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Neurobehavior disinhibition, parental substance use disorder, neighborhood quality and development of cannabis use disorder in boys[☆]

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Abstract

This prospective investigation examined the contribution of neighborhood context and neurobehavior disinhibition to the association between substance use disorder (SUD) in parents and cannabis use disorder in their sons. It was hypothesized that both neighborhood context and son's neurobehavior disinhibition mediate this association. Two hundred and sixteen boys were tracked from ages 10–12 to age 22. The extent to which neighborhood context and neurobehavior disinhibition mediate the association between parental SUD and son's cannabis use disorder was evaluated using structural equation modeling. The best fitting model positioned neighborhood context and neurobehavior disinhibition as mediators of the association between parental SUD and cannabis use disorder in sons. Neurobehavior disinhibition also was a mediator of the association between neighborhood context and son's cannabis use. The implications of this pattern of association between parental SUD, neighborhood context and individual risk for SUD for improving prevention are discussed.

Keywords

Cannabis; Disinhibition; Neighborhood; Substance use disorder; Familial transmission; Structural equations modeling

1. Introduction

A wide spectrum of illegal and socially non-normative behaviors occur with high prevalence in neighborhoods that have a high rate of poverty and unemployment (Laumann et al., 1994; Sampson et al., 1997). Low collective efficacy among residents of disadvantaged neighborhoods, in conjunction with greater opportunities for socially proscribed behaviors,

[☆]Supplementary information for this article is available. Please see Appendix A for more information.

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Contributors

Authors Tarter, Vanyukov, Mezzich, Reynolds, and Kirisci designed the study and the protocol. Authors Tarter, Ridenour, Reynolds, Mezzich, and Vanyukov conducted literature searches and summaries of previous related work. Dr. Ridenour undertook the statistical analysis, and authors Ridenour and Tarter wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

None of the authors have a conflict of interest pertaining to this investigation.

have been theorized to promote tolerance of illegal behavior, including selling and using drugs (Galea et al., 2004; Schuck and Widom, 2005). Notably, offer rates for cocaine have been reported to be up to six times higher in 6–8th grade youths in severely disadvantaged neighborhoods (Crum et al., 1996). Illegal drugs are not only more readily available in poor neighborhoods (Crum et al., 1996); there are also opportunities for consumption outside public view and police surveillance such as in abandoned buildings, concealed alleys, and in houses where drugs are bought and used in a communal setting (e.g. “crack house”).

Attention disturbances and low behavior control, even when measured neurophysiologically, are more common among youths residing in a disadvantaged neighborhood (Manuck et al., 2005). A higher concentration of neurotoxins, particularly lead, which impair cognitive and behavioral development, has been frequently reported in poor neighborhoods (CDC, 1997). The same psychological disturbances are, however, also evinced by youths prior to development of substance use disorder (SUD) (Cole et al., 1993; Kirisci et al., 2005; Mezzich et al., 2007a) and have been reported to comprise transmissible features of SUD liability (Button et al., 2006; Vanyukov et al., 2007). Inasmuch as SUD is linked to social decline (Buu et al., 2007), a higher proportion of children residing in poor neighborhoods have one or more parents with SUD compared to youths living in more optimal neighborhoods. These findings raise the prospect that neighborhood context might operate as a mediator of the association between parental SUD and child’s risk for SUD.

Research conducted to date has not disaggregated the relative contribution of parental SUD, neighborhood quality, and child’s psychological dysregulation on the development of SUD. Each of these correlated factors predict SUD; however, their pattern of interrelationships on development of SUD has not been studied. Fig. 1 depicts the array of these variables and their potential patterns of relationships within eight models devised to illuminate the best fitting and parsimonious characterization of the development of cannabis use disorder taking into account parental SUD, neighborhood quality and individual susceptibility.

Model 1

Unmediated Model. In this model, neighborhood quality (NQ) and neurobehavior disinhibition (ND) do not contribute to the prediction of son’s cannabis use disorder (CD) beyond the contribution of parental SUD.

Model 2

Full Model. In this model, each variable occurring earlier in the development of CD directly predicts all subsequent variables (i.e., CD depends on all variables).

Model 3

Neurobehavior disinhibition indirectly leads to cannabis use disorder. In this model, ND contributes to cannabis use (CU), but not CD, beyond the contribution of other variables.

Model 4

Neurobehavior disinhibition does not predict cannabis use. In this model, ND does not contribute to CU, but does contribute to CD beyond use of cannabis.

Model 5

Neurobehavior disinhibition does not predict cannabis use or disorder. This model asserts that ND does not predict CU or CD beyond the contribution of NQ and parental SUD.

Model 6

Neighborhood quality indirectly leads to cannabis use. In this model, NQ does not directly predict CU; rather, its contribution is through ND.

Model 7

Neighborhood Quality is Not a Predictor. In this model, NQ is predicted by parental SUD; however, it is not a predictor of ND or CU.

Model 8

Parental SUD indirectly leads to cannabis use and disorder. This model asserts that the contribution to CU by parental SUD is accounted for by both NQ and ND (i.e., there are not direct paths between parental SUD to CU or to CD).

In summary, this study seeks to shed light on the pathway to CD in a longitudinal study of boys tracked from late childhood (ages 10–12) to young adulthood (age 22) taking into account parental SUD history, NQ and severity of ND. Based on previous reports indicating that psychological dysregulation (including ND) may be a transmissible component of SUD risk (McGue et al., 2001; Silberg et al., 2003), it was hypothesized that severity of ND (capturing the cognitive, emotional and behavioral components of dysregulation) mediates the association between poor NQ and CD. In addition, based on the finding that SUD may lead to downward social mobility, it was theorized that NQ mediates the association between parental SUD and severity of ND in male offspring.

2. Methods**2.1. Subjects**

The sample consisted of 22 year old men who have been enrolled since age 10–12 in a longitudinal study conducted by the Center for Education and Drug Abuse Research. Exclusion criteria included a history of neurological injury, chronic or life threatening illness, physical disability, uncorrectable sensory impairment, full scale WISC-III-R IQ less than 80 and evidence of fetal alcohol effects determined upon physical examination conducted by a trained nurse.

2.2. Recruitment plan

The participants were recruited through their biological fathers who either qualified for a DSM-III-R lifetime diagnosis of SUD consequent to use of illegal drugs or had no axis I psychiatric disorder. These two subgroups of sons, respectively, are labeled in this study as “high average risk” and “low average risk” subgroups, consistent with the concepts of Faraone and Tsuang (1995). This group assignment was unchanged during the course of the study as none of the baseline low average risk fathers developed SUD. The attrition rate from baseline (age 10–12) to follow-up (age 22) was 7.7%. As can be seen in Table 1, there are no differences between retained and attrited subjects on key personal and demographic characteristics, including the two predictor variables, NQ and ND.

Because the population-level occurrence of illegal-drug SUD may be as low as 10% (Compton et al., 2007), it is difficult to locate men with this diagnosis who have a current or past spouse and also have a healthy biological child between 10–12 years of age, all willing to participate in research of this type. Several recruitment strategies were thus employed, including random digit dialing conducted by a market research firm, advertising in print media and public service announcements in electronic media. Approximately 20% of the men with SUD were recruited after discharge from treatment. The same procedures were used to recruit men without SUD

except that none were accrued from treatment facilities. Previous analyses have revealed that the men with and without SUD map closely to their respective populations (Tarter and Vanyukov, 2001).

In accord with an IRB-approved protocol, the goals of the study were described to each family member at the outset of the test session. Next, the father, mother and their son were escorted to private rooms where written informed consent was obtained from the parents and written assent from the son. The boys and their parents were additionally informed that their privacy was protected by a Certificate of Confidentiality issued by the National Institute on Drug Abuse. Special effort was made to ensure that the boys were not coerced to participate in the study. Urine and breath samples were collected and analyzed before commencing the research protocol to ensure that performance was not influenced by the acute effects of drugs or alcohol. The protocol was administered in fixed order. Following completion of the evaluation, each family member was debriefed and paid for their time and travel expenses.

2.3. Instrumentation and assessments

2.3.1. Substance use disorder severity in parents (offspring ages 10–12)—An expanded version of the *Structured Clinical Interview for DSM-III-R* (Spitzer et al., 1987) was administered to each parent at the time the boys were enrolled. SUD diagnoses were consensually formulated in a clinical conference chaired by a psychiatrist certified in addictions psychiatry, attended by another psychiatrist or psychologist and the clinical associates who conducted the interviews. SUD severity, indexed as a continuous latent variable, was derived by first clarifying that the various SUD diagnoses are indicators of a unidimensional trait using confirmatory factor analysis followed by application of item response theory analysis to specify the location of each diagnosis and combination of SUD diagnoses on the SUD severity trait (Kirisici et al., 2006; Vanyukov et al., 2003).

2.3.2. Neighborhood quality (offspring ages 10–12)—Census data were used to create two subscales of NQ: *concentrated disadvantage* and *residential instability* (Browning and Olinger-Wilbon, 2003; Sampson et al., 1997; Schuck and Widom, 2005). The concentrated disadvantage variable was derived by computing the mean of the proportion of households in the neighborhood having the following characteristics: (1) total income below poverty; (2) a female as the head; (3) receiving public assistance; (4) having an unemployed parent; and (5) residents under 18 years of age. The standardized alpha coefficient for this construct was 0.95. The residential instability variable was derived as the mean of two inter-correlated variables ($r = 0.28, p < 0.001$), proportion of (a) households in the neighborhood domiciled by residents who moved since the last census and (b) vacant houses. Because the concentrated disadvantage and residential instability variables were correlated ($r = 0.52, p < 0.001$), a combined mean score of concentrated disadvantage and residential instability was used to index NQ. The standardized alpha coefficient of the combined variable was 0.87.

2.3.3. Neurobehavior disinhibition (at age 10–12)—The score on the ND trait has been previously shown to predict occurrence of SUD between childhood and adulthood as well as psychosocial characteristics during adolescence that in turn predict SUD (Habeych et al., 2005; Kirisici et al., 2005). In addition, this trait has excellent psychometric properties (Tarter et al., 2003; Mezzich et al., 2007b), as measured via a second order factor of the component processes, consisting of tests of executive cognitive function, emotion modulation and behavior control.

2.3.4. Cannabis use (at age 19)—Section 1A of the revised *Drug Use Screening Inventory* (Tarter, 1990) documented frequency of CU during the 30 days preceding the age

19 assessment. The distribution among offspring was 56.6% (no use), 12.7% (1–2 times), 11.0% (3–9 times), 7.0% (10–19 times) and 12.7% (20+ times).

2.3.5. Cannabis use disorder (by age 22)—The same procedure used to formulate diagnoses in the parents was employed for their sons when they attained 22 years of age. However, because the DSM-IV had been published by the time of this outcome, this latter taxonomy was employed. Seventy-one participants qualified for a diagnosis of CD: 35.2% abuse, 45.1% dependence, 19.7% abuse and dependence. In view of findings that these latter categories might not be distinct (Hasin and Grant, 2004; Langenbucher et al., 2004; Ridenour et al., 2005) the outcome variable was a diagnosis of either abuse or dependence.

2.4. Statistical analysis

Descriptive statistics were computed followed by bivariate correlations. Based on the type of data, either product moment, logistic, polyserial or polychoric techniques were employed. Next, MPlus software was used for structural equation modeling to evaluate the eight models described in our introduction (Muthen and Muthen, 2007; version 4.2).

The method of maximum likelihood was used for model estimation, with testing of specific path coefficients and construction of 95% confidence intervals based upon the Wald test. The COUNT option modeled mediators as either a Poisson variable or a zero-inflated Poisson variable (CU). Three fit statistics (likelihood-ratio χ^2 , Akaike's Information Criterion and Bayesian Information Criterion) estimated the fit of competing models to the data.

Bootstrap solutions are not an option when MPlus uses numerical integration (as with Poisson variables), nor are standard delta method tests for indirect effects. Evidence that a variable (M) mediates the association between two other variables (x and y) consists of (a) all three must be associated at the specified alpha value and (b) the bivariate association between x and y (τ) becomes markedly attenuated when M is modeled as a mediator within the x and y pathway (Little et al., 2007; MacKinnon et al., 2007). Within an experimental context, MacKinnon (2000) extended the single delta method (Sobel, 1982) to testing multiple mediators. If the statistical association between parental SUD severity and son's CD was not entirely accounted by the model mediators, the multivariate delta method was used to test each mediator separately (MacKinnon, 2000).

3. Results

Among the 216 sons providing data for the longitudinal models, 17.4% had smoked marijuana within 30 days preceding their age 19 interview; 28.5% qualified for CD by age 22. Other descriptive statistics appear in the *Drug and Alcohol Dependence* online supplement. Because the continuous variables were non-normal, they were analyzed as Poisson or zero-inflated Poisson variables. All bivariate associations between predictors and CD were significant by conventional p -values (Table 2; Panel A). In particular, parental SUD had statistically robust associations with male offspring CD at age 22 (odds ratios for mother and father SUD were 2.1 and 1.5, respectively). Correlations among model variables, also presented in Table 2 (Panel B), reached $p < 0.05$ except for the association between maternal SUD severity and NQ.

3.1. Best fitting model

Notwithstanding the tangible unadjusted odds ratios for the predictive association of parental SUD and offspring CD, the Full Model estimates (path diagram available in the *Drug and Alcohol Dependence* online supplement) are null for direct paths from maternal and paternal SUD severity to CD in male offspring (z -values were -1.12 and 0.29 , respectively), with meditational paths specified for NQ and ND. Under this same model, paths from NQ to son

CU ($z = 0.107$) and CD ($z = -0.47$) were null. Thus, to test the fit of more parsimonious models, the direct paths to son's CD from maternal SUD, paternal SUD and NQ were dropped from all competing models (i.e., fixed to zero).

The Unmediated Model fit the data worse than the other models (Table 3). Compared to the Full Model, two of the more parsimonious models provided equivalent fit to the data: "Neighborhood Quality Indirectly Leads to Cannabis Use" (Model 6, LR $\chi^2 = 0.09$, $df = 1$, $p > 0.05$) and "Parental SUD Indirectly Leads to Cannabis Use and Disorder" (Model 8, LR $\chi^2 = 2.29$, $df = 2$, $p > 0.05$). Compared to "Neighborhood Quality Indirectly to Cannabis Use" (Model 6), "Parental SUD Indirectly Leads to Cannabis Use and Disorder" (Model 8) provided a slightly improved fit to the data, although the likelihood ratio χ^2 vs. previously best fitting model = 2.2, 1 df , was not statistically significant. The more parsimonious "Parental SUD Indirectly Leads to Cannabis Use and Disorder" (Model 8), therefore, qualified as best fitting the data.

The "Parental SUD Indirectly Leads to Cannabis Use and Disorder" model (Model 8, Fig. 2) positions ND in an integral role for development of CD. Specifically, ND in childhood directly predicts use of cannabis 7–9 years later (z -value = 2.31, $p < 0.05$) as well as CD by age 22 above and beyond the CU association (z -value = 1.69, $p = 0.05$). Direct paths to ND were found from NQ, paternal SUD and maternal SUD, but none of these antecedents qualified for direct paths to CU or CD. As such, ND is in a mediational position leading from NQ and parental SUD onwards toward development of CU and CD.

4. Discussion

To recapitulate briefly, this investigation posited that maternal and paternal SUD severity, NQ and ND measured at age 10–12 would predict frequency of recently active CU 7–9 years later and onset of CD by age 22. Structural equation model testing provided support that these latter variables predict son CU and CD. ND was found to account entirely for the association between (a) the antecedents parental SUD and NQ and (b) later son CU. The notion that ND predicts CD over and above an association with CU deserves closer scrutiny. In our data and modeling, we specified the CU construct as recently active use at age 19, whereas CD was cumulative to age 22. As such there remains an open question that we cannot resolve presently: is there a statistically robust association linking ND to the conditional probability of CD, once CU has occurred? What we can envision is an ND–CD association, net of ND's association with CU in the 30 days before the age 19 assessment.

Poor NQ also seems to be related to risk for CD via its association with ND. If our model is correct, one straightforward intervention would address high risk children in disadvantaged neighborhoods as in public housing. In addition, if this model is correct, modification of the adverse aspects of the neighborhood environment that influence ND might have a positive impact on reducing children's risk for CD. Toward this goal, enhancing opportunities for adult supervised prosocial recreation (e.g. parks, community center, etc.) might diminish opportunities to affiliate with other high risk youths, which is associated with propensity for drug use (Gardner et al., 2008; Rosenberg and Anthony, 2001). It also might enable acquisition of self-regulation (Audrain-McGovern et al., 2004; Caldwell, 2004). Albeit untested, hiring high risk youths to work on neighborhood improvement jobs, involving a mentoring (apprentice) relationship, might provide them the opportunity to acquire prosocial attitudes and self-management skills, while also strengthening bonds to NQ. Long-term effects of this type of prosocial participation might include increased personal and community efficacy with enhanced social capital of the neighborhood. Inasmuch as low collective efficacy has been found to be related to higher rates of antisociality and drug use (Sampson and Raudenbush, 1999), engaging high risk youth in a shared goal of neighborhood improvement may yield

long-term commitment to and investment in the community. Alternatively, early intervention to prevent social decline after onset of parent SUD might serve well as an approach to lower SUD risk in their children.

It is noteworthy that, to date, interventions directed at reducing disinhibitory behavior have had only modest effects (e.g., see Derzon et al., 2005; Springer et al., 2004), although exceptions exist (Kellam et al., 2008). These interventions are typically administered in a group setting and involve only a few sessions. Hence, they may lack sufficient impact on modifying behavior, especially among youths with high disinhibition. Moreover, because the components of SUD risk are multifaceted, it would appear important to design interventions that encompass multiple cognitive, emotional and behavioral processes (Tarter et al., 2003). Speculation regarding the particular prevention modality notwithstanding, the results of this study shed light on a possibility that it is important to conjointly target the social context of neighborhood and individual liability.

4.1. Limitations

In addition to those mentioned already, four limitations of this study are noteworthy. First, it is possible that variables not included in the model may have accounted for the pattern of associations. Clearly, there are many facets of disinhibition (Tarter et al., 2003) as well as of the neighborhood which influence children. Future studies thus need to more precisely specify features of the neighborhood that most influence development of ND and subsequent manifestation of CU and CD. It is also noteworthy that the sample was confined to boys. Inasmuch as SUD development differs between genders (Ridenour et al., 2006; Wagner and Anthony, 2007), the relationship between NQ and ND may lead to SUD differently in boys and girls. Third, the high-risk study design may have yielded a sample that limits generalizability of the results although previous analyses have shown that the boys comprising this sample are similar to other samples (Tarter and Vanyukov, 2001). Given the relatively small sample size, the effects reported herein are large enough to have reached statistical significance. Nevertheless, these findings point to need for large scale replication. Finally, with so many constructs at play in models of this type, and with so many coefficients to estimate (or to constrain), the results are advanced as the best and most definitive estimates, based on the models as specified.

4.2. Summary

If our model is correct, ND mediates the association between NQ and CU and CD as well as directly predicts these latter outcomes. These findings underscore the importance of both contextual and individual factors on the risk for CD. Moreover, parental SUD predicts NQ which in turn predicts CD and there may be a stronger link from paternal SUD to son CD (as compared to the corresponding estimated relationship from maternal SUD to son CD). These results, considered in aggregate, help support the now mature concept known as “comprehensive drug abuse prevention programming,” with a multi-prong strategy to prevent CD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drugalcdep.2009.01.009.

Fig. 1.

Eight competing conceptual models of how parental substance use disorder, neurobehavior disinhibition and neighborhood quality contribute to son substance use disorder. *Note:* SUD = substance use disorder. ND = neurobehavioral disinhibition. CU = cannabis use. CD = cannabis use disorder. NQ = neighborhood quality.

Fig. 2. Path diagram results for the best fitting model. *Note:* Path coefficients are raw coefficients (parenthetical values are confidence intervals); *B* designates the standardized coefficient and OR designates the odds ratio predicting Cannabis Use Disorder. (*) Path coefficient *p*-value was statistically greater than zero $p < 0.05$.

Table 1
Comparison of retained and attrited subjects at baseline.

	Retained (n = 216)	Attrited (n = 18)	F	p
Family socioeconomic status	41.5 (14.13)	41.00 (14.03)	0.02	0.88
IQ	111.2 (16.12)	105.7 (13.69)	2.01	0.16
Size of sibship	1.79 (1.11)	1.61 (0.78)	0.43	0.51
Neighborhood Quality Index	0.18 (0.09)	0.16 (0.06)	1.12	0.29
Neurobehavior Disinhibition	51.36 (10.16)	52.30 (12.85)	0.14	0.71
	n	n	Attrited (%)	
Ethnicity				
Caucasian	163	11	6.7	
African-American	46	3	6.5	
Other/biracial	7	4		

Note: Family socioeconomic status was measured using the Hollingshead Index (Hollingshead, 1975). IQ was measured using the Wechsler Intelligence Scale for Children-III, Full Scale score (Wechsler, 1991).

Table 2

Panel A					
Variable	Mean (SD)	Range	OR		
Neighborhood quality (census)	0.18 (0.09)	0–100%	13.2 ^{**}		
Concentrated disadvantage	0.16 (0.15)	0–100%	6.8 [*]		
Families in poverty	0.12 (0.15)	0–100%	4.6 [*]		
Female head of household	0.22 (0.18)	0–100%	5.6 [*]		
Public assistance	0.11 (0.12)	0–100%	9.2 [*]		
Unemployed	0.05 (0.03)	0–100%	<i>a</i>		
Residents younger than 18	0.23 (0.06)	0–100%	3.7 [*]		
Residential instability	0.20 (0.06)	0–100%	2.0		
Moved since last census	0.33 (0.10)	0–100%	1.9		
Vacated living units	0.07 (0.06)	0–100%	<i>a</i>		
Severity of SUD in mother (self-report)	0.13 (0.05)	(Standard deviations)	2.1 [*]		
Severity of SUD in father (self-report)	0.07 (0.07)	(standard deviations)	1.5 [*]		
Son cannabis use by age 19 (self-report)	1.1 (1.5)	0–4	3.8 [*]		
Son neurobehavioral disinhibition (see text)	51.3 (9.8)	(standard deviations)	1.1 [*]		
Panel B					
Correlations between study variables					
	1	2	3	4	5
1. Son CD by age 22					
2. Father SUD severity	0.17 ^A				
3. Mother SUD severity	0.26 ^A	0.44 ^B			
4. NQ	0.19 ^A	0.23 ^B	0.15 ^B		
5. Son CU at age 19	0.85 ^C	0.27 ^A	0.30 ^A	0.22 ^A	
6. ND	0.39 ^A	0.38 ^B	0.26 ^B	0.29 ^B	0.36 ^A

Note: N = 216. OR = odds ratio. Note: N = 216. All correlations significant at $p < 0.05$ except between neighborhood quality and mother's SUD severity.

A Polyserial correlation.

B Pearson correlation.

C polychoric correlation. SUD = substance use disorder. ND = neurobehavioral disinhibition. CU = cannabis use. CD = cannabis use disorder. NQ = neighborhood quality.

* $p < 0.05$.

** $p < 0.10$.

a Variance was too small to provide a stable estimate of OR. SD = standard deviation.

Table 3

Tests of fit to data of the competing models.

Model	AIC	BIC	LR χ^2 (df) versus:	
			Unmediated model	Full model
1. Unmediated model	5615.3	5666.7	N/A	N/A
2. Full model	5546.8	5618.8	89.96 (6)**	N/A
3. ND indirectly leads to CD	5547.8	5616.4	86.99 (4)**	2.97 (1)
4. ND does not predict CU	5551.1	5616.3	82.14 (3)**	7.82 (2)**
5. ND does not predict CU or CD	5614.1	5669.0	13.13 (0)**	76.83 (5)**
6. NQ indirectly leads to CU	5545.0	5613.5	89.87 (4)**	0.09 (1)
7. NQ is not a predictor	5547.2	5605.5	81.59 (1)**	8.37 (4)
8. Parental SUD indirectly leads to CU and CD (Fig. 2)	5543.6 ^F	5605.3 ^F	77.67 (3)**	2.29 (2)

Note: $N = 216$. AIC = Akaike's Information Criterion (smaller values indicate better fit). BIC = bayesian information criterion (smaller values indicate better fit). LR χ^2 = likelihood ratio (LR) χ^2 .

^F Best fitting model according to the column fit statistic. ND = neurobehavioral disinhibition. CU = cannabis use. CD = cannabis use disorder. NQ = neighborhood quality. SUD = substance use disorder.

**
 $p < 0.01$.