the proposed model. Having obtained excellent model data fit, it is now opportune to build a more comprehensive model in future research aimed at understanding SUD etiology.

Conclusions

This study demonstrated that transmissible liability and advanced pubertal maturation are independent risk factors for development of SUD. Each factor, however, correlates with and predicts deviant peer affiliation and substance use presaging SUD. These findings inform prevention programs by demonstrating the need to minimize the negative influence of peers who, via selection and contagion, potentiate substance use initiation and subsequently SUD. Future studies are necessary to determine whether tracking pubertal maturation in conjunction with transmissible risk improves detection of youths requiring SUD prevention.

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Figure 1.
Theoretical model demonstrating the hypothesized relationship between pubertal stage, transmissible risk and affiliation with deviant peers, portending SUD outcome.

Figure 2.
Results of path analysis. Only standardized coefficients which are significant are presented.

Table 1

Demographics and comparison of retained and attrited subjects.

	Retained		Attrited		F	p
	M	SD	M	SD		
Age 10–12 Assessment (N = 500)						
Family SES	41.46	13.47	38.95	12.63	3.95	.05
Grade in school	4.55	1.14	4.51	1.02	.19	.67
Full scale IQ	110.13	16.01	103.62	15.35	18.48	<.001
Married parents %	75.2		75.1		$\chi^2=.00$	.99
European-American %	76.6		75.1		$\chi^2=.13$	.72
Transmissible liability index (TLI)	.12	1.00	.23	1.05	1.13	.29
Pubertal stage	1.46	.54	1.42	.52	.55	.46
Peer delinquency	4.02	8.31	4.52	8.05	.41	.52
Substance use	.72	.81	.60	.88	2.20	.14
ADHD	14.4		19.8		$\chi^2=2.28$	.13
ODD	11.2		13.0		$\chi^2=.35$	.55
CD	12.3		8.0		$\chi^2=1.50$	.22
Age 16 Assessment (N=404)						
Transmissible liability index (TLI)	.02	1.02	.24	1.01	3.96	.05
Pubertal stage	2.78	.41	2.76	.45	.08	.77
Peer delinquency	9.84	8.59	9.76	8.36	.01	.93
Substance use	1.96	3.45	2.27	3.29	.66	.42

Table 2

Results of significant path analysis

Paths Age 10–12 to Age 16	β	Z	p
Transmissible risk → Peer delinquency	.110	2.671	.008
Transmissible risk → Substance use	.125	3.166	.002
Transmissible risk → Transmissible risk	.361	9.791	< .001
Pubertal stage → Peer delinquency	.106	2.897	.004
Pubertal stage → Substance use	.137	3.376	.001
Pubertal stage → Pubertal stage	.246	5.766	< .001
Peer delinquency → Transmissible risk	.048	1.973	.049
Peer delinquency → Substance use	.077	2.406	.016
Peer delinquency → Peer delinquency	.106	5.456	< .001
Substance use → Peer delinquency	.138	5.192	< .001
Substance use → Substance use	.154	4.812	< .001