



# Externalizing behavior and emotion dysregulation are indicators of transmissible risk for substance use disorder



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## HIGHLIGHTS

- TLI evaluates the component of SUD risk having intergenerational continuity.
- Transmissible liability index (TLI) measured at ages 10–12 and 16 predicts SUD, number of SUDs and severity of SUD at age 22 after controlling for the influence of externalizing behavior and emotion dysregulation.
- This study provides further support for using TLI to objectively quantify SUD risk but potentially also has practical utility for detecting youths requiring prevention intervention.

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## ABSTRACT

**Background:** Psychological items discriminating children of fathers diagnosed with an illicit drug-related substance use disorder and normal controls are indicators of a unidimensional construct termed transmissible liability index (TLI) (Vanyukov et al., 2009). TLI is a highly heritable (Vanyukov et al., 2009; Hicks, Iacono, McGue, 2012) and valid (Vanyukov et al., 2009; Hicks et al., 2009; Kirisci et al., 2013a) measure of childhood liability to substance use disorders (SUDs).

**Aims:** This longitudinal study determined whether TLI has incremental validity for predicting SUD beyond commonly measured psychological indicators of risk.

**Methods:** TLI and measures of executive cognitive capacity, emotion dysregulation and externalizing disturbance were administered to boys at ages 10–12 and 16. SUD outcome determined at age 22 was assessed as (1) any SUD, (2) the number of drug-specific SUDs, and (3) SUD severity.

**Results:** TLI predicted SUD beyond the contribution of measures of emotion dysregulation, executive cognitive capacity and externalizing disturbance. The association of emotion dysregulation and externalizing behavior at ages 10–12 and 16 with SUD at age 22 was also reduced to non-significance after controlling for transmissible risk measured by TLI.

**Conclusions:** TLI's incremental validity beyond these latter indicators of risk points to its utility for identifying vulnerable youths requiring intervention.

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## 1. Introduction

Substance use disorder (SUD) in parents is well known to be associated with psychological dysregulation in their children (Vanyukov et al., 2009). Diverse characteristics have been shown to comprise indicators of a unidimensional construct corresponding to the transmissible component (correlated between generations) of non-drug-specific liability to SUD (Vanyukov et al., 2009). This construct, termed the *transmissible liability index (TLI)*, has been shown to be a valid childhood measure of liability for SUD, predicting the age of substance use initiation, SUD

risk, and the rate of SUD development (Hicks, Iacono, & McGue, 2012; Kirisci et al., 2013a; Vanyukov et al., 2009). TLI is highly heritable (Hicks et al., 2012; Vanyukov et al., 2009), consistent with its derivation as a measure of transmissible liability. Moreover, TLI predicts all DSM-IV SUD categories (Ridenour, Tarter, Kirisci, & Vanyukov, 2011), consistent with results demonstrating that genetic and phenotypic commonalities among substance-specific SUD liabilities (Kendler, Jacobson, Prescott, & Neale, 2003a; Kendler, Prescott, Myers, & Neale, 2003b; Tsuang et al., 1998). Further indicating that TLI is a measure of common (general) SUD liability, it has been shown that cannabis use during adolescence mediates the association between TLI score in childhood and diagnosis of alcohol use disorder in adulthood, and alcohol use mediates the association between TLI and cannabis use disorder (Hicks et al., 2012).

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Indeed, the order of drug use initiation specified in the “gateway hypothesis” (Kandel & Yamaguchi, 2002) is less informative than TLI for modeling SUD development between childhood and adulthood (Tarter et al., 2012a).

Investigations exploring the utility of TLI in the elucidation of SUD etiology have yielded promising results. For example, youths scoring high on TLI exhibit a linear increase in risk following the first cannabis use that subsequently culminates in cannabis disorder, whereas youths who score low on TLI exhibit no change in risk after onset of consumption (Kirisci, Tarter, Ridenour, Reynolds, & Vanyukov, 2013b). The extent to which this increment in severity reflects a differentially strong reinforcing experience following substance use among high-risk youths or the influence of substance using peers on socialization remains to be determined. Notably, non-normative socialization mediates the association between TLI scores in childhood and SUD in adulthood (Tarter et al., 2011) and the TLI score in childhood predicts elevated testosterone level and attenuated cortisol reactivity in mid-adolescence presaging SUD in adulthood (Tarter et al., 2013) suggesting that both pharmacological and social factors potentiate transmissible risk leading to development of SUD. In sum, the emerging research demonstrates the utility of the TLI for elucidating the mechanisms and etiological pathways to SUD.

Whereas these findings indicate that TLI measures transmissible risk for SUD and is heuristic for researching etiology, the relationship between TLI and psychological processes commonly reported to contribute to SUD liability has not been investigated. Accordingly, this study evaluated the association between TLI and psychological processes most often implicated in SUD risk, pertaining to cognition, emotion and behavior, namely executive cognitive capacity, emotion dysregulation and externalizing disturbance. It was hypothesized that these latter variables are facets of SUD liability measured by TLI. Hence, the hypothesis was tested that TLI in childhood and adolescence not only accounts for the relationships of these variables with the SUD outcome, but predicts that outcome over and above their contribution.

## 2. Methods

### 2.1. Participants

The participants in this study were part of a longitudinal study of the etiology of SUD consequent to use of illicit drugs, conducted under the aegis of the NIDA-funded Center for Education and Drug Abuse Research (CEDAR) established in 1990. Using the family/high-risk paradigm, boys (N = 490) were enrolled when they were 10–12 years of age and followed up at ages 16 and 22. The boys are currently undergoing assessments until age 30, at which time the project will be completed. Because comprehensive protocols are administered, the subjects were enrolled over many years, hence the sample is in varying stages of the follow-up. This report pertains to the portion of the sample that has attained age 22 because insufficient subjects have yet to be followed up beyond that point to enable valid statistical analysis. The sample was confined to boys because TLI was under development for girls. Recruitment was conducted

through the biological fathers (probands) who either qualified for DSM-III-R lifetime SUD diagnosis consequent to consumption of an illegal compound (N = 249) or had no adult psychiatric disorder (N = 241). The DSM-III-R criteria were used to ascertain the sample because this longitudinal project was initiated prior to publication of the DSM-IV. Multiple recruitment sources were used to minimize bias that could potentially occur if all of the subjects were recruited from one source. The SUD fathers were recruited using public service announcements, advertisement and a market research firm that conducted random-digit dialing. Approximately 25% of the SUD + men were accrued from treatment facilities. Proband fathers without SUD were recruited using the same procedures except that none were obtained from treatment facilities.

Boys were excluded from the study if they had a lifetime history of psychosis, chronic illness, neurological disability, uncorrectable sensory handicap, Full Scale IQ below 80 on the WISC-III-R, or signs of fetal alcohol effects determined upon physical examination conducted by a trained registered nurse.

Table 1 presents the baseline personal and demographic characteristics of the sample (N = 305) and those who attrited (N = 185). Attrition, defined as either a failure to locate the individual or refusal to participate at the age 22 evaluation, was 38%. As can be seen, the participants who attrited scored about three points lower on the Hollingshead Index of Socioeconomic Status (SES) and almost seven points lower on Full Scale IQ measured by the Wechsler Intelligence Scale for Children (WISC-III-R). No differences were observed between the retained and attrited segments on TLI (the predictor variable), grade in school, or ethnicity.

### 2.2. Measures

#### 2.2.1. Transmissible liability index (TLI) (ages 10–12 and 16)

TLI was derived using a previously described multistage procedure (Vanyukov et al., 2003a,b). First, investigators at the Center for Education and Drug Abuse Research (CEDAR) catalogued the psychological traits (N = 34) most frequently reported in the empirical literature to be associated with risk for SUD. Next, items (N = 441) from a large battery of psychological questionnaires and psychiatric interviews administered to the parents, teachers and the boys contained in CEDAR's database were assigned to these traits. Exploratory factor analysis (EFA) was performed on the items in each provisional trait. Items having loading >.4 were retained and submitted to confirmatory factor analysis (CFA). The constructs that satisfied the criterion of unidimensionality were contrasted between boys having SUD + and SUD – fathers. The items contained in the thirteen constructs that discriminated the sons in these two groups were then submitted to EFA and further pruning if they had loading below .4. CFA was conducted on the remaining items to verify the unidimensionality of the resulting construct. Lastly, item response theory (IRT) was conducted to calibrate the items, estimating their item threshold and item discrimination parameters. The threshold parameter relates the probability of endorsing a particular characteristic (item) to severity of SUD liability whereas the discrimination parameter specifies the ability of the item to differentiate individuals according to severity of SUD liability. In sum, from a roster

**Table 1**  
Baseline (age 10–12) Characteristics of retained and attrited segments of the sample.

	Retained (n = 305)		Attrited (n = 185)		F	p
	Mean	SD	Mean	SD		
School grade	4.57	1.12	4.51	1.01	.28	.594
Socioeconomic status	41.95	13.50	38.89	12.84	6.14	.014
Full Scale IQ	110.30	15.82	103.58	15.21	21.43	<.001
	n	%	n	%	$\chi^2$	p
White	232	76.1	137	74.1	1.09	.580
Black	65	21.3	40	21.6		
Other	8	2.6	8	4.3		
SUD + parent	147	48.2	94	50.8	.31	.575
SUD – parent	158	51.8	91	49.2		

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