Available online at www.sciencedirect.com
SCIENCE DIRECT®
Drug and Alcohol Dependence 77 (2005) 13–21
DRUG and ALCOHOL DEPENDENCE
www.elsevier.com/locate/drugalcdep

Childhood risk categories for adolescent substance involvement: a general liability typology

Duncan B. Clark*, Jack R. Cornelius, Levent Kirisci, Ralph E. Tarter

Departments of Psychiatry and Pharmaceutical Sciences, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213, USA

Received 18 October 2003; received in revised form 21 June 2004; accepted 23 June 2004

Abstract

Childhood risks for adolescent substance involvement include parental substance use disorders (SUDs), psychological dysregulation and early tobacco and alcohol experimentation. This study was designed to identify childhood risk categories predicting accelerated adolescent substance involvement across drug types and stages. The index subjects were 560 children recruited from high risk (n = 266) or low risk (n = 294) families based on fathers' SUDs. Assessments were conducted at approximately ages 11 (baseline), 13, 16, and 19 years. Childhood predictors included parent SUDs, early tobacco or alcohol use (i.e., substance use), and neurobehavior disinhibition (ND) as determined by indicators of cognitive, affective and behavioral disinhibition. A cluster analysis defined five risk categories based on baseline characteristics as follows: (1) High (n = 31; 100% had both parents with SUDs, 100% had early substance use, and the mean ND score = 58.9); (2) Intermediate-High (n = 76; 45% had one parent with SUD, 100% early substance use and ND = 51.9); (3) Intermediate (n = 76; 100% both parents with SUDs, 0% early substance use and ND = 51.4); (4) Intermediate-Low (n = 161; 100% with one SUD parent; 0% early substance use and ND = 49.9) and; (5) Low (n = 216; no parental SUD, no early substance use and ND = 47.5). Compared with all other groups, children in the High risk group had significantly accelerated substance involvement across all substance types and stages. The ordering of risk categories from low to high was also consistent for all substance involvement outcomes. The findings indicate that these five risk categories constitute general liability classes for adolescent substance involvement, and may identify homogeneous groups of children requiring distinct preventive interventions.

Keywords: Children; Adolescents; Family; Personality; Risk factors

1. Introduction

Risk factors for adolescent substance involvement that may be identified in childhood include parental substance use disorders (SUDs), psychological dysregulation, and early alcohol and tobacco experimentation. While prospective evidence has accrued that these risk factors generally predict substance involvement, their relative predictive utilities across multiple substance types and stages have yet to be definitively established. To the extent that these risk characteristics are complementary, their combination may synergistically predict substance involvement outcomes. In this study, we consider the utility of these childhood risk factors singly and combined for prospectively predicting adolescent substance involvement across multiple substance types and stages.

The children of parents with alcohol use disorders, compared with reference children, have accelerated onset of adolescent alcohol involvement and increased rates of alcohol use disorders (Chassin et al., 2002; Lieb et al., 2002; Sher et al., 1991; Schuckit and Smith, 1996). While SUDs have been shown to aggregate in families (Merikangas et al., 1998), prospective studies have only recently examined substance involvement outcomes for the offspring of parents with disorders involving illicit drugs. Compared with reference children, children of parents with these drug use disorders have been shown to have earlier involvement with alcohol and tobacco, higher rates of adolescent illicit drug use, and increased drug use disorder symptoms (Clark et al., 1999).

* Corresponding author. Tel.: +1 412 246 5186; fax: +1 412 246 6550.
E-mail address: clarkdb@upmc.edu (D.B. Clark).

0376-8716/$ – see front matter © 2004 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.drugalcdep.2004.06.008

Psychological dysregulation, defined as delayed or deficient development of behavioral, emotional and cognitive regulation, has been hypothesized to be a risk factor for the development of SUDs (Clark and Winters, 2002; Tarter et al., 1999). Children of parents with SUDs have increased rates of mental disorder reflective of psychological dysregulation, including conduct disorder, attention deficit hyperactivity disorder, depression, and anxiety disorders (Clark et al., 1997, 2004; Wilens et al., 2002). In some studies, these mental disorders predict substance involvement in adolescence (Clark et al., 1999; Biederman et al., 1997). Tarter et al. (in press) have developed an index of psychological dysregulation, termed neurobehavior disinhibition (ND), using measures of behavioral, emotional and cognitive regulation. In a subset (n = 112) of the sample described here, childhood ND predicted SUDs in late adolescence.

While experimentation with tobacco and alcohol are normative in adolescence, consumption of these substances in childhood is atypical (Johnson et al., 2001). Tobacco and alcohol use has been found to be more common among children of parents with SUDs than among reference children (Clark et al., 1998a). Childhood tobacco and alcohol use predicts problems with these substances as well as illicit drug involvement in adolescence (Clark et al., 1998a; Bentler et al., 2002; Boyle et al., 1992).

Parent SUDs, ND and childhood tobacco and alcohol use are distinct features, each likely having strengths and weaknesses in the prediction of substance involvement types and stages. We anticipated that utilization of multiple childhood characteristics to define risk levels would improve the prediction of adolescent substance involvement. If predictive of accelerated substance involvement across multiple substance types and stages, these risk groups could be considered general liability classes.

1.1. Study aims

The aims of this study were: (1) to determine whether parental SUDs, ND, and childhood tobacco and alcohol use similarly predict adolescent substance involvement across multiple substance types and stages; (2) to use cluster analysis to construct homogeneous groups of children based on parental SUDs, ND, and childhood tobacco and alcohol use; and (3) to determine the predictive validity of childhood risk classes across substance types and stages. The hypothesis was that childhood risk categories constitute general risk classes optimally predicting accelerated substance involvement across all substance types and stages.

2. Methods

2.1. Participants

The subjects were 560 children (425 boys, 135 girls) recruited through their biological fathers and initially assessed in late childhood at approximately ages 10 through 12 years old (mean age = 11.4 ± .9). The recruitment procedure was designed to yield a group of children at high average risk for substance use disorders (SUD), identified by having fathers with histories of drug use disorders (abuse or dependence involving illicit substances), and a comparison group at low average risk, identified by having fathers without substance use disorders or other major mental disorders. The study required the family to have a child in the age range of 10 through 12 years, participation of both the biological father and mother, and willingness to participate in long-term follow-up assessments. To ascertain the requisite families, multiple recruitment sources were utilized. To identify and recruit families with SUD fathers, recruitment occurred through multiple sources, including SUD and psychiatric treatment programs, social service agencies, newspaper and radio advertisements, and a sampling frame purchased from a marketing firm. To recruit comparison families with fathers without SUDs or other mental disorders, advertisements and a sampling frame were used. After a complete description of the study was provided to the parents and children, written informed consent was obtained from parents and assent was obtained from children. The study was approved by the University Institutional Review Board.

Children were initially classified into two groups based on paternal SUD history: (1) children of fathers with SUD histories (SUD+ Fathers: n = 266); and (2) children of fathers without SUD histories (SUD− Fathers: n = 294). Fathers were considered to have SUD histories if they had ever met DSM-III-R criteria (APA, 1987) for abuse or dependence involving substances other than nicotine, caffeine or alcohol. The presence of other mental disorders and SUDs (including alcohol use disorders) was not an exclusionary criterion for the HAR group. The fathers in the LAR group had never met DSM-III-R criteria for any SUD, or any other major adulthood Axis I mental disorder. For the families of SUD+ Fathers, the following characteristics were noted: index children were 77% male, 23% female; 67% European American, 30% African American, 3% other; mean age was 11.3 ± .9 household socioeconomic status by Hollingshead Index was 36.2 ± 12.4. For the families of SUD− Fathers, the following characteristics were noted: index children were 75% male, 25% female; 78% European American, 19% African American, 3% other; mean age was 11.4 ± .9; household socioeconomic status by Hollingshead Index was 44.2 ± 13.4.

Data collected at the baseline assessment were used to determine risk characteristics. In addition to the baseline assessment (age 10–12 years), follow-up assessments occurred in early adolescence (age 12–14 years), middle adolescence (age 15–17 years), and early adulthood (age 18–21 years). This sample includes additional subjects and follow-up data not reported in previous articles (Clark et al., 1997, 1999; Tarter et al., 2003).

2.2. Measures

2.2.1. Parental substance use disorders

Diagnoses were made by DSM-III-R (APA, 1987), the latest DSM edition when the study was initiated. For index cases and parents, SUD items were assessed by a semi-structured interview developed for CEDAR using questions from the Structured Clinical Interview for Diagnosis (SCID: Spitzer et al., 1988). Screening information was gathered on all classes of substances and detailed information was collected on the most frequently used substance classes (Clark et al., 2001). Diagnoses were determined by DSM-III-R criteria in a consensus conference using the best estimate diagnostic procedure (Kosten and Rounsaville, 1992). Additional information about the diagnostic procedure, rater training and interrater reliabilities may be found in prior publications (Clark et al., 1997, 1998a, 2001).

2.2.2. Neurobehavior disinhibition

ND was a latent variable derived from indicators of affective, behavioral, and cognitive regulation (see Tarter et al., 2003 for details). The affective dimension was determined by the total score on the revised Dimensions of Temperament Survey (Windle, 1992). The behavioral dimension was determined by disruptive behavior disorder symptoms reported by the mother on the K-SADS-E (Orvaschel et al., 1982) and the total score on the Pelham & Murphy Disruptive Behavior Disorders Rating Scale by teacher report (Tarter et al., in press). The cognitive dimension was determined by measures of executive cognitive functions, including the Stroop, Porteus Mazes, vigilance, motor restraint, forbidden toys, and Block Design test of the WISC-III-R. ND scores were derived by using item response theory methods applied to these indicators of affect, behavior and cognitive regulation. The ND scale has been shown to be unidimensional, stable over a 4–6 year period, and predictive of SUD outcomes (Tarter et al., 2003).

2.2.3. Index substance involvement

Substance use onsets and phases were assessed by a method developed for this project to separately evaluate tobacco, alcohol, cannabis, cocaine, and other drug classes (see Clark et al., 2001 for additional details). At the baseline assessment, subjects were asked whether they had used specific substances. For each substance used by the subject, onsets were determined for first use, regular use, first problem and meeting DSM-III-R criteria for a substance use disorder. The onset dates were estimated to the nearest month. Prior research has shown that onset dates for SUD symptoms and diagnoses can be reliably assessed in adolescent samples (Martin et al., 2000). First use was defined as the first time the subject used the identified substance, and was thus synonymous with "any use" with the exception of alcohol. Alcohol use was defined here by quantity as a minimum of one standard drink per drinking episode, since experimentation with lesser amounts have not been shown to consistently indicate a risk characteristic or a clinically significant outcome (e.g., Clark et al., 1998a). Substance use frequency was determined and regular use was defined as one or more use per month for a consumption phase. Substance-related problems were defined as any DSM-III-R abuse or dependence symptom, queried by SCID items. SUDs were determined by the method described above for parents. Note that a history of use of tobacco or alcohol at the baseline assessment was used as a risk variable, and other substance involvement variables were used as outcome characteristics.

2.3. Data analyses

The cluster analysis used parental SUDs, childhood tobacco or alcohol use, and ND from the childhood assessment as the defining variables. Parental SUDs were scaled according to the number of parents with SUDs (i.e., 0–2), and childhood substance use was scaled according to whether none, one or both alcohol and tobacco had been used (i.e., 0–2). The most common cluster analysis methods are hierarchical methods and *k*-means cluster analysis. Hierarchical methods have been recommended for categorical data (Everitt et al., 2001, p. 178), such as the parent SUD and early substance use variables here. A hierarchical cluster analysis using Ward's method by squared Euclidian distance specified five subject clusters. In this application, the hierarchical method and a *k*-means cluster analysis yielded similar results, with significantly associated classification assignments follows (likelihood ratio χ^2 = 1132.4, d.f. = 16, $P < .01$; kappa agreement statistic = .61, $P < .001$). In addition, group comparisons on risk characteristics were conducted to verify that internally valid clusters were generated.

The substance involvement outcome data were "right-censored," since onsets may have occurred in some subjects after the final assessment conducted for this study. Survival analysis was therefore the appropriate statistical methodology (Klein and Moeschberger, 1997). The survival function gives the probability that a subject will "survive" (i.e., will not manifest the outcome) at a specific time. The proportional hazards or Cox model performs regression analysis with survival data (Cox, 1972). Proportional hazards models were developed for 13 variables: (1) regular tobacco use, (2) daily tobacco use, (3) regular alcohol use, (4) alcohol problems, (5) alcohol use disorders, (6) first cannabis use, (7) regular cannabis use, (8) cannabis problems, (9) cannabis use disorder, (10) first cocaine use, (11) regular cocaine use, (12) cocaine problems, and (13) cocaine use disorders. Predictions of these substance involvement outcomes were examined for individual risk variables as well as for risk groups (i.e., clusters). Where risk groups showed overall significant differences, paired comparisons were conducted. To present a manageable number of paired comparisons in Results, statistics for paired comparisons representing threshold pairs are presented. Risk Groups more different than those

indicated were also significantly different, and Risk Groups more similar than the pairs described were not significantly different. The presentation includes representative survival plots.

3. Results

3.1. Childhood risk group characteristics

The internal validity of the classification process was verified by statistically significant group differences among subjects in the five risk levels on the specified defining variables, including parent SUDs (χ^2 = 1025.3, d.f. = 8, P < .001), childhood alcohol or tobacco use (χ^2 = 548.6, d.f. = 8, P < .001), and ND (F = 11.5, d.f. = 4.555, P < .001). The lowest risk children (i.e., Low Risk) were characterized by parents without SUDs, the absence of childhood alcohol or tobacco use, and low mean scores on ND (47.5 ± 8.4). The Intermediate-Low Risk group was characterized by one parent with SUDs, the absence of childhood alcohol or tobacco use, and higher mean ND score (49.9 ± 9.9) than the Low Risk group (F = 6.6, d.f. = 1.375, P = .01). The Intermediate Risk children had two parents with SUDs, and moderate scores on ND (51.4 ± 8.7) similar to the Intermediate-Low group (F = 1.2, d.f. = 1.235, P = .3), as well as an absence of childhood alcohol or tobacco use. Of the children in the Intermediate-High Risk group, 45% had one parent with SUD, and all had tried one or both licit drugs. The mean ND of the Intermediate-High Risk group was moderate (51.9 ± 11.3), similar to Intermediate Risk children (F = .1, d.f. = 1.150, P = .7). The High Risk children had two parents with SUDs, had tried one or both licit drugs, and the highest mean ND score (58.9 ± 13.0) compared with Intermediate-High (F = 7.7, d.f. = 1.105, P = .006) and other groups.

The five risk groups were compared on demographic characteristics (Table 1). The groups were not significantly different on gender, ethnic groups, or age at baseline assessment. The groups were significantly different on socioeconomic status (SES) by Hollingshead two-factor index (Hollingshead and Redlich, 1958), with the High Risk group being significantly lower than other groups (versus Intermediate-High: F = 19.4, d.f. = 1.105, P < .001; versus Intermediate: 4.1, d.f. = 1.105, P = .04). Subsequent analyses controlled for these demographic characteristics.

3.2. Tobacco involvement prediction

3.2.1. Regular use

For regular use of tobacco, all three individual risk variables significantly predicted onset age, as did the overall Risk Groups variable (Table 2). Comparing group pairs, the onset of regular tobacco use was significantly accelerated in the High Risk group compared with the Intermediate-High Risk group (Wald χ^2 = 6.7, d.f. = 1, P = .009) as well as all other groups. Onset in the Intermediate-High Risk group was accelerated compared with the Intermediate-Low Risk (Wald χ^2 = 6.6, d.f. = 1, P = .01) and Low Risk groups. Onsets were not significantly different in the Intermediate-High and Intermediate Risk groups, and there were no significant differences among pairs involving Intermediate, Intermediate-Low and Low Risk groups.

3.2.2. Daily use

For daily tobacco use, all three individual risk variables significantly predicted onset age, as did the overall Risk Groups variable. Comparing onsets between pairs of Risk Groups, the High Risk group was significantly accelerated compared with the Intermediate-High Risk group (Wald χ^2 = 10.5, d.f. = 1, P = .001) and all other groups. Onset in the Intermediate-High Risk group was accelerated compared with Intermediate-Low (Wald χ^2 = 7.8, d.f. 1, P = .005) and Low Risk groups. Fig. 1 presents the survival plot depicting the proportion of each group with onset of daily tobacco use over time.

Table 1
Demographic characteristics for five groups of children defined by risk for substance involvement

	Variable							
	Lowest, n = 216 (%)	Intermediate-Low, n = 161 (%)	Intermediate, n = 76 (%)	Intermediate-High, n = 76 (%)	Highest, n = 31 (%)	χ^2	d.f.	P
Gender								
Male	72	76	72	87	84	8.6	4	.07
Female	28	24	28	13	16			
Ethnic group								
White	76	69	62	80	74	10.0	8	.27
African American	21	27	36	17	23			
Other	3	4	3	3	3			
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	F	d.f.	P
Age at baseline	11.3 ± .9	11.3 ± 1.0	11.1 ± .9	11.5 ± .09	11.6 ± .9	2.0	4.555	.10
SES	45.1 ± 13.1	38.3 ± 12.6	34.6 ± 10.9	42.2 ± 13.7	29.6 ± 12.6	18.3	4.555	<.001

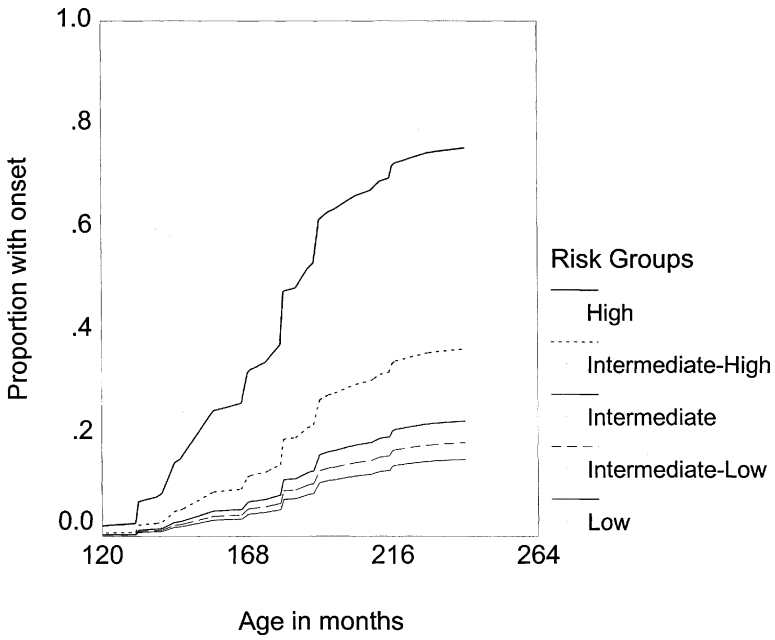

Fig. 1. Daily tobacco use survival plots by childhood risk category.

3.3. Alcohol involvement prediction

3.3.1. Regular use

For the regular use of alcohol, Parent SUDs and Childhood Alcohol or Tobacco Use significantly predicted onset age, whereas ND did not. Overall, Risk Groups significantly predicted onset age. Onset in the High Risk group was significantly accelerated compared with the Intermediate-High Risk group (Wald χ^2 = 10.4, d.f. = 1, P = .001) and all other groups. Onset in the Intermediate-High Risk group was accelerated compared with Intermediate-Low (Wald χ^2 = 3.9, d.f. 1, P = .05) and Low Risk groups.

3.3.2. Problems

For alcohol problems, Parent SUDs and Childhood Alcohol or Tobacco Use significantly predicted onset age, whereas ND did not. Overall, Risk Groups significantly predicted onset age (Fig. 2). The High Risk group was significantly accelerated compared with Intermediate-High Risk group (Wald χ^2 = 10.0, d.f. = 1, P = .002) and all other groups. The Intermediate-High Risk group was accelerated compared with the Low Risk group (Wald χ^2 = 5.5, d.f. 1, P = .02).

3.3.3. Disorders

For alcohol use disorders, Parent SUDs and Childhood Alcohol or Tobacco Use significantly predicted onset age, whereas ND did not. Overall, Risk Groups significantly predicted onset age. The High Risk group was significantly accelerated compared with the Intermediate-High Risk group (Wald χ^2 = 7.4, d.f. = 1, P = .007) and all other groups. The Intermediate-High Risk group was accelerated compared with the Low Risk group (Wald χ^2 = 4.4, d.f. = 1, P = .04).

3.4. Cannabis involvement prediction

3.4.1. First use

For first use of cannabis, the three individual risk variables significantly predicted onset age, as did the overall Risk Groups variable (Fig. 3). Onset in the High Risk was significantly accelerated compared with Intermediate-High Risk group (Wald χ^2 = 14.8, d.f. = 1, P < .001) and all other groups. Onset in the Intermediate-High Risk group was accelerated compared with the Intermediate-Low Risk group (Wald χ^2 = 12.0, d.f. = 1, P = .001), and in the Intermediate Risk group compared with the Low Risk group (Wald χ^2 = 6.9, d.f. = 1, P = .009).

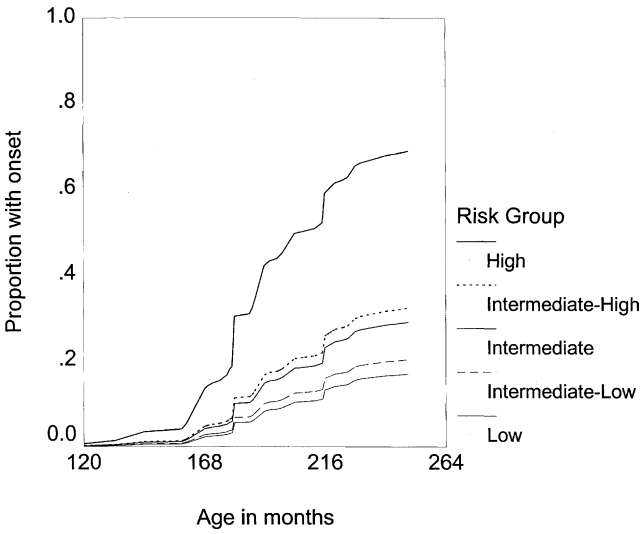

Fig. 2. Alcohol problems survival plots by childhood risk category.

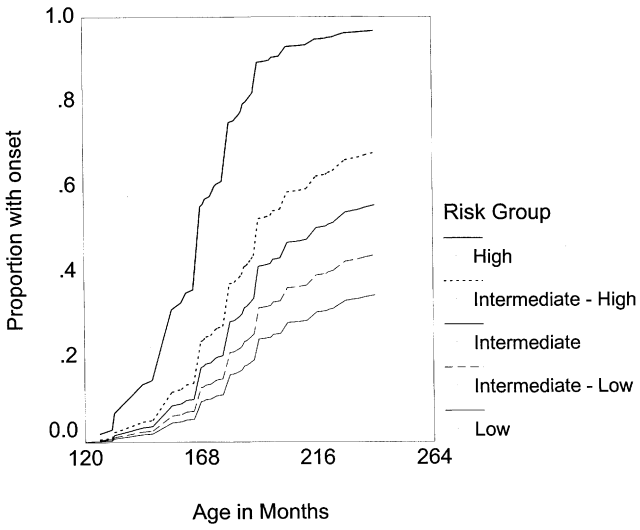

Fig. 3. Cannabis use survival plots by childhood risk category.

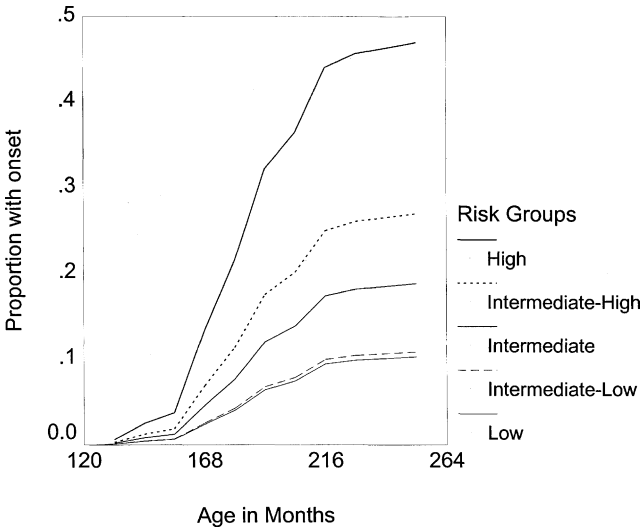

Fig. 4. Cannabis use disorders survival plots by childhood risk category.

3.4.2. Regular use

For regular use of cannabis, the three individual risk variables significantly predicted onset age, as overall Risk Groups. Onset in the High Risk was significantly accelerated compared with Intermediate-High Risk group (Wald χ^2 = 9.5, d.f. = 1, P = .002) and all other groups. Onset in the Intermediate-High Risk group was accelerated compared with the Intermediate-Low Risk group (Wald χ^2 = 13.1, d.f. = 1, P < .001), and in the Intermediate Risk group compared with the Intermediate-Low (Wald χ^2 = 4.8, d.f. = 1, P = .03) and Low Risk groups.

3.4.3. Problems

For cannabis problems, the three individual risk variables significantly predicted onset age, as did the overall Risk Groups variable. Comparing group pairs, onset in the High Risk was significantly accelerated compared with Intermediate-High Risk group (Wald χ^2 = 5.7, d.f. = 1, P = .02) and all other groups. Onset in the Intermediate-High Risk group was accelerated compared with the Intermediate-Low Risk group (Wald χ^2 = 15.7, d.f. = 1, P < .001), and in the Intermediate Risk group compared with the Intermediate-Low (Wald χ^2 = 4.7, d.f. = 1, P = .03) and Low Risk groups.

3.4.4. Disorders

For cannabis use disorders, the three individual risk variables significantly predicted onset age, as did the overall Risk Groups variable (Fig. 4). Comparing group pairs, the High Risk group had significantly accelerated onset compared with Intermediate-High Risk group (Wald χ^2 = 4.4, d.f. = 1, P = .04) and all other groups. The Intermediate-High Risk group had accelerated onset compared with the Intermediate-Low Risk group (Wald χ^2 = 8.3, d.f. = 1, P = .004).

3.5. Cocaine involvement prediction

3.5.1. First use

For first use of cocaine, the three individual risk variables significantly predicted accelerated onset, as did the overall Risk Groups variable (Fig. 5). The Intermediate-High through Low Risk groups were not significantly different on onset of first use of cocaine (Wald χ^2 = .3, d.f. = 1, P = .6). Since there were relatively fewer subjects with cocaine use, the High Risk group was compared with all other groups combined to improve statistical power. Onset of cocaine use in the High Risk group was significantly accelerated compared with the other groups combined (Table 2).

3.5.2. Regular use

For regular use of cocaine, Parent SUDs and ND significantly predicted accelerated onset, whereas Child Substance

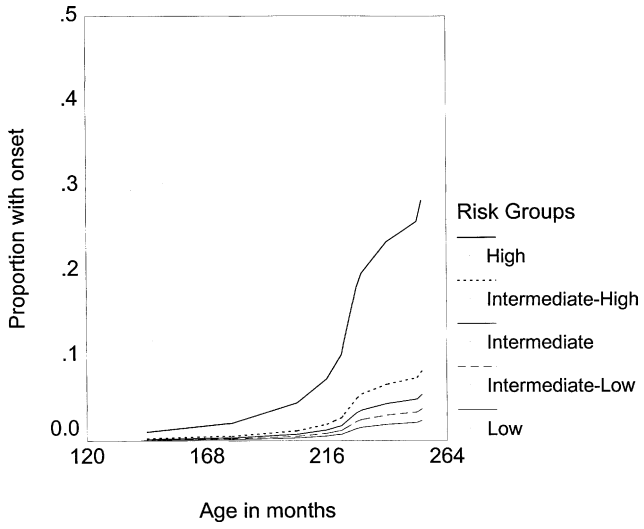

Fig. 5. Cocaine use survival plots by childhood risk category.

Table 2
Survival analysis statistics for predictions of substance involvement variables by individual risk characteristics and a five group risk classification

		Parent SUDs		Child tobacco or alcohol use		Neurobehavior disinhibition		Risk Groups	
		Wald χ^2	*P*	Wald χ^2	*P*	Wald χ^2	*P*	Wald χ^2	*P*
Tobacco	Regular use	13.5	.001	44.8	<.001	6.2	.01	48.8	<.001
	Daily use	15.7	<.001	50.5	<.001	11.1	.001	57.1	<.001
Alcohol	Regular use	10.5	.005	24.7	<.001	.5	.5	42.8	<.001
	Problems	19.1	<.001	26.7	<.001	1.1	.3	40.2	<.001
	Disorder	18.0	<.001	12.3	.002	3.3	.07	31.9	<.001
Cannabis	First use	26.2	<.001	60.5	<.001	10.3	.001	81.4	<.001
	Regular use	18.4	<.001	39.6	<.001	5.8	.02	56.8	<.001
	Problems	15.2	<.001	37.8	<.001	11.1	.001	53.2	<.001
	Disorder	11.5	.003	20.3	<.001	15.6	<.001	33.3	<.001
Cocaine	First use	12.0	.002	8.8	.01	9.4	.002	18.4	<.001
	Regular use	8.8	.01	1.4	.5	8.6	.003	5.3	.02
	Problems	8.6	.01	4.1	.1	7.4	.007	14.5	<.001
	Disorder	1.6	.4	6.6	.04	8.6	.003	12.5	<.001

Note: With Bonferroni correction, tests interpreted as significant were $P < .004$ (.05/13). For parent SUD, d.f. = 2; for child substance use, d.f. = 2; for NBD, d.f. = 1; for Risk Group, d.f. = 4. All statistical tests control for SES, gender and ethnic group. For cocaine involvement, High group was compared with other groups were combined in Risk Group analyses (d.f. = 1). NBD: neurobehavioral disinhibition score.

Use did not. The overall Risk Groups variable predicted accelerated onset. Onsets in the Intermediate-High through Low Risk groups were not significantly different (Wald $\chi^2 = .2$, d.f. = 1, $P = .7$). Onset in the High Risk group was significantly accelerated compared with the other groups combined (Table 2).

3.5.3. Problems

For regular use of cocaine, Parent SUDs and ND significantly predicted onset age, whereas Child Alcohol or Tobacco Use did not. The overall Risk Groups variable predicted onset age. Onsets in the Intermediate-High through Low Risk groups were not significantly different (Wald $\chi^2 = .3$, d.f. = 1, $P = .6$). Onset in the High Risk group was significantly accelerated compared with the other groups combined (Table 2).

3.5.4. Disorders

For cocaine use disorders, Child Alcohol or Tobacco Use and ND significantly predicted onset age, whereas Parental SUDs did not. The overall Risk Groups variable predicted onset age. Onsets in the Intermediate-High through Low Risk groups were not significantly different (Wald $\chi^2 = .01$, d.f. = 1, $P = .9$). Onset in the High Risk group was significantly accelerated compared with the other groups combined.

4. Discussion

The childhood risk factors investigated here were all predictive of some substance involvement outcomes, with variation in the degree to which specific outcomes by substance type and stage were correctly predicted. As expected, parent SUDs predicted most substance involvement outcomes. According to the conservative interpretation adopted for these statistical results, however, parent SUDs did not significantly predict the onset of regular use of alcohol, and three of four cocaine involvement variables. Childhood alcohol or tobacco use produced very robust predictions of accelerated onsets of all stages of tobacco, alcohol, and cannabis involvement. On the other hand, none of the four cocaine involvement variables were significantly predicted by this risk characteristic. ND showed a complementary prediction pattern. ND did not significantly predict tobacco and alcohol involvement with one exception. On the other hand, ND strongly predicted the acceleration of three of the four stages of cocaine involvement. One might envisage that parental SUDs, childhood substance use, and ND would contain redundant information. These results rather indicate that these characteristics are complementary, identifying different facets of substance involvement liability. Compared with the less consistent results for individual risk variables, the overall childhood risk class variable produced highly significant predictions of substance involvement onset ages across 12 of 13 substance types and stages.

The substance involvement outcomes of the three lower risk groups were similar for most variables. From the standpoint of their risk variable characteristics, the Intermediate, Intermediate-Low and Low Risk groups were fundamentally different. The Intermediate group of children had two parents with a history of substance use disorders, the Intermediate-Low group one parent with substance use disorders, and the Low group had parents without a history of substance use disorders. Furthermore, the ND score was significantly higher in the Intermediate-Low group than in the Low group. These differences in risk characteristics justify examining these children as separate groups. Compared with the Low risk group, the Intermediate risk group had accelerated onset of cannabis involvement, including first use, regular use, and problems. Wile the Intermediate-Low and Low Risk groups did not show significant differences on substance involvement out-

comes, studies with larger samples and longer follow-up periods will be necessary to determine whether this was due to inadequate statistical power in this study or the fundamental similarity of these groups.

The assessment of substance involvement was designed to be reasonably comprehensive as well as diachronic, i.e., continuous over time. Chronologically accurate determinations of consumption are optimally derived from frequent assessments, and inquiries involving long periods of retrospection yield less reliable variables (Clark and Winters, 2002). The decay in reliability of substance involvement reports was minimized in this study by completing the initial assessment at an age when subjects typically had little or no substance use history, and performing subsequent assessments at 2–3 year intervals. Tobacco experimentation and alcohol use of a standard drink or more constitute risk indicators at the relatively young age of the initial assessment in this study, and become more normative at older ages (Clark et al., 1998a). While DSM diagnostic criteria have been found to be reasonably reliable when applied to adolescents, several validity issues have been identified for the alcohol use disorder criteria (Clark, 2004), and similar problems have been noted for other substances (e.g., Chung et al., 2004). Nevertheless, the five risk categories identified here showed similar results across substance types and stages, suggesting that the ordering of risk categories indicated by the included outcomes would likely be similar for other substance involvement outcome measures or definitions.

The genetic and environmental mechanisms through which paternal SUDs influence offspring outcomes have yet to be fully understood. The parents' manifestations of psychological dysregulation have been found to be predictive of similar offspring characteristics in a manner suggesting non-environmental transmission consistent with a genetic hypothesis (Clark et al., 1997; Cadoret et al., 1995). Parent characteristics may also constitute environmental influences (Moss et al., 1997). While not definitive, observational findings such as those presented here may be informative in illuminating causal relationships (Clark and Winters, 2002; Clogg and Haritou, 1997; Cooper, 1999). More comprehensive studies are needed to determine the degree to which these risk factors were due to genetic and environmental effects or their interaction. Given the exploratory nature of this study, we elected to interpret statistical tests as significant with a $P < .05$ threshold. There were a relatively large number of such tests, and some may find this criterion too liberal. Therefore, specific P-values were provided, and some comparisons may thus be interpreted as non-significant. Another study limitation was that the extent to which the sample was representative of high and low risk populations of children was not testable here. Replications of these findings will be needed with samples acquired by other more systematic methods.

The characterization of parents by their history of SUDs represents an oversimplified description. Parents with SUDs typically have other mental disorders, and the latter characteristics may be important to take into consideration in defining risk groups. Parents with SUDs vary in their history of other forms of psychopathology, transmission of such mental disorders from parents to child may occur independent of parents' SUDs (Clark et al., 2004), and offspring psychopathology predicts substance involvement (Clark et al., 1999). Further studies may be able to refine the risk categories developed here.

Consistent with prior studies (Clark et al., 1998b), the progression from tobacco and alcohol experimentation through substance use disorders involving illicit drugs occurred rapidly in the highest risk children. Preventive programs likely need to focus on disrupting the link between childhood risk factors and adolescent substance involvement. For high risk children, prevention may require programs with considerable cost. Interventions focused on treatment for manifestations of psychological dysregulation may offer an effective strategy for SUD prevention in some high risk children (Vitaro and Dobkin, 1996). Such costly programs are impractical as well as unnecessary for lower risk children. Through the identification and validation of childhood risk levels, research such as this project may constitute the basis for selective application of specialized preventive interventions optimized for children at specified risk levels.

Acknowledgments

This work was conducted at the Center for Education and Drug Abuse Research and was supported by NIDA P50-DA05605 and R01-DA14635 and NIAAA K02-AA00291. Requests for reprints should be sent to Dr. Clark, 3811 O'Hara Street, Pittsburgh, PA 15213.

References

American Psychiatric Association 1987. Diagnostic and Statistical Manual of Mental Disorders, third ed. (DSM III-R). American Psychiatric Association, Washington, DC.

Bentler, P.M., Newcomb, M.D., Zimmerman, M.A., 2002. Cigarette use and drug use progression: growth trajectory and lagged effects hypotheses. In: Kandel, D.B. (Ed.), Stages and Pathways of Drug Involvement: Examining the Gateway Hypothesis. Cambridge University Press, Cambridge, UK, pp. 223–253.

Biederman, J., Wilens, T., Mick, E., Farone, S.V., Weber, W., Curtis, S., Thornell, A., Pfister, K., Jetton, J.G., Soriano, J., 1997. Is ADHD a risk factor for psychoactive substance use disorders? Findings from a four-year prospective follow-up study. J. Am. Acad. Child. Adol. Psychiatr. 36, 21–29.

Boyle, M.H., Offord, D.R., Racine, Y.A., Szatmari, P., Fleming, J.E., Links, P., 1992. Predicting substance use in late adolescence: results of the Ontario Child Health Study Follow-up. Am. J. Psychiatr. 149, 761–767.

Cadoret, R.J., Yates, W.R., Troughton, E., Woodworth, G., Stewart, M.A., 1995. Adoption study demonstrating two genetic pathways to drug abuse. Arch. Gen. Psychiatr. 52, 42–52.

Chassin, L., Pitts, S.C., Prost, J., 2002. Binge drinking trajectories from adolescence to emerging adulthood in a high-risk sample: predictors and substance abuse outcomes. J. Cons. Clin. Psychol. 70, 67–78.

Chung, T., Martin, C.S., Cornelius, J.R., Winters, K.C., Langenbucher, J.W., 2004. Limitations in the assessment of DSM-IV cannabis tolerance as an indicator of dependence in adolescents. Exp. Clin. Psychopharmacol. 12, 136–146.

Clark, 2004. The natural history of adolescent alcohol use disorders. Addiction, in press.

Clark, D.B., Cornelius, J.R., Wood, D.S., Vanyukov, M., 2004. Psychopathology risk transmission in children of parents with substance use disorders. Am. J. Psychiatr. 161, 685–691.

Clark, D.B., Kirisci, L., Moss, H.B., 1998a. Early adolescent gateway drug use in sons of fathers with substance use disorders. Addict. Behav. 23, 561–566.

Clark, D.B., Kirisci, L., Tarter, R.E., 1998b. Adolescent versus adult onset and the development of substance use disorders in males. Drug Alcohol Depend. 49, 115–121.

Clark, D.B., Moss, H., Kirisci, L., Mezzich, A.C., Miles, R., Ott, P., 1997. Psychopathology in preadolescent sons of substance abusers. J. Am. Acad. Child. Adol. Psychiatr. 36, 495–502.

Clark, D.B., Parker, A.M., Lynch, K.G., 1999. Psychopathology, substance use and substance related problems. J. Clin. Child. Psychol. 28, 333–341.

Clark, D.B., Pollock, N.A., Mezzich, A., Cornelius, J., Martin, C., 2001. Diachronic assessment and the emergence of substance use disorders. J. Child. Adol. Subs. Abuse. 10 (4), 13–22.

Clark, D.B., Winters, K.C., 2002. Measuring risks and outcomes in substance use disorders prevention research. J. Cons. Clin. Psychol. 70, 1207–1223.

Clogg, C.C., Haritou, A., 1997. The regression method of causal inference and a dilemma confronting this method. In: McKim, V.R., Turner, S.P. (Eds.), Causality in Crisis? University of Notre Dame Press, South Bend, IN.

Cooper, G.F., 1999. An overview of the representation and discovery of causal relationships using Bayesian networks. In: Glymour, C., Cooper, C.F. (Eds.), Computation, Causation, and Discovery. AAAI/MIT Press, Menlo Park, CA.

Cox, D.R., 1972. Regression models and life tables. J. R. Stat. Soc. 34, 187–220.

Everitt, B.S., Landau, S., Leese, M., 2001. Cluster Analysis, fourth ed. Arnold, London.

Hollingshead, A.B., Redlich, F.C., 1958. Social Class and Mental Illness: A Community Study. Wiley, New York.

Johnson, L.D., O'Malley, P.M., Bachman, J.G., 2001. Monitoring the Future National Survey Results on Drug Use, 1975–2000, vol. I. Secondary School Students (NIH Publication No. 01-4924). National Institute on Drug Abuse, Bethesda, MD, 492 pp.

Klein, J.P., Moeschberger, M.L., 1997. Survival Analysis: Techniques for Censored and Truncated Data. Springer, New York.

Kosten, T.A., Rounsaville, B.J., 1992. Sensitivity of psychiatric diagnosis based on the best estimate procedure. Am. J. Psychiatr. 149, 1225–1227.

Lieb, R., Merikangas, K.R., Hoefler, M., Pfister, H., Isensee, B., Wittchen, H.U., 2002. Parental alcohol use disorders and alcohol use and disorders in offspring: a community study. Psychol. Med. 32 (1), 63–78.

Martin, C.S., Pollock, N.K., Bukstein, B.G., Lynch, K.G., 2000. Inter-rater reliability of the SCID alcohol and substance use disorders section among adolescents. Drug Alcohol Depend. 59, 173–176.

Merikangas, K.R., Stolar, M., Stevens, D.E., Goulet, J., Preisig, M.A., Fenton, B., Zhang, H., O'Malley, S.S., Rounsaville, B.J., 1998. Familial transmission of substance use disorders. Arch. Gen. Psychiatr. 55 (11), 973–979.

Moss, H.B., Clark, D.B., Kirisci, L., 1997. Developmental timing of paternal substance use disorder offset and the severity of problem behaviors in their prepubertal sons. Am. J. Addict. 6, 30–37.

Orvaschel, H., Puig-Antich, J., Chambers, W., Tabrizi, M.A., Johnson, R., 1982. Retrospective assessment of prepubertal major depression with the Kiddie-SADS-E. J. Am. Acad. Child. Adol. Psychiatr. 21, 393–397.

Schuckit, M.A., Smith, T.L., 1996. An 8-year follow-up of 450 sons of alcoholic and control subjects. Arch. Gen. Psychiatr. 53, 202–210.

Sher, K.J., Walitzer, K.S., Wood, P.K., Brent, E.E., 1991. Characteristics of children of alcoholics: putative risk factors, substance use, and abuse, and psychopathology. J. Abnormal Psychol. 100, 427–428.

Spitzer, R., Williams, B., Gibbon, M., 1988. Structured Clinical Interview for DSM-III-R. New York State Psychiatric Institute, Biometrics Research, New York.

Tarter, R., Kirisci, L., Mezzich, A., Cornelius, J., Pajer, K., Vanyukov, M., Gardner, W., Clark, D.B., 2003. Neurobehavior disinhibition in childhood predicts early age onset substance use disorder. Am. J. Psychiatr. 160, 1078–1085.

Tarter, R., Vanyukov, M., Giancola, P., Dawes, M., Blackson, T., Mezzich, A., Clark, D.B., 1999. Epigenetic model of substance use disorder etiology. Dev. Psychopathol. 11, 657–683.

Vitaro, T.E., Dobkin, P.L., 1996. Prevention of substance use/abuse in early adolescents with behavior problems. J. Alcohol Drug Educ. 41, 11–38.

Wilens, T.E., Biederman, J., Bredin, E., Hahesy, A.L., Abrantes, A., Neft, D., Millstein, R., Spenser, T.J., 2002. A family study of the high-risk children of opiod- and alcohol-dependent parents. Am. J. Addict. 11 (1), 41–51.

Windle, M., 1992. The Revised Dimensions of Temperament Survey (DOTS-R): simultaneous group confirmatory factor analysis for adolescent gender groups. Psychol. Assess. 4, 228–234.