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EMPIRICAL RESEARCH

Increased Pre- and Early-Adolescent Stress in Youth with a Family History of Substance Use Disorder and Early Substance Use Initiation

Nora E. Charles · Charles W. Mathias · Ashley Acheson · Bethany C. Bray · Stacy R. Ryan · Sarah L. Lake · Yuanyuan Liang · Donald M. Dougherty

Abstract Individuals with a family history of substance use disorders (Family History Positive) are more likely to have early-onset substance use (i.e., prior to age 15), which may contribute to their higher rates of substance use disorders. One factor that may differentiate Family History Positive youth who engage in early-onset substance use from other Family History Positive youth is exposure to stressors. The aim of this study was to quantify how exposure to stressors from age 11–15 varies as a function of family history of substance use disorders and early-onset substance use. Self-reported stressors were prospectively compared in a sample of predominately (78.9 %) Hispanic youth that included 68 Family History Positive youth (50 % female) who initiated substance use by age 15 and demographically matched non-users with (n = 136; 52.9 % female) and without (n = 75; 54.7 % female) family histories of substance use disorders. Stressors were assessed at 6-month intervals for up to 4 years. Both the severity of stressors and the degree to which stressors were caused by an individual's own behavior were evaluated. All three groups differed from one another in overall exposure to stressors and rates of increase in stressors over time, with Family History Positive youth who engaged in early-onset substance use reporting the greatest exposure to stressors. Group differences were more pronounced for stressors caused by the participants' behavior. Family History Positive users had higher cumulative severity of stressors of this type, both overall and across time. These results indicate greater exposure to stressors among Family History Positive youth with early-onset substance use, and suggest that higher rates of behavior-dependent stressors may be particularly related to early-onset use.

Keywords Substance use · Stress · Risk · Early adolescence

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Introduction

Youth with a family history of substance use disorders (Family History Positive) are three (Chassin et al. 1999) to nearly eight (Kilpatrick et al. 2000) times more likely to develop substance use disorders than are peers without such family histories (Family History Negative). The higher lifetime rates of substance use disorders among Family History Positive individuals may relate to differences present during adolescence, when Family History Positive individuals use substances at earlier ages and have a steeper increase in substance use over time (Chassin et al. 1996). Greater substance use among Family History Positive youth has been attributed to inherited traits associated with vulnerability to substance use disorders, such as

greater sensitivity to rewards (Andrews et al. 2011); greater impulsivity and antisocial tendencies (Sher et al. 1991), and more externalizing behaviors (Tarter et al. 2003). Family History Positive individuals also report more exposure to both major (Anda et al. 2002) and more moderate (Charles et al. in press) stressors during childhood, especially in the domains of family problems (Pillow et al. 1998), academic problems, issues with peers, and financial stress (Hussong et al. 2008). It has previously been suggested that this increased exposure to stressors in early life contributes to the increased risk for substance use disorders among Family History Positive youth (Sher et al. 1997). However, there is limited research on stressors experienced by Family History Positive youth specifically during adolescence, when substance use initiation becomes increasingly likely, and it is not known how exposure to stressors during this time may relate to early-onset (e.g., before age 15) substance use.

Adolescence is a period marked by physical and psychological changes such as greater involvement in peer relationships and increased autonomy. Some of these changes likely contribute to the increase in exposure to stressors that is typically seen after the transition from childhood to adulthood (Rudolph and Hammen 1999). Although some increase in exposure to stressors during this time is expected, particularly high levels of stress during adolescence have been associated with increased depressive symptoms (Ge et al. 2001) and externalizing symptoms (Grant et al. 2004). Several theories have been developed to explain how exposure to stressors may specifically relate to substance use. The stress-coping model (Wills and Shiffman 1985) and self-medication model (Khantzian 1985) of substance abuse suggest that substance use increases as users attempt to regulate their emotions and manage reactions to negative or stressful experiences. Other researchers have suggested that exposure to stressors impacts brain reward circuitry, resulting in increased sensitivity to the rewarding properties of substances and greater substance use (Koob and Le Moal 1997). These theories suggest that exposure to stressors is associated with higher levels of substance use, but do not address the question of whether stressors play a role in the early initiation of substance use. Previous research on the association between stressors and substance use during adolescence also does not address this question, as these studies have primarily used one of three approaches: (1) cross-sectional analyses, (2) retrospective reports collected from adults, or (3) prospective examinations of adolescents that focus on changes in substance use over time. Cross-sectional research has found that both severe stressors, such as experiencing or witnessing violence (Vermeiren et al. 2003) or being abused (Anda et al. 2002), as well as more moderate stressors, such as problems at school (Charles

et al. in press), work-related stress (Wiesner et al. 2005), and family conflict (Pillow et al. 1998) are more common among substance-using adolescents and young adults. The results of retrospective studies also indicate adults who had early-onset substance use (Rothman et al. 2008), who binge drink (Pilowsky et al. 2009) or drink heavily (Dube et al. 2002), and those with substance use disorders (Anda et al. 2006) report more stressors associated with childhood abuse and family dysfunction than do adults with no history of substance use disorders. Fewer studies have used prospective approaches, but exposure to stressors during adolescence has been associated with a greater escalation in substance use from early- to mid-adolescence (Hoffmann et al. 2000) and more substance use disorder symptoms by mid- to late-adolescence (Windle 2000). Taken together, these results suggest that exposure to stressors during childhood and adolescence is associated with both current and future substance use.

Although a number of studies have examined exposure to stressors and substance use, research in this area has been limited in four ways: (1) failing to account for influence of family history of substance use disorder, (2) focusing on checklist assessment methods, (3) not specifically analyzing stressors occurring during adolescence when substance use is typically initiated, and (4) lacking consideration for the individual's role in creating stressful situations. First, the contribution of a family history of substance use disorders has been understudied. No studies we are aware of have compared exposure to stressors during adolescence in Family History Positive and Family History Negative youth, or related exposure to stressors with substance use among Family History Positive youth. Given evidence of both increased exposure to stressors (Charles et al. in press) and increased risk for substance use disorders (Kilpatrick et al. 2000) among Family History Positive youth, the association between these factors may be especially important in this at-risk group. A second limitation of previous research has been the use of checklists, which contain a limited set of potential stressors (Dishion and Skaggs 2000) and typically only focus on more severe stressors such as being abused or witnessing violence (e.g., Kilpatrick et al. 2000). Third, many studies have not specifically assessed stressors occurring during adolescence, often grouping together all events occurring prior to age 18 (e.g., Anda et al. 2002). This is an important point, given that adolescence is a time of significant and rapid change that is associated with increases in both exposure to stressors (Rudolph and Hammen 1999) and likelihood of alcohol and drug use [Substance Abuse and Mental Health Services Administration (SAMHSA) 2012]. As a result, stressors occurring during early- to mid-adolescence may contribute uniquely to the development of substance use. In particular, stressors

during this time may relate to early-onset substance use (i.e., prior to age 15), which has been related to the development of substance use disorders (SAMHSA 2012). A final limitation is that no previous studies in this area have distinguished between stressors resulting from an individual's own actions (i.e., behavior-dependent) from those caused by outside forces (i.e., behavior-independent). This may be an important factor, given that research with other populations has found increases in behavior-dependent stressors (e.g., interpersonal conflict), but not behavior-independent stressors (e.g., being the victim of a crime), among individuals with bipolar disorder (Romero et al. 2009) and those with depression and anxiety (Connolly et al. 2010). A similar pattern may be present among Family History Positive youth and may relate to their risk for early-onset substance use, yet no research to date has examined this directly.

The Current Study

Previous research has documented an association between increased exposure to stressors and elevated substance use. It has been suggested that exposure to stressors can increase substance use through both emotional (e.g., Wills and Shiffman 1985) and neurobiological pathways (e.g., Koob and Le Moal 1997). However, it is not known whether the type and degree of stressors experienced during early to mid-adolescence relates specifically to early-onset substance use, which is a risk factor for developing a substance use disorder (SAMHSA 2012). In addition, it is not known whether these associations may be more pronounced among youth with a family history of substance use disorders, given their increased exposure to stressors (e.g., Charles et al. in press) and greater risk for substance use disorders (e.g., Chassin et al. 1999), or whether these Family History Positive individuals contribute to their relatively greater exposure to stress through behaving in ways that causes them to encounter more stressors. To address these gaps in the literature, this study was designed to measure a broad range of stressors occurring between ages 11–15 in Family History Positive and Family History Negative youth. Total stressors, behavior-independent stressors, and behavior-dependent stressors will be examined separately and prospectively. Exposure to stressors from age 11–15 will be compared across three groups: Family History Positive youth with early-onset substance use and two groups of non-users: one that is Family History Positive and one that is Family History Negative. It was hypothesized that Family History Positive youth would report greater overall exposure to stressors during adolescence than would Family History Negative youth, and that Family History Positive youth with early-onset substance

use would report greater overall exposure to stressors than would those without early-onset substance use. In addition, it was hypothesized that Family History Positive youth who initiated substance use during adolescence would report more behavior-dependent stressors than would youth who did not initiate substance use.

Methods

Participants

Participants were 279 adolescents (132 boys, 147 girls), most of whom had a family history of substance use disorders (Family History Positive; $n = 204$) and some of whom had no history of substance use disorders in their parents or grandparents (Family History Negative; $n = 75$). These adolescents were selected from a larger cohort of an ongoing longitudinal study of the development of substance use and impulsivity. Briefly, the most common substance use disorders in Family History Positive parents were alcohol dependence (42.2 %), cocaine dependence (26.2 %), and cannabis dependence (19.3 %). Families were recruited when youth were age 10–12 and followed for a maximum of 48 months (Median = 30 mo) prior to the current analyses. Exclusion criteria for the larger study were: regular substance use by the child (defined as use at least once per month for six consecutive months; Clark et al. 2005); positive urine-drug test at time of screening; low IQ (<70); or physical/developmental disabilities that would interfere with the ability to understand or complete study procedures. Current psychiatric diagnoses were exclusionary for the FH− group; oppositional defiant disorder, conduct disorder, ADHD, dysthymia, and anxiety disorders were allowed for Family History Positive youth because these disorders are commonly co-morbid with substance use involvement (Iacono et al. 2008).

One parent or guardian participated with each child; this included biological fathers (12.9 %), biological mothers (86 %) and other relatives (1.1 %). Study procedures were approved by the Institutional Review Board and participant data was further protected by a Certificate of Confidentiality from the Department of Health and Human Services.

Participant Selection and Classification

Two types of participants were selected and included from a larger longitudinal cohort ($n = 279$): Family History Positive adolescents who initiated substance use prior to age 15 (i.e., FH+ users; $n = 68$); and demographically matched Family History Positive adolescents who had not initiated substance use (i.e., FH+ non-users; $n = 136$)

were selected from the larger longitudinal study [described in Ryan et al. (in press)]. A 2–1 nearest neighbor propensity score matching without replacement method was used for selection of the Family History Positive non-users. Propensity scores were computed from a logistic regression model including the following pretreatment variables as covariates: number of visits, sex, ethnicity (Hispanic, non-Hispanic), race (Caucasian, African-American), age at most recent study visit (Median = 13.9 years), and number of parents and grandparents with substance use disorders (1–6). Our goal was to reduce the imbalance in covariates of interest between the Family History Positive non-user group and the Family History Positive user group on the aggregate level, which was achieved after propensity score matching. The main comparison of interest was between these two matched groups of Family History Positive adolescents (users and non-users). Very few Family History Negative youth in the larger study had initiated substance use ($n = 6$); those who had not initiated substance use ($n = 75$) were included in these analyses.

Study Procedures

Parents and children were placed in separate rooms to complete a battery of self-report, interview, and behavioral measures. At study entry, information was collected about demographic characteristics, family history of substance use disorders, family socioeconomic status, lifetime psychiatric symptoms, exposure to stressors, and substance use. Psychiatric symptoms, stressors, and substance use were re-assessed at biannual follow-up visits.

Measures

Parent and Grandparent Psychiatric Diagnosis

The Family History Assessment Module (FHAM; Janca et al. 1992) is a semi-structured interview that assesses major psychiatric disorders, including substance use disorders, in family members of the person being interviewed. For this study, parents were interviewed about psychiatric diagnoses in their children's parents, grandparents, and siblings. All Family History Positive participants had a biological father with a past or present substance use disorder; additional diagnoses in parents or other relatives were not exclusionary. All Family History Negative participants had no parents or grandparents with lifetime histories of substance use disorders.

Substance Use

Adolescent substance use was assessed using breath alcohol tests, urine-drug tests, and self-reports. Breath samples were tested using the AlcoTest® 7110 MKIII C device (Draeger Safety Inc., Durango, CO) and urine was tested using the Panel/Dip Drugs of Abuse Testing Device (Redwood Biotech, Santa Rosa, CA). Adolescents' self-reported substance use was collected at every visit using a drug history interview that assessed patterns of use for a number of licit and illicit drugs. All information regarding adolescent substance use was kept confidential from the parent/legal guardian. When breath/urine tests indicated substance use but no use was self-reported, participants were informed of their drug test results and re-interviewed regarding their substance use. Either self-reported drug use or a positive urine/breath test was considered sufficient to indicate substance use.

Socioeconomic Status

The Four Factor Index of Socioeconomic Status (Hollingshead 1975) assesses the socioeconomic status of a family based on parent education and occupation.

Intelligence

The Wechsler Abbreviated Intelligence Scale (The Psychological Corporation 1999) is a standardized measure of general intelligence in children and adults. IQ scores have a mean of 100 and a standard deviation of 15.

Adolescent Psychiatric Diagnosis

The Kiddie and Young Adult Schizophrenia and Affective Disorders Schedule, Present State and Lifetime (K-SADS; Kaufman et al. 1997) assesses past and present Axis I diagnoses in the adolescents. Both parents and children are interviewed about the presence of psychiatric symptoms.

Exposure to Stressors

The Stressful Life Events Schedule (SLES; Williamson et al. 2003) is a standardized semi-structured interview used to gather descriptions of stressors. The SLES interview assesses 80 different types of stressors that can be classified into ten categories: (1) Abuse (e.g., being physically or sexually abused); (2) Housing (e.g., moving, home requiring repairs); (3) Family (e.g., relationships problems, changes in household composition); (4) School/Work (e.g., academic problems, changing schools); (5) Crime (e.g., family or friends committing crimes, being the victim of a crime); (6) Medical (e.g., hospitalizations, illnesses for the child and close others); (7) Peers (e.g., problems in peer relationships, romantic relationships); (8) Deaths (e.g., deaths of friends or family members); (9) Money (e.g., parental unemployment, financial crises); and

(10) Other (four additional items that did not fit into other categories: "Have you revealed to anyone that you are bisexual/homosexual?", "Have you lost a pet or has your pet died or run away?", "Have you received any unexpected bad news?", and "Have you had to break any bad news to someone, which was not about your relationship with him/her?").

The severity and behavior dependence of reported stressors is rated by trained research staff using a standardized procedure (James et al. 2013). Briefly, the SLES interviewer meets with a group of three additional team members trained in rating SLES events to review each reported stressor. Participants' membership in the Family History Positive or Family History Negative group is not identified during these meetings. Each of the team members rates the severity and dependence of each event and then the group discusses any discrepancies in ratings to come to a final consensus rating. Severity ratings range from 1 (minimally stressful) to 4 (extremely stressful) and behavior dependence ratings range from 1 (totally independent) to 4 (totally dependent). If raters are not in agreement, the group comes to a consensus through discussion of event details and consultation with expert raters not involved in the original rating. We have previously found that the initial ratings of individuals within the consensus rating group have substantial agreement with the final rating for stressor severity (average $K = .65$) and excellent agreement for behavior dependence (average $K = .81$) across all event categories. In addition, these levels of agreement are maintained over at least a one-year period of consistent ratings (James et al. 2013). In this study, the cumulative severity of stressor exposure is calculated by squaring and summing the consensus objective severity ratings, so that more severe ratings are more heavily weighted (Williamson et al. 2003). Stressors whose consensus behavior dependence ratings were a 1 (totally independent) or a 2 (probably independent) were classified as behavior-independent and those whose consensus behavior dependence ratings were a 3 (probably dependent) or 4 (totally dependent) were classified as behavior-dependent.

The training procedure used to prepare research team members to administer and rate the SLES included several steps. First, an expert trainer was established. The team member that was designated as the expert trainer was trained by the developer of the SLES measure and then completed approximately 1200 observed SLES interviews and ratings under the supervision of the developer. Second, the expert trainer trained three staff members (i.e., expert trained raters) who practiced administration of the SLES interview under observation and led consensus meetings with the expert trainer present. Expert trained raters followed the same procedure to train all subsequent staff. To ensure the continued quality of ratings obtained from consensus meetings over the course of the study, the expert rater periodically joined consensus meetings to confirm the accuracy of ratings based on the standard criteria used in training.

Analyses

Propensity score matching was performed using Stata (version 13, StataCorp, College Station, TX). Other analyses were conducted using SPSS (version 21) software (IBM Corp., Armonk, NY) and SAS (version 9.3) software (SAS Institute, Inc., Cary, NC). Demographic information and frequency of psychiatric diagnoses were examined using Chi square tests or one-way ANOVA followed by LSD t test, as appropriate. Total numbers of stressors and overall cumulative severity of stressors were compared using one-way ANOVA followed by LSD t-test. Hierarchical linear modeling (HLM) was used to characterize the cumulative severity of stressors from age 11–15. HLM extends multiple linear regression modeling to repeated-measures data, provides a framework for analyzing individual change over time, and can accommodate time-invariant and time-varying predictors to determine whether individual characteristics are related to initial status or change over time. Change in cumulative severity of stressor exposure was modeled as a function of age in half-year increments from 11 to 15 years; group membership (Family History Positive user, Family History Positive non-user, Family History Negative non-user) was then added as a predictor of initial status and change over time. Additionally, tests of these models were also repeated, controlling for affiliation with delinquent peers (Peer Delinquency Scale; Loeber 1989), to test whether differences in stress trajectories between the groups are explained by differences in association with delinquent peers from age 11 to age 15. All models were fit using a compound symmetry covariance structure for the repeated-measures; SAS PROC MIXED was used to fit all models.

Results

Participant Characteristics

Demographics

Group demographics are presented in Table 1. The average age of participants at initial assessment was 11.6 years, they were of average IQ, and were predominantly Hispanic. Groups did not differ in age, sex, or ethnicity, though Family History Negative (FH−) youth had higher SES and IQs than did both groups of Family History Positive (FH+) youth. Within the FH+ group, users and non-users did not differ on any demographic variables. The prevalence of psychiatric

Table 1 Demographic and psychiatric details of the sample

	FH+ users N = 68	FH+ non-users N = 136 Mean (SD)	FH− non-users N = 75	Significance of three-group comparison F (p value)
Age at study entry	11.8 (0.8)	11.6 (0.9)	11.6 (1.0)	1.09 (.34)
Wechsler abbreviated scale of intelligence	93.8 (11.1)	94.4 (10.2)	102.5 (11.9)	16.18 (<.001)
Four factor index of socioeconomic status	31.6 (12.0)	31.7 (10.9)	43.5 (11.0)	30.53 (<.001)
		Number (%)		χ^2 (p value)
Sex				
Boys	34 (50.0)	64 (47.1)	34 (45.3)	.32 (.85)
Girls	34 (50.0)	72 (52.9)	41 (54.7)	
Ethnicity n (%)				
White/Caucasian	8 (11.8)	12 (8.9)	16 (21.3)	11.46 (.08)
Black/African-American	8 (11.8)	17 (12.5)	5 (6.7)	
Hispanic/Latino	51 (75)	107 (78.7)	52 (69.3)	
Other/Multiethnic	1 (1.5)	0 (0)	2 (2.7)	
Current psychiatric disorders				
Anxiety disorder	5 (6.7)	32 (23.5)	0 (0)	20.10 (<.001)
ADHD	21 (30.9)	35 (25.7)	0 (0)	27.26 (<.001)
ODD	9 (13.2)	12 (8.8)	0 (0)	10.94 (.004)

FH+ users: children with a family history of substance use disorders and early-onset use; FH+ non-users: children with a family history of substance use disorders and no early-onset use; FH− non-users: children without a family history of substance use disorders and no early-onset use. Diagnosis totals do not equal total n for the groups due to children with multiple diagnoses

ADHD attention deficit hyperactivity disorder, *ODD* oppositional defiant disorder

* $p < 0.01$, ** $p < .001$ difference between groups

diagnoses also varied across groups. By design, no FH– child met criteria for any externalizing or internalizing disorder, though some children in the FH+ group had current psychiatric disorders. Anxiety disorders and attention-deficit/hyperactivity disorder (ADHD) were the most common diagnoses, with nearly 20 % of FH+ youth having an anxiety disorder and nearly 30 % having ADHD. The prevalence of psychiatric disorders did not differ between FH+ non-users and FH+ users.

Substance Use

The mean age of substance use initiation was 13.5 years. The most commonly used substances were marijuana (64.7 %) and alcohol (60.3 %). Tobacco use was less common (38.2 %), and few participants reported using any other substances (11.8 %). Approximately half (51.5 %) reported using more than one substance.

Frequencies of Stressors

In total, 4863 stressors spanning the ages of 11–15 were reported and assessed. The three groups differed significantly from one another $(F(2,552) = 77.67, p < .001)$ in terms of average number of stressors reported per individual: FH+ users reported 27.1 $(SD = 14.2)$ stressors; FH+ non-users reported 16.3 $(SD = 9.4)$ stressors; and FH− non-users reported 10.4 $(SD = 7.5)$ stressors. Table 2 presents the associations between the total number of stressors reported, number of stressors within each category, and substance use status (0 = no use, 1 = use). Generally, higher overall numbers of stressors were more closely related to values for School/Work, Family, Peer, and Health stressors. Most of the subscales were positively related to substance use; values for School/Work, Family, Peers, and Crime were highest.

The most common stressors reported within each category are presented in Table 3. The frequencies of behavior-independent and behavior-dependent stressors across different categories are presented in Table 4. Briefly, the most common stressors were in the areas of Family, Health, School/Work, and Peers, and a higher number of stressors were behavior-independent than behavior-dependent (72.4 vs. 27.6 %). Compared to the other groups, FH+ users reported more behavior-independent and behavior-dependent stressors overall. FH+ users

Table 2 Associations between numbers of stressors in each category, total number of stressors, and substance use for the entire sample

	School/work	Money	Abuse	Family	Death	Peers	Housing	Health	Crime	Other	Total
Money	.373***										
Abuse	.142*	.173**									
Family	.396***	.391***	.142*								
Death	.233***	.153*	.009	.169**							
Peers	.512***	.294***	.175**	.384***	.164**						
Housing	.292***	.315***	−.043	.252***	.100	.052					
Health	.406***	.184**	.158**	.358***	.128*	.416***	.126*				
Crime	.300***	.240***	.002	.384***	.175**	.375***	.076	.325***			
Other	.234***	.244***	.184**	.253***	.060	.234***	.116	.314***	.216***		
Total stress	.755***	.522***	.212***	.710***	.302***	.770***	.363***	.662***	.534***	.468***	
Substance use	.362***	.136*	.088	.309***	.113	.457***	.024	.277***	.347***	.174**	.464***

* $p < 0.05$, ** $p < .01$, *** $p < .001$ difference between groups

Table 3 Total number of occurrences for the most common stressors reported in each category

Category	Most common stressors	Independent events	Dependent events
Abuse	Has anyone sexually abused you?	6	0
	Has anyone physically abused you?	1	0
Housing	Have you changed residences?	208	15
	Have there been any problems with your housing situation (e.g., overcrowding, pest infestations?)	71	2
Family	Has anyone moved into or out of your home?	416	1
	Have there been any changes in your parent(s), job(s), such that your parent(s) is/are away from home more often or at home more often?	107	0
School/Work	Have you had any difficulties with your performance at school, such as failing finals, classes, or grades and/or receiving deficiency reports or letters about your poor performance?	183	342
	Have you changed schools?	304	30
Crime	Were any close friends and/or family members caught committing any crimes?	103	1
	Were any close friends and/or family members a victim of a crime?	25	0
Health	Have any of your close friends and/or family members been hospitalized or had surgery?	229	0
	Did any of your close friends and/or family members have any serious injury, accident, or health emergency?	143	1
Peers	Have you started or ended a romantic relationship?	86	431
	Did you lose or have a falling out with a good friend?	40	125
Deaths	Have any of your close relatives (not immediate family) passed away?	137	0
	Have any of your close friends passed away?	37	0
Money	Was a parent fired, dismissed, or laid off from his/her job?	68	0
	Has your family had any financial crises?	87	0
Other	Have you lost a pet or has your pet died or run away?	234	5
	Have you received any unexpected bad news?	34	3

Independent events stressors caused by forces outside the individual's control; *dependent events* stressors resulting from an individual's own actions

reported more behavior-independent stressors in the areas of School/Work, Family, Peers, Health, and Crime and more behavior-dependent stressors in the areas of School/Work, Family, Peers, Health, Crime, and Other. There was also a group by behavior-dependence interaction such that the cumulative severity of behavior-dependent stressors

Table 4 Number and type of stressors per child reported by each group

Types of stress	Independent events					Dependent events				
	A FH+ users N = 68	B FH+ non-users N = 136	C FH− non-users N = 75	Omnibus test F (p value)	Group differences	A FH+ users N = 68	B FH+ non-users N = 136	C FH− non-users N = 75	Omnibus test F (p value)	Group differences
	Number of stressors M (SD)					Number of stressors M (SD)				
School/work	2.9 (1.9)	2.3 (1.9)	1.6 (1.2)	9.4 (<.001)	A>B>C	2.9 (2.4)	1.4 (1.5)	0.9 (1.4)	23.8 (<.001)	A>B, C
Money	0.9 (1.1)	0.8 (1.1)	0.3 (0.6)	8.3 (<.001)	A, B>C	0	0	0	0	
Abuse	0.04 (0.2)	0.02 (0.1)	0 (0)	1.65		0	0	0	0	
Family	4.0 (3.0)	2.7 (2.5)	1.3 (2.0)	19.7 (<.001)	A>B>C	0.8 (0.9)	0.4 (0.7)	0.3 (0.6)	8.8 (<.001)	A>B, C
Death	0.8 (1.0)	0.6 (0.8)	0.5 (0.7)	2.0		0	0	0	0	
Peers	1.4 (1.5)	0.8 (1.2)	0.5 (1.0)	10.0 (<.001)	A>B, C	5.2 (4.5)	1.7 (2.5)	1.1 (2.0)	39.6 (<.001)	A>B, C
Housing	1.1 (1.5)	1.2 (1.6)	0.7 (1.1)	3.8 (.02)	B<C	0.1 (0.3)	0.1 (0.4)	0	2.8	
Health	4.0 (3.0)	2.6 (2.3)	2.3 (2.2)	10.6 (<.001)	A>B, C	0.2 (0.4)	0.04 (0.2)	0.04 (0.2)	4.5 (.01)	A>B, C
Crime	1.2 (1.5)	0.5 (0.9)	0.2 (0.5)	19.0 (<.001)	A>B, C	0.1 (0.3)	0.02 (0.2)	0	8.0 (<.001)	A>B, C
Other	1.3 (1.9)	1.0 (1.3)	0.7 (1.0)	3.0	A>C	0.4 (0.6)	0.1 (0.4)	0.01 (0.1)	11.2 (<.001)	A>B, C
Total	17.7 (9.0)	12.6 (7.4)	8.2 (5.3)	47.8 (<.001)	A>B>C	9.5 (6.8)	3.8 (3.7)	2.4 (3.1)	50.6 (<.001)	A>B>C

FH+ users: children with a family history of substance use disorders and early-onset use; FH+ non-users: children with a family history of substance use disorders and no early-onset use; FH− non-users: children without a family history of substance use disorders and no early-onset use

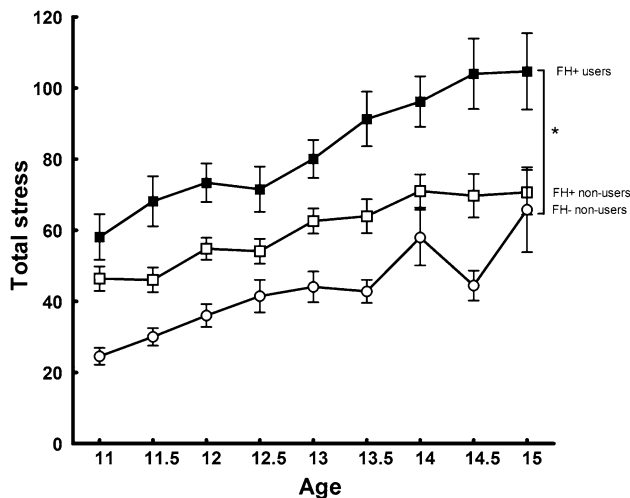* $p < 0.05$, ** $p < .01$, *** $p < .001$

Fig. 1 Cumulative severity of stressors over time in youth with a family history of substance use disorders and early-onset substance use (FH+ users); youth with a family history of substance use disorders and no early-onset substance use (FH+ non-users); and youth without a family history of substance use disorders and no early-onset substance use (FH− non-users). Exposure to stressors increases over time and change over time differs significantly across all three groups. *p < .001 difference across all three groups

was higher among FH+ users than for the other two groups, $F(2,552) = 5.02$, $p = .007$.

Cumulative Severity of Total Stressors Over Time

Increases in cumulative severity of stressors reported over time were examined using hierarchical linear modeling and results are presented in Fig. 1 and Table 5. The cumulative severity of total stressors significantly increased across all participants from age 11 to age 15. FH+ users and FH+ non-users did not differ from each other at age 11, but both had greater exposure to stressors than did FH− non-users at

initial assessment. Over the course of the study, exposure to stressors increased more among FH+ users than among the other two groups, whose rate of increase did not differ significantly. These relationships all remained significant when peer delinquency was included in the model.

Cumulative Severity of Behavior-Independent and Behavior-Dependent Stressors Over Time

Increases in cumulative severity of behavior-independent and behavior-dependent stressors over time were examined using separate hierarchical linear models. For behavior-independent stressors, the three groups did not differ at age 11 but the increase in cumulative severity of stressors from age 11–15 differed significantly across all three groups. FH+ users experienced the greatest increase in behavior-independent stressors, FH+ non-users experienced a more modest increase, and FH− non-users experienced the least change (see Fig. 2a; Table 5). For behavior-dependent stressors, FH+ non-users and FH− non-users had greater exposure to stressors at age 11 than did FH+ users. Over time, FH+ users experienced a greater increase in cumulative severity of behavior-dependent stressors than did the other two groups, who did not differ from one another (see Fig. 2b; Table 5). When peer delinquency was included in the model, the unexpected finding that FH+ users had fewer behavior-dependent stressors than the other groups at age 11 was no longer significant. The other associations remained significant.

Discussion

Youth with a family history of substance use disorders (Family History Positive youth) are more likely to develop substance use disorders than are peers without such family

Table 5 Group comparisons at study entry and trajectories over time

	FH+ users versus FH+ non-users		FH+ users versus FH− non-users		FH+ non-users versus FH− non-users	
At study entry						
Behavior-independent	−1.33	(2.86)	−1.02	(3.27)	0.31	(2.82)
Behavior-dependent	−3.36*	(1.11)	−3.07*	(1.28)	0.29	(1.10)
Total	3.54	(5.53)	16.87*	(6.31)	13.33*	(5.44)
Over time						
Behavior-independent	2.22***	(0.33)	3.67***	(0.40)	1.45*	(0.37)
Behavior-dependent	2.22***	(0.14)	2.47***	(0.17)	0.25	(0.16)
Total	5.09***	(0.47)	6.09***	(0.57)	1.00	(0.52)

FH+ users: children with a family history of substance use disorders and early-onset use; FH+ non-users: children with a family history of substance use disorders and no early-onset use FH− non-users: children without a family history of substance use disorders and no early-onset use. Beta weights with standard errors in parentheses
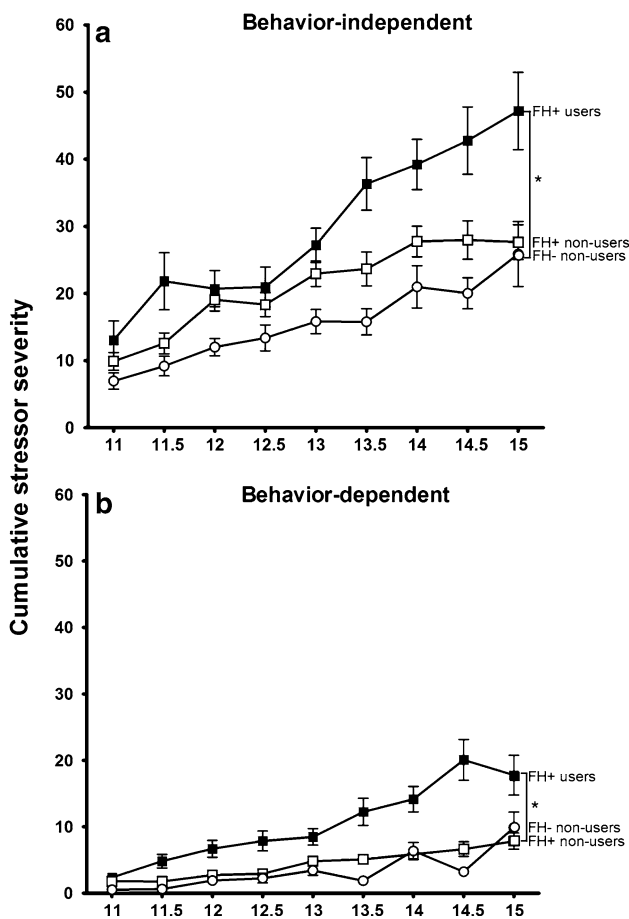
* $p < .05$, ** $p < .01$, *** $p < .001$

Fig. 2 Cumulative severity of behavior-independent (**a**) and behavior-dependent (**b**) stressors over time in youth with a family history of substance use disorders and early-onset substance use (FH+ users); youth with a family history of substance use disorders and no early-onset substance use (FH+ non-users); and youth without a family history of substance use disorders and no early-onset substance use (FH− non-users). FH+ users report a greater increase in both types of stressors. Although there were more behavior-independent stressors overall, the group difference for behavior-dependent stressors is larger than that for behavior-independent stressors. *$p < .001$ difference across all three groups

histories (Family History Negative youth). It is possible that environmental differences between Family History Positive and Family History Negative youth contribute significantly to their patterns of substance use beginning as early as adolescence. Previous research has established that Family History Positive youth have greater exposure to stressors during childhood (e.g., Charles et al. in press). Given that adolescence is usually associated with an increase in exposure to stressors (Rudolph and Hammen 1999), Family History Positive adolescents are especially likely to experience high levels of stressors during this developmental period. This elevated exposure to stressors during adolescence may contribute to early-onset substance use, which in turn increases risk for developing a substance

use disorder. This study provides a partial test of that model by focusing on whether stressors occurring in early-to mid-adolescence, an understudied developmental period for research of this type, differ as a function of family history of substance use disorders and early-onset substance use. The results provide new information about differences in exposure to a broad range of stressors occurring between ages 11 and 15 in a large, well-characterized sample of youth with a family history of substance use disorders who initiated substance use prior to age 15 (Family History Positive users) and two demographically matched groups of non-users with (Family History Positive non-users) and without (Family History Negative non-users) family histories of substance use disorders.

All three groups differed from one another in overall exposure to stressors, with Family History Positive users reporting the greatest exposure and Family History Negative non-users reporting the least exposure. The increased exposure to stressors among Family History Positive users was found for both behavior-independent and behavior-dependent stressors, but the magnitude of this group difference was greater for behavior-dependent stressors. When trajectories of stressor exposure over time were examined, each group differed significantly from one another: Family History Positive users reported the greatest increase in cumulative exposure to stressors from age 11 to age 15, Family History Positive non-users reported a more modest increase, and Family History Negative non-users reported the least increase in stressors. The pattern for behavior-independent stressors was similar to that for total stressors, but for the behavior-dependent stressors, the Family History Positive non-users and Family History Negative non-users did not differ from one another and both increased significantly less than did the Family History Positive user group. Taken together, these results indicate greater exposure to stressors during preadolescence and early adolescence among Family History Positive youth with early-onset substance use, and suggest that behavior-dependent stressors may be especially related to early initiation of substance use.

The present research extends the literature on the impact of exposure to stressors on adolescent development in important ways. First, this study expands on research showing normative increases in exposure to stressors from childhood to adolescence (Rudolph and Hammen 1999) by demonstrating that the magnitude of this increase is relatively greater among Family History Positive youth compared with Family History Negative youth, and suggesting that this difference could relate to their different levels of risk for developing a substance use disorder. Second, the finding that increased exposure to stressors among Family History Positive youth is associated with early-onset substance use is consistent with other research suggesting that the effects of stressors on adolescent

behavior may depend on moderating factors that predispose an adolescent to certain types of outcomes. For example, exposure to stressors predicts depressive symptoms in adolescents with depressed mothers (Hammen et al. 2004) and predicts criminal behavior in youth affiliated with delinquent peers (Agnew 2008). Therefore, exposure to stressors during adolescence can be thought of as a factor that exacerbates tendencies for which there is already some vulnerability, and early-onset substance use may be a particular concern for Family History Positive youth exposed to stressors during adolescence.

In addition, this work adds to the understanding of the specific association between stressors and adolescent substance use in two important ways. First, compared to previous research using checklists of stressors (e.g., Dishion and Skaggs 2000), this study used an interview format that queried not only severe stressors, such as being abused, but also more moderate and mild stressors, such as peer conflict. Assessing this broad range of stressors improves understanding of which types of stressors are most prevalent among Family History Positive youth and which are most associated with early-onset substance use. Second, this study extends previous research relating stressors and substance use by specifically assessing stressors during preadolescence and early adolescence. These results are consistent with studies indicating that Family History Positive individuals, relative to Family History Negative peers, experience more stressors prior to age 18 (e.g., Anda et al. 2002), as well as research associating stressors during childhood (e.g., Charles et al. in press) and up to age 18 (e.g., Dube et al. 2006) with early-onset substance use. The findings from the current study add to this literature by demonstrating the magnitude and types of stressors occurring from age 11–15 vary as a function of both family history status and early-onset substance use.

Another important way in which this study extends previous research is the separate examination of behavior-independent and behavior-dependent stressors. Much of the existing research on stressors during childhood and adolescence is based on the assumption that stressors cause emotional and behavioral problems, with less attention paid to whether the stressor is the result of the individual's actions (i.e., behavior-dependent) or external sources (i.e., behavior-independent). However, there is a growing body of research that suggests a reciprocal relationship between stressors and emotional and behavioral problems. This research has primarily focused on depression (for review, see Hammen 2006), though similar results have been reported anxiety disorders (Connolly et al. 2010), bipolar disorder (Romero et al. 2009), and personality disorders (Daley et al. 1998), as well as traits such as neuroticism (Kendler et al. 2003). In the present study, Family History Positive users had greater exposure to stressors overall but a relatively larger increase for behavior-dependent stressors than behavior-independent stressors. The most common behavior-dependent stressors reported by the Family History Positive user group were in the areas of School/Work and Peers. The School/Work items include events such as being disciplined at school and not completing schoolwork. The Peers items include conflicts with peers as well as problems related to romantic relationships and sexual behavior. These types of events are likely to be associated with traits such as greater impulsivity and antisocial tendencies (Sher et al. 1991), hyperactivity and cognitive deficits (Pihl et al. 1990), and more externalizing behaviors (Tarter et al. 2003), which are more common among Family History Positive individuals. This suggests that some of the association between having a family history of substance use disorders and risk for substance use disorders may be the result of inherited traits, such as impulsivity, increasing exposure to stressors that, in turn, increase risk for substance use.

The interpretation of these results must be made in the context of the limitations of this investigation. The SLES measures itself, although more comprehensive than many measures used in previous research, is a self-report measure that requires youth to accurately report their exposure to stressors. As a result, it is possible that some stressors may have been omitted from reports and that those that were reported may have included incomplete or inaccurate information. Additionally, the ratings derived from the SLES involve the research team coming to a consensus about different aspects of the stressors. Although raters in this study were extensively trained and monitored by expert raters, it is possible that there were biases that could have affected the rating process. Future research on exposure to stressors and substance use during adolescence may seek to overcome these limitations by including information about the nature and severity of stressors from additional reporters, such as parents. This methodology would maximize confidence in the measurement of stressors and, accordingly, understanding of their relation to the development of substance use.

Although there were limitations, this study also has significant strengths that include using a large sample size, following participants longitudinally, and assessing a wide range of stressors in a detailed manner. The methodology used in this study overcomes some of the limitations of previous research that was cross-sectional or limited in scope and size. In addition, this study extends previous research by focusing specifically on stressors occurring during preadolescence and early adolescence. It is possible that stressors occurring during this important developmental period are especially related to the development of substance use, as it is during this time that the risk for initiating substance use increases sharply. Finally, this

study is the first to examine the unique associations of behavior-independent and behavior-dependent stressors with substance use during adolescence. The results of those analyses, in particular, suggest some areas of focus for future research. Given that a relatively larger proportion of the increased stressors observed among Family History Positive users resulted from behavior-dependent stressors, it would be advantageous to develop prevention and early intervention techniques that target behaviors which could lead to this type of stressor, such as reducing aggression, impulsivity, or other problematic behaviors. In addition, we are continuing to follow this cohort prospectively and our future research will explore how stressors, especially behavior-dependent stressors, relate to the development of more regular substance use and substance use disorders.

Conclusion

The results of this study make an important contribution to the study of adolescent substance use by clarifying associations between family history of substance use disorders, exposure to stressors from age 11–15, and early-onset substance use. The finding that Family History Positive youth experience greater exposure to stress during early- to mid-adolescence than do Family History Negative youth extends previous research showing that Family History Positive youth have greater exposure to stressors during childhood (e.g., Charles et al. in press). In addition, the different trajectories of stressor exposure between Family History Positive youth with and without early-onset substance use suggests that the association between exposure to stressors and the development of substance use disorders (e.g., Anda et al. 2002) may occur via a pathway that includes early-onset substance use. Finally, this study indicates that behavior-dependent stressors are particularly relevant for early-onset substance use, which has interesting implications for clinical practice if behavior modifications are able to reduce exposure to behavior-dependent stressors.

Author Contributions NC conducted literature searches, summarized previous related work, contributed to data collection and statistical analyses, and wrote the initial draft of the manuscript. CM designed and coordinated the study, participated in the interpretation of results, and contributed to the initial draft of the manuscript. DD designed and coordinated the study and participated in the interpretation of results. SR made final determination of participants' psychiatric diagnoses. BB and YL conducted the statistical analyses. AA and SL participated in the interpretation of results and helped draft the manuscript. All authors contributed to revisions and approved the final manuscript.

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