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Does the "Gateway" Sequence Increase Prediction of Cannabis Use Disorder Development Beyond Deviant Socialization? Implications for Prevention Practice and Policy

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Abstract

Background—This study was conducted to test whether non-normative socialization mediates the association between transmissible risk measured in childhood and cannabis use disorder manifested by young adulthood, and whether the sequence of drug use initiation ("gateway", i.e., consuming legal drugs before cannabis, or the reverse) increases accuracy of prediction of cannabis use disorder.

Methods—Sons of fathers with or without substance use disorders (SUD) related to illicit drugs were tracked from 10–12 to 22 years of age to model the association between transmissible risk for SUD, socialization (peer deviance), order of drug use initiation ("gateway" or reverse sequence), and development of cannabis use disorder. Path analysis was used to evaluate relationships among the variables.

Results—Non-normative socialization mediates the association between transmissible risk measured during childhood and cannabis use disorder manifest by young adulthood. The sequence of drug use initiation did not contribute additional explanatory information to the model.

Conclusions—The order of drug use initiation does not play a substantial role in the etiology of cannabis use disorder.

Keywords

gateway hypothesis; cannabis use; transmissible liability index (TLI)

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1. Introduction

Policies aimed at curtailing substance use have been largely guided by ideology and political expediency effected primarily through the criminal justice system. The Eighteenth Amendment of the U.S. Constitution and the Volstead Act banning manufacture, transport and selling of alcohol beverages between 1919 and 1933, for example, culminated a long struggle spearheaded by the Anti-Saloon League, Prohibition Party, and Woman's Christian Temperance Union. Similarly, the first Director of the Federal Bureau of Narcotics, Harry J. Anslinger, demonized marijuana for primarily political reasons, namely to bolster the visibility, prestige and budget of the Federal Bureau of Narcotics (Booth, 2004).

To this day, the U.S. Federal government allocates more resources for prevention by attempting to eliminate the supply of drugs than interventions directed at lowering demand. Despite enormous costs associated with investigation, prosecution and incarceration, the prevalence of consumption of illegal drugs nevertheless remains high. Results from a recent national survey in the U.S. reveal, for example, that the one-year prevalence of marijuana use is 34.8% among 12th grade students (Johnston et al., 2010). This constitutes approximately a 10% increase since 1991. During the period spanning 1981–1992, the past-year prevalence of cannabis use disorder (abuse or dependence) among marijuana users increased from 30.2% to 35.6% (Compton et al., 2010).

The onset of cannabis use disorder usually occurs before 20 years of age (Wagner and Anthony, 2007). Accordingly, prevention requires interventions that focus on ameliorating etiological influences within a developmental perspective. Currently, however, the rubric for understanding the etiology of substance use and SUD within a developmental framework remains unsettled. Two competing models vie as the framework for explaining the onset of cannabis use behavior, the necessary prodrome to cannabis use disorder. According to the most well-known version of the various stepping-stone models, referred to as the "gateway hypothesis" (GH) (Kandel and Yamaguchi, 1999), consumption of legal, "soft" illegal and "hard" illegal drugs constitutes specific developmental stages. Each stage is posited to have a forward influencing effect on the propensity to use the drug comprising the next developmental stage in a presumed invariant sequence that is contingent also on the presence of drug-specific risk factors. As stated by Kandel and Yamaguchi (1999), *"One licit drug is required to make the progression to marijuana use"* (p. 71). In addition, it is suggested that the transition from one stage to the next comprises a causal sequence: *"the identification of drug specific risk factors for progression is technically related to the demonstration of causal linkages between stages"* (p. 64). Although the gateway sequence and its presumed constituent stages are not claimed to extend to diagnosis of substance use disorder (SUD), the development of the prodrome, cannabis use, is considered to reflect a particular stage within a temporal sequence.

In stark contrast to the GH, the *common liability to addiction (CLA)* model posits that a complement of psychological characteristics is associated with risk for all SUD categories (Vanyukov et al., 2003a,b; Vanyukov et al., this issue). Accordingly, the characteristics associated with risk for developing the prodromes, namely alcohol and drug use, are also congenerous to all drugs that have abuse potential. Key support for the CLA stems from research conducted on twins and showing that up to 100% of genetic variance and up to 80% of phenotypic variance are shared among all SUD categories (Kendler et al., 2003; Tsuang et al., 1998). Additional support for common liability is derived from research showing that the different SUD categories in the DSM are indicators of a continuous latent trait (Kirisci et al., 2002). Moreover, this trait and the variety of SUDs can be mapped on a latent dimension corresponding to severity of externalizing disorder (Krueger et al., 2002), thus illustrating that socially non-normative behaviors, including deviance proneness

(Mason et al., 2007; Sher, 1991; Windle, 1990) and problem behavior syndrome (Donovan et al., 1998; Jessor, 1987) are integral to the propensity to consume all types of abusable drugs. In this model, deviant or non-normative socialization, defined as a lifestyle featured by low adherence to societal mores and laws, leads to substance use initiation as one manifestation of nonconformance. Indeed, the strong genetic overlap between SUD and antisocial behavior (Grove et al., 1990; Fu et al., 2002; Kendler et al., 2003b) suggests that using illegal drugs and SUD are manifestations of deviant socialization.

Thus, whereas the GH asserts that using each substance comprises a discrete developmental stage, the CLA model posits that biobehavioral processes congenerous to all SUD categories, via interaction with, and possibly resulting in selection of, multiple facets of the environment, predispose to consumption of substances leading to SUD. Inasmuch as these two conceptual models are not mutually exclusive (despite the assertion that they are antithetical [Kandel and Yamaguchi, 1999]), since the putative gateway sequence may manifest in context of non-normative socialization, it was determined in this study whether the order of drug use initiation -“gateway” (alcohol and/or tobacco to marijuana) or, alternatively, reverse (marijuana to alcohol and/or tobacco) – adds information about etiology beyond non-normative socialization predisposed by transmissible (heritable) liability that is congenerous to all SUDs.

The conceptual differences between the gateway hypothesis and CLA model regarding the nature of the developmental process leading to cannabis use and ultimately diagnosis of cannabis use disorder have, however, important ramifications for prevention policy and practice. In particular, it is important to ascertain whether a specific order of drug use initiation has any bearing on identifying youths who are at high risk for SUD beyond the trivial fact that initiation of drug use in general is a necessary condition for SUD development. Specifically, prevention of cannabis use guided by the gateway hypothesis should optimally focus on youths who consume alcohol or tobacco and possess the specific characteristics associated with risk for transitioning to marijuana use. To date, however, specific or unique factors associated with risk of using marijuana have not been reported. On the other hand, prevention within the CLA framework emphasizes deployment of interventions beginning in early childhood that could potentiate normative socialization. Prevention in this framework entails inculcating attitudes, values and behaviors that are consistent with prevailing societal mores. For instance, affectional bonding between the mother and baby establishes the basis for a synergistic relationship, thereby catalyzing long-term parental investment in childrearing. Poor attachment hampers the child’s development and frequently leads to lifelong social maladjustment (Allen et al., 1996) which, in turn, amplifies risk for substance use and SUD. Temperament deviations in the toddler augment risk for conduct disorder in later childhood (Maziade et al., 1990) and substance use up to two decades later (Caspi et al., 1996). Significantly, children under 3 years of age understand that a rule specifies obligations regarding how to behave in particular circumstances (Gopnik, 2009). Hence, children at a very young age are amenable to learning adherence to prosocial behavior although this may be hampered in children disadvantaged by temperament makeup and quality of attachment to caregivers. Even at an early age (20–64 months), disregard for rules is significantly albeit moderately heritable, but, more importantly, genetic factors account for over 90% of continuity in this trait, with the rest of covariance between the point measurements being due to individual environment/error (Petitclerc et al., 2011). In effect, the CLA model conceptualizes SUD as one developmental outcome of non-normative socialization presaged by psychological characteristics reflecting transmissible SUD liability and adverse rearing experiences. Whereas the opportunistic character of the sequence is explicitly rejected by the GH proponents (Kandel, 2002), within the CLA framework, the “gateway” order of drug use initiation – from licit to illicit drugs – is defined opportunistically, by substance availability, one of the determinants of which is

the legality of the drug. Thus, while the contribution of that order to the SUD risk is expected to be minimal, the reversals of the licit-illicit sequence could be related to a higher SUD risk rather than treatable simply as "error" (Kandel, 1975), because they might indicate a higher liability to step over marijuana's illegality threshold before less societally proscribed and frequently more available (albeit still illegal for under-21 individuals) alcohol use.

We hypothesized that non-normative socialization evinced during adolescence (indicated by peer deviance) mediates the association between transmissible risk for SUD in childhood and cannabis use disorder in adulthood. We also evaluated whether the sequence of drug transitions, namely alcohol or tobacco use followed by marijuana use ("gateway"), or marijuana use followed by alcohol/tobacco (reverse) contributes additional explanatory information to the etiology of cannabis use disorder.

2. Methods

2.1 Subjects

Boys were ascertained at age 10–12 through proband fathers who qualified for SUD consequent to consumption of an illegal drug or had no adult onset Axis 1 psychiatric disorder. This ascertainment criterion was applied because the aim of this research program is to elucidate the etiology of SUD involving illegal drugs. Men with alcohol use disorder or tobacco dependence were not excluded from recruitment provided that they also satisfied diagnostic criteria for lifetime SUD associated with use of illegal drugs. Eighty percent of the SUD+ fathers were recruited via public service announcements, advertisements and a market research firm that conducted random digit dialing. The remaining 20% were enrolled following discharge from treatment facilities. Based on the assumption that men receiving clinical intervention for SUD have more severe disturbance, recruiting their children in this study enhances the likelihood that the sample encompasses the full range of liability. The most frequent SUD diagnoses (abuse or dependence) in the men, based on results of the Structural Clinical Interview for Diagnosis (SCID; Spitzer et al., 1987), pertained to use of cannabis (34.2%), cocaine (23.8%), opiates (11.2%), and amphetamines (8.4%). An alcohol use disorder without co-occurring SUD concomitant to using an illegal drug was an exclusion criterion. Comorbid alcohol use disorder was, however, diagnosed in 42.6% of SUD+ fathers. The most frequent non-SUD psychiatric disorders were depression (15.8%), antisocial personality (12.2%) and anxiety spectrum disorder (8.8%). The SUD- men were recruited using the same methods with the exception that none were accrued from treatment facilities.

At the time of recruitment the biological sons of the probands underwent a physical examination, urine drug screen, and intelligence evaluation using the WISC-III-R to ensure that they were in good health, drug-free, and had at least low normal intelligence. Follow-up evaluations were conducted when the boys attained 16 and 22 years of age. Only one boy in each family was evaluated to avoid biased results associated with correlated data. Because recruitment of girls began several years after the boys, an insufficient number were available to conduct statistical analysis; hence this study was confined to boys.

From the baseline sample of 500 boys, 254 participated in the age 22 follow-up. The remainder from the baseline sample of 500 either declined participation (154) or had not yet attained 22 years of age (92) at the time of this report prepared. The diagnosis was by a clinical committee following a review of the SCID administered at age 22 (Spitzer et al., 1987). Table 1 presents the results of comparisons between retained and attrited subjects at the time of baseline evaluation. As can be seen, IQ was higher in the retained subjects; however, both groups scored in the normal range. The scores on a predictor variable (TLI)

and other important sample characteristics were not different between boys at age 10–12 who either participated or did not participate in the age 22 follow-up.

2.2 Instrumentation

2.2.1 Transmissible Liability Index (TLI) (age 10–12)—Transmissible risk, defined as the component of phenotypic variance associated with SUD liability that is correlated across generations, was measured by the *Transmissible Liability Index (TLI)*. The rationale for and method of deriving the TLI have been previously described (Kirisci et al., 2009; Vanyukov et al., 2003a,b; Vanyukov et al., 2009). Specifically, the TLI, a continuous scale, is derived using item response theory and family/high-risk design from psychological characteristics associated with transmissible risk for all categories of SUD. Notably, genetic factors account for between 75–85% of TLI variance (Vanyukov et al., 2009; Hicks et al., this issue). Moreover, a modified TLI derived from variables in the National Epidemiological Survey of Alcohol and Related Conditions is a significant predictor of all DSM-IV categories of SUD (Ridenour et al., 2011). Internal reliability of the TLI exceeds 0.90, indicating that transmissible risk for the variety of SUDs comprises a unidimensional trait. The 45 items comprising the TLI, listed in previous publications (Kirisci et al., 2009; Vanyukov et al., 2009), reflect broadly the features associated with psychological self-regulation, and accordingly, encompass primarily indicators of impulse control, emotion modulation, and attention.

2.2.2 Peer Milieu Index (age 16)—The *Peer Milieu Index* (PMI) measures adherence to social mores by the friendship network. The questionnaire was composed of items having face validity (e.g., “Were there any children in your group of friends of which your parents disapproved (last 6 months)?’ and “How many of your friends obey school rules?”) from the *Child Report on Peer Environment* (Center for Education and Drug Abuse Research, 1989), *Conventional Activities of Friends Scale* (Loeber et al., 1998), *Opportunity/Resistance Scale* (Loeber et al., 1998), *Parents and Peers Scale* (Loeber et al., 1998), and *Peer Delinquency Scale* (Loeber et al., 1998). Prior research has shown that the PMI (age 16) is psychometrically sound and predicts cannabis use disorder at age 22 (Feske et al., 2008). Alpha coefficient is .80.

2.2.3 Alcohol, tobacco and marijuana use (age 10–22)—The central premise of the gateway hypothesis is that consumption of legal drugs invariantly precedes marijuana consumption (Kandel and Yamaguchi, 1999). Whether this order has practical ramifications was determined by analyzing the contribution of the substance use initiation order coded as a binary variable (“gateway” sequence - alcohol and/or tobacco use precedes cannabis use; or the reverse sequence - cannabis use precedes alcohol and/or tobacco use) to risk for developing cannabis use disorder. The self-report *Substance Use History Questionnaire*, developed at the Center for Education and Drug Abuse Research (CEDAR), was administered to ascertain age of onset (measured in postnatal months) of alcohol, tobacco, and cannabis use.

2.2.4 Cannabis Use Disorder—Diagnostic formulation was conducted when the boys attained 22 years of age using an expanded version of the Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al., 1987). Questions were added to the SCID to more fully characterize antisocial and substance use behavior (Clark et al., 2001). The results of the SCID, in conjunction with medical, legal, psychiatric, and social history information obtained from official records and other questionnaires were reviewed by a clinical committee consisting of a psychiatrist certified in addiction psychiatry (chair), another psychiatrist or clinical psychologist, and the clinical associates who conducted the interviews. Following review of all information, the committee assigned “best estimate”

lifetime diagnoses (Leckman et al., 1982). DSM-III-R criteria were used because this longitudinal project was initiated prior to publication of the DSM-IV manual. The outcome variable was lifetime cannabis use disorder (abuse or dependence).

2.3 Procedure

Written assent and written informed consent were obtained respectively from the boys (age 10–12 and 16) and their parents prior to administering the research protocols. Informed consent was obtained from the boys prior to the follow-up assessment conducted at age 22. The research protocols and procedures for obtaining informed consent have been approved annually since 1990 by the University of Pittsburgh Institutional Review Board. Privacy was additionally protected by a *Certificate of Confidentiality* issued by the National Institute on Drug Abuse. Breath alcohol and urine drug screens were performed before the test session to ensure that the results were not confounded by the acute effects of alcohol or drugs. A positive result required rescheduling the participant. The assessments were individually conducted by experienced master-level research associates in a sound attenuated room. The questionnaires, formatted for scoring using optical scan procedures, were reviewed for completeness after the test session. Prior to discharge from the laboratory, the participants were debriefed and compensated for their time.

2.4 Statistical Analysis

Path analysis with dichotomous outcome was conducted to model the trajectory to cannabis use disorder taking into account transmissible liability (TLI, age 10–12), peer milieu during mid-adolescence (PMI, age 16), and cannabis use disorder (age 22) and the order of drug use initiation ("gateway" or reverse). The model parameters were estimated using Mplus (Muthén and Muthén, 2001). Mplus uses the weighted least square parameter estimation method with diagonal weight matrix with robust standard errors. Four indices of model fit were used: the χ^2 goodness-of-fit index, root mean square error approximation (RMSEA), comparative fit index (CFI), and Tucker-Lewis index (TL). A non-significant χ^2 value ($p \geq .05$) indicates that the data are consistent with the model. RMSEA values greater than .08 reflect poor model-data fit, values between .05 – .08 indicate acceptable fit, and values of less than .05 reflect good fit (MacCallum et al., 2004). For the CFI and TL, values greater than .90 and .95 indicate good model fit (Loehlin, 2004).

Mediated paths were tested using the method described by Sobel (1982) using the following formula implemented in Mplus: $z=b_1b_2/\sqrt{b_2^2\sigma_{b_1}^2+b_1^2\sigma_{b_2}^2}$, where b_1 is the regression coefficient between predictor and mediator, b_2 is the regression coefficient between mediator and dependent variable, and σ^2 is the square of the estimate of the standard error of the corresponding regression coefficient. All of the variables used in the path analysis were manifest variables.

The difference in pseudo-R^2 between the full and reduced models was used to evaluate the sequence's contribution to the explanatory power of the model for the disorder outcome beyond the contribution of socialization.

3. Results

In the sample of 254 boys studied, 95 developed cannabis use disorder by age 22. Out of the latter, 76 (80%) conformed to the "gateway" sequence and 19 (20%, and 7.5% of the entire sample) exhibited the reverse sequence (cannabis before alcohol use), in contravention to the gateway hypothesis "requirement" of licit substance use before progressing to marijuana use (Kandel and Yamaguchi, 1999). Regardless of the disorder diagnosis, there were no non-users of alcohol/tobacco among individuals who used marijuana (before or after alcohol/

tobacco use initiation), but among alcohol/tobacco users in this sample, 27% never used marijuana. The subsample evincing both alcohol/tobacco and marijuana use (n=171) was used for the analysis of the contribution of the order of use initiation in the risk for cannabis use disorder.

Figure 1 presents the results of the analysis. Only significant paths, with corresponding standardized path coefficients (partial regression coefficients) are depicted. The model fits well (please see fit indices shown in the figure).

As can be seen, the Transmissible Liability Index (TLI) at age 10–12 predicts peer deviance at age 16 (path coefficient $\beta = .24$; $p < 0.001$), which, in turn, predicts absence or presence of cannabis use disorder by age 22 ($\beta = .40$; $p < 0.001$). Whereas the TLI is predictive of CUD diagnosis in bivariate analysis (OR = 1.82; 95% CI: 1.13–2.94), this relationship is entirely mediated by peer deviance (PMI), with a highly significant indirect path ($p = 0.001$). There is no significant relationship between the sequence of drug use initiation and the other independent variables. The association between the sequence variable and the risk for CUD, with the reverse (non-“gateway”) sequence tending to be related to a higher risk for the disorder, does not reach significance either ($p = 0.054$), Accordingly, dropping the sequence variable from the model does not result in an appreciable change in its explanatory power for the more parsimonious model: the pseudo-R^2 changes nonsignificantly from 40 to 37%.

4. Discussion

Non-normative socialization mediates the association of transmissible SUD risk and cannabis use disorder by young adulthood. In effect, affiliation with socially deviant peers in adolescence is an intermediate outcome linking transmissible risk and cannabis use disorder. These findings indicate that the psychological dispositions underlying transmissible risk bias the ontogenetic trajectory to low compliance with authority and subsequently affiliating with norm-violating youths presaging cannabis use disorder. Considering that TLI is highly heritable (Vanyukov et al., 2009; Hicks et al., this issue), as well as the mediation of the TLI-CUD risk relationship by the PMI, the data suggests that these relationships are indicative of the active genotype-environment correlation (Scarr and McCartney, 1983) augmenting addiction risk.

The sequence of drug use initiation – whether “gateway” or reverse - does not add information for understanding the development of cannabis use disorder. The irrelevance of the sequence for the disorder risk corresponds to its unrelatedness to the mechanisms of addiction, apart from drug use per se that is obviously a necessary (but not sufficient) condition. The lack of the sequence’s upstream or downstream mechanistic associations is consistent with its opportunistic character, whereas this notion is explicitly rejected by the gateway hypothesis (Kandel, 2002). The differences between the prevalences of alcohol/tobacco use among marijuana users and of marijuana use among alcohol/tobacco users are also in conformance with the higher availability of alcohol/tobacco. Even though alcohol/tobacco use is illegal for children, this legal obstacle is conditional on age rather than virtually absolute as in the case of marijuana and other illicit drugs, which can contribute to the differences in the availability of respective substances and in the mechanisms involved in behaviors needed to procure these substances.

These mechanisms, however, do not seem to be related to those that are involved in the risk for addiction. Indeed, this is consistent with the fact that the gateway sequencing hypothesis does not extend to disorders, but deals with the order of drug use initiation only. Nevertheless, the finding that this order is not related to addiction risk is relevant because the gateway hypothesis has considerably influenced policy and interventions ultimately targeting addiction.

Mediation of the relationship between addiction risk measured in children and their CUD diagnosis as adults by peer deviance, an "environmental" variable, points to social behavior as a mechanism of realization of the transmissible SUD risk. This behavior is indeed non-specific in respect to drugs, apart from clustering of respective addictions created by the social boundaries of the classification of substances into licit and illicit. The profound influence of social factors and thus social behavior is illustrated by the fact that this clustering involves *genetic* causes of variation in liabilities to addictions, resulting in two distinct albeit highly correlated respective sources of genetic variance, each common to all disorders within the two groups (Kendler et al., 2007).

The results of this study are consistent with our prior findings suggesting the association of affiliation with (deviant) peers (and earlier detachment from parents) with elevated SUD risk related to parental SUD burden (Kirillova et al., 2008), and the role of parenting in the risk for SUD (Vanyukov et al., 2007) pertaining to socialization mechanisms. Importantly, the relationship of parenting with the risk for frequent SUD precursors – disruptive behavior disorders – as well as for SUD was moderated by variation in the *MAOA* gene, shown previously to influence the relationship between parenting and antisocial behavior (Caspi et al., 2002). The role of socialization in the mediation of transmissibility or, more narrowly, heritability of SUD liability is also supported by our recent finding of the association between the vasopressin receptor *AVPR1A* gene and SUD risk (Maher et al., 2011). This gene has been shown to influence variation in social behavior, including attachment and bonding, in humans and other animals (reviewed in Insel, 2010). In line with those findings, the *AVPR1A*-SUD liability association in our study was shown to be mediated by the characteristics of marital satisfaction/bonding. This association was also dependent on sex (nonsignificant in females), consistent with sex dimorphism of the roles of vasopressin and oxytocin in mate behavior and bonding.

Involvement with parents, needed to instill prosocial/cooperative behavior (Landry et al., 2006; Landry et al., 2008) *and prevent deviant peer affiliation*, ideally should commence during parent-infant bonding when the baby signals cooperative intent using pointing gestures (Tomasello et al., 2007). Notably, performing tasks collaboratively with the mother is related to better physiological regulation compared to performing tasks alone (Calkins et al., 2008), and parental withdrawal from a collaborative task causes the child to attempt to re-engage the parent (Tomasello and Herman, 2010). Hence, *a* synchronous parent-child relationship that provides opportunity for sustained parental mentoring is essential for inculcating prosocial behavior. Considering that cooperative behavior has lasting positive impact on social adjustment (Gauvin, 1992), it may, therefore, be important to emphasize this developmental outcome in childhood for prevention of SUD. The extent to which suboptimal parenting and child's characteristics contribute to this developmental outcome in youths who subsequently use drugs and develop SUD remains to be delineated.

Consolidating a cooperative disposition in children who are at high risk for SUD is, however, beset by major obstacles. In particular, prevention interventions need to simultaneously take into account conjoint individual and contextual influences concomitant to phenotype environment correlation. Because genetic factors largely account for transmissibility of liability for SUD (Vanyukov et al., 2009; Hicks et al., this issue), children who are at high risk likely have biological parents who similarly possess the psychological characteristics associated with high transmissible risk, namely behavior undercontrol and emotion dysregulation. These characteristics in parents militate against establishing a synchronous relationship with their children. Moreover, parents having high transmissible risk are likely to qualify for SUD diagnosis that frequently occur in conjunction with psychiatric disorders and social maladjustment. Consequently, children who are at high transmissible risk for SUD have the difficult challenge of acquiring cooperative behavior

because disruptive parental behavior hampers establishing a sustained synchronous relationship with their offspring. Furthermore, an adverse sociodemographic environment is more likely to be present in youths who are at high transmissible risk for SUD. For example, socioeconomic decline occurs commonly in adults with SUD. Consequently, children who are at high transmissible risk are more likely to domicile in neighborhoods where abusable substances are readily available (Crum et al., 1996), and violation of social mores and laws is tolerated (Sampson et al., 1997). In fact, such violation, in contrast to normative behavior, may incur benefits in this environment, being an adjustment to it (Mealey, 1995; Vanyukov, 2004). It is important to emphasize that cannabis using youths are inclined toward affiliating with peers who similarly do not adhere to the law, thereby reflecting the influence of social selection. Cannabis use is an overt indicator of a certain degree and direction of behavioral deviation, facilitating homophily (affiliation with phenotypically similar individuals) for such deviations, with potential population genetic effects (Vanyukov et al., this issue). This may offset the benefits of family-focused interventions. Similarly, effectiveness of community-focused interventions may be negated by an adverse family environment. Likewise, eliminating the influence of socially deviant peers may not alleviate risk associated with adverse family or neighborhood environment. In effect, youths having high transmissible liability for SUD are also more likely to be exposed to multiple adverse environments (family, peers, neighborhood) that potentiate non-normative socialization.

This study adds to an accumulating empirical literature refuting a central premise of the gateway hypothesis. Specifically, it was shown that use of a legal substance, at least for adults, frequently does not lead to using an illegal drug as claimed by Kandel and Yamaguchi (1999). Twenty percent of the affected sample used cannabis before alcohol. Other authors have reported even higher rates of non-conformance with the gateway sequence. Young et al. (1995), for example, observed that cannabis was the first drug used by 42% of delinquent youths. Golub and Johnson (2002) reported that cocaine was used before marijuana in 75% of inner city youths. Mackesy-Amiti et al. (1997) and Blaze-Temple and Lo (1992) similarly found that hard drugs were used by a sizable portion of their sample before beginning consumption of marijuana. These findings strongly disconfirm the tenet that the order of drugs used comprises an invariant developmental process. Furthermore, this study shows that the order of substance use (“gateway” or otherwise) has no bearing on clinical outcome.

Several limitations of this study are noted. Importantly, the sample was confined to boys. Girls demonstrate greater willingness for cooperative behavior and are more socially responsive than boys (Forman and Kochanska, 2001). Hence, the trajectory to cannabis use disorder described herein may not apply to girls. Moreover, it should be pointed out that this study was confined to evaluating the role of transmissible SUD risk in socialization. Future research needs to more comprehensively model socialization and development of cannabis use disorder by also including a measure of non-transmissible risk. Results of a preliminary study points to the plausibility of developing a measure of non-transmissible risk for SUD (Kirisci et al., 2009). Upon finalization of development of this measure, the mediating role of socialization on both the transmissible and non-transmissible components of SUD risk will be more fully understood. Also, it should be noted that the model tested was confined to affiliation with deviant peers as a mediator of transmissible risk during childhood and a predictor of cannabis use disorder. This pathway most likely captures only one facet of the etiological trajectory to cannabis use disorder. Lastly, it is recognized that the outcome variable in this study was circumscribed to cannabis use disorder. Although this clinical outcome pertains to the most frequently used illegal drug, it remains to ascertain whether non-normative socialization similarly accounts for the development of other SUDs.

In conclusion, this study demonstrated that non-normative socialization mediates the association between transmissible risk and development of cannabis use disorder in young adulthood. The sequence of drug transitions specified in the gateway hypothesis does not contribute information for understanding the etiology of cannabis use disorder.

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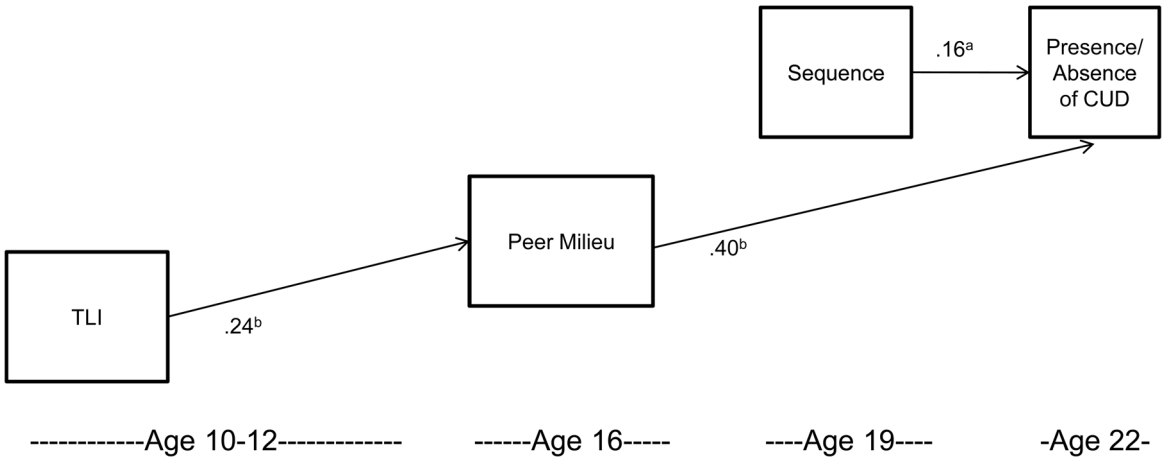

Model fit: χ^2=.30, df=1, p=.58, CFI=.99, TLI=.99, RMSEA<.001
a: p=.054, b: p<.001

Figure 1.
Longitudinal path analysis of the relationships among the order of drug use initiation, transmissible liability to addiction, peer deviance and the diagnosis of cannabis use disorder

Table 1

Personal and demographic characteristics of attrited and retained segments of the sample

	Attrited N = 154 Mean (sd)	**Retained N=254 Mean (sd)**	**F**	**p**
Socioeconomic Status[1]	38.83 (12.87)	41.10 (13.75)	2.74	.098
Full Scale WISC-III-R IQ	104.10 (15.61)	110.37 (16.20)	14.73	<.001
Grade in school	4.56 (1.02)	4.59 (1.13)	.10	.746
Transmissible Liability Index (TLI)	.08 (1.08)	−0.6 (1.02)	1.73	.19
European American	73.4%	75.6%		
African American	26.6%	24.4%	.25	.618

[1]Hollingshead criteria