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Adverse childhood experience effects on opioid use initiation, injection drug use, and overdose among persons with opioid use disorder

Michael D. Stein^{a,b}, Micah T. Conti^{a,c}, Shannon Kenney^{a,d}, Bradley J. Anderson^a, Jessica N. Flori^{a,c}, Megan M. Risi^{a,c}, and Genie L. Bailey^{c,d}

^aBehavioral Medicine, Butler Hospital, Providence, RI, 02906

^bBoston University School of Public Health, Boston, MA 02118

^cStanley Street Treatment and Resources, Inc., Fall River, Massachusetts 02720

^dWarren Alpert Medical School of Brown University, Providence, RI, 02912

Abstract

Introduction—Adverse childhood experiences are associated with the development of substance use disorders. With opioid use disorder, a growing concern in the United States, we were interested in examining the relationship between adverse experiences and three landmarks of opioid use: age of opioid initiation, injection drug use, and lifetime overdose.

Methods—Between May and December 2015, we interviewed consecutive persons seeking inpatient opioid detoxification. Participants were asked about age of opioid initiation, last month injection drug use, and lifetime history of overdose, and completed the ten-item Adverse Childhood Experience (ACE) questionnaire.

Results—Participants ($n=457$) averaged 32.2 (± 8.64) years of age, 71.3% were male, and 82.5% were non-Hispanic White. The mean score on the ACE scale was 3.64 (± 2.75). Mean age at time of initiating opioid use was 21.7 (± 7.1) years, 68.7% had injected drugs within the past month, and 39.0% had overdosed. After adjusting for age, gender, and ethnicity, the ACE score was inversely associated with age of initiating opioid use ($b = -0.50$, 95% CI $-0.70; -0.29$, $p < .001$),

Correspondence: Michael D. Stein, M.D., Professor of Health Law, Policy and Management, Boston University School of Public Health, 715 Albany Street, Boston, MA 02118, Telephone: (617) 414-0319, mdstein@bu.edu.

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Contributors

Drs. Bailey, Flori, and Risi collected the data used in the current manuscript. Drs. Stein, Conti, and Anderson generated the design and analyses used in the current study. Drs. Conti and Kenney conducted the literature review, wrote the Introduction, Methods, and Discussion, and revised the final draft of the manuscript. Dr. Anderson conducted statistical analyses, wrote the Results section, and reviewed manuscript drafts. All authors reviewed and provided feedback on drafts of the manuscript, and contributed to and have approved the final manuscript.

Conflict of Interest

Dr. Bailey reports personal fees from BioDelivery Science International, Inc., grants, personal fees and other from Braeburn Pharmaceuticals, Inc., personal fees from Camurus AB, grants from Orexo, grants and other from Reckitt-Benckiser (Indivior), other from Titan Pharmaceuticals, Inc., outside the submitted work. (ICMJE form available upon request.)

and positively associated with recent injection drug use (OR = 1.11, 95% CI 1.02; 1.20, $p = .014$) and the likelihood of experiencing an overdose (OR = 1.10, 95% CI 1.02; 1.20, $p = .015$) in a graded dose response manner.

Conclusion—Greater adverse childhood experiences are associated with three landmarks of opioid use risk. ACE screening may be useful in identifying high-risk subsets of opioid-using populations.

Keywords

opiates; detoxification; adverse childhood experiences

1.0 Introduction

Opioid use disorder is a growing public health concern. In addition to its high prevalence, the morbidity and mortality associated with opioid use has increased dramatically, with incidents of overdose nearly quadrupling over the past decade (NSDUH, 2014)).

Previous studies investigating the precursors of substance misuse have focused on childhood adversity, often childhood sexual abuse (CSA) (Darke et al., 2005; Heffernan et al., 2000; Kendler et al., 2000), which is strongly associated with experiencing other adverse events in childhood (Dong, Anda, et al., 2004). The Adverse Childhood Experiences (ACE; Felitti et al., 1998) questionnaire was developed to examine the long-term effects of childhood experiences on medical problems and examines a wide array of childhood adversity. Greater number of ACEs experienced (e.g., abuse, neglect, household dysfunction) have been correlated with several adult physical illnesses such as obesity, diabetes, ischemic heart disease, and frequent headaches (Anda et al., 2010; Dong et al., 2004; Felitti et al., 1998; Monnat and Chandler, 2015). Additionally, ACE scores are associated with several psychiatric problems including depressive disorders, psychosis, and suicidality (Brodsky and Stanley, 2008; Chapman et al., 2004; Trotta et al., 2016). ACE scores are also associated with smoking, alcohol abuse, and illicit drug use (Allem et al., 2015; Anda et al., 2002; Douglas et al., 2010; Dube et al., 2002; Dube et al., 2003).

With respect to opioid use, adverse experiences during childhood (e.g., parental substance use, emotional neglect, physical and sexual abuse) have been linked to opioid dependence (Afifi et al., 2012; Moselhy et al., 2010) and earlier age of injection drug use (IDU) initiation (Taplin et al., 2014).

In the present study, we explored three landmarks of opioid use: age of opioid initiation, current IDU, and lifetime overdose and their relationship to ACE score. Age of opioid use initiation is a critical developmental concern, as those who initiate drug use at an earlier age are more likely to develop drug dependence problems (Anthony and Petronis, 1995; Baldwin et al., 2013; Chen et al., 2009; King and Chassin, 2007). Another milestone in the history of an opioid user is the transition from prescription opioids to injection heroin use. IDU is associated with serious medical complications, including HIV and HCV infection (Bruneau et al., 2012; Torres et al., 2011) as well as a greater risk for overdose (Lake et al., 2015). Many injection heroin users have a history of problematic prescription opioid use prior to heroin

initiation (Muhuri et al., 2013; Pollini et al., 2011) and IDU suggests an escalation in addiction severity. In this cross-sectional study of opioid users entering a detoxification program, we hypothesized that higher ACE scores (i.e., reported adverse experiences during childhood) would correlate with an increased probability of each of these risk outcomes.

2.0 Methods

Between May and December 2015, consecutive persons seeking inpatient opioid detoxification were approached by research staff upon admission to Stanley Street Treatment and Resources, Inc. (SSTAR) in Fall River, Massachusetts to participate in a survey. SSTAR's program has 38 beds and is a 24-hour medically supervised detoxification facility that provides evaluation and withdrawal management followed by referral to outpatient substance use treatment.

Five hundred thirty consecutive patients admitted to SSTAR for detoxification during the recruitment period met eligibility criteria (i.e., 18 years or older and English-speaking) to provide verbal informed consent as approved by the Butler Hospital Institutional Review Board and were invited to participate in the current study. Forty-two refused participation or were missed by research staff due to early discharge. The remaining 488 consented to a face-to-face, 15-minute, structured, standardized interview within the first 24 hours of admission after withdrawal symptoms had relented; no compensation was provided. A total of 457 participants completed the interview and were available for analysis.

2.1 Measures

Sample descriptors included age, gender, race and ethnicity. Participants were asked about age of opioid initiation, last month IDU (yes/no), and, "Since your first drug use, have you ever overdosed?" We asked participants about the presence of adverse childhood experiences they experienced using the ten-item ACE questionnaire (Felitti et al., 1998). Internal consistency reliability of the 10-item index was .79 in this sample.

2.2 Analytical Methods

ACE scores were calculated as the sum of ten yes/no questions about abuse, neglect, and household dysfunction. We report descriptive statistics to summarize the characteristics of the sample. Between sex differences in ACE item responses were measured using t-tests for differences in means and χ^2 tests for differences in counts. Adjusting for age, gender, and race/ethnicity, multivariate linear regression was used to estimate the adjusted association of ACE scores with age of opioid initiation; tests of significance and 95% confidence interval estimates were based on heteroskedastic Huber-White standard errors. We used multivariate logistic regression to estimate the adjusted association of ACEs with the likelihood of recent IDU and lifetime drug overdose. Because age of opioid use may have been initiated prior to age 18, we conducted an auxiliary analysis to estimate the adjusted association of ACE scores with age of opioid initiation among persons ($n = 321$) who initiated opioid use at age 18 or older.

3.0 Results

3.1 Demographics

As shown in Table 1, participants ($n = 457$) averaged $32.2 (\pm 8.64)$ years of age, 71.3% were male, 8.8% were Hispanic, 86.9% were White, 5.5% were Black, and 7.7% identified other racial origins. Race/Ethnicity was dichotomized to contrast non-Hispanic Whites to all minorities in subsequent analyses. Age at time of initiating opioid use ranged from 12 – 54 years with a mean of $21.7 (\pm 7.12)$, Median = 20) years. Past 30-day IDU was reported by 68.7% of the sample and 39.0% reported a drug overdose at least once in their life.

3.2 ACE Distribution

Individual ACE items and prevalence are shown in Table 2. The most frequently endorsed items were having parents who were separated or divorced (59.5%), living with a problem drinker or someone who used drugs (51.4%), and having an adult in the household who often swore at or humiliated them (47.5%). The mean score on the 10-item scale was $3.64 (\pm 2.75)$, Median = 3.0). Sixty-seven (14.7%) participants did not endorse any item, 168 (36.8%) had scores between 1 and 3, and 222 (48.6%) had scores of 4 or higher. Compared to males, females were significantly ($\chi^2 = 55.87, p < .001$) more likely to endorse being touched or fondled in a sexual way, feeling that no one in their family loved or thought they were important ($\chi^2 = 6.66, p = .010$), having a mother or stepmother who pushed, shoved, or grabbed them ($\chi^2 = 5.53, p = .019$), living with a problem drinker or alcoholic ($\chi^2 = 4.10, p = .043$), and saying that a household member was depressed, mentally ill, or attempted suicide ($\chi^2 = 9.31, p = .002$). Overall, mean ACE scores for females (4.39 ± 2.92) were significantly ($t = 3.80, p < .001$) higher than for males (3.33 ± 2.63).

3.3 Adjusted Association of ACEs with Landmarks of Opioid Use

After adjusting for age, gender, and race/ethnicity, the ACE score was inversely associated with age of opioid use initiation ($b = -.50, 95\%CI -0.70; -0.29, p < .001$) (Table 3). A 1-point increase in the ACE was associated with a 1.11 (95%CI 1.02; 1.20) factor increase in the expected likelihood of a recent IDU and a 1.10 (95%CI 1.02; 1.20) factor increase in the expected odds of reporting a lifetime overdose. Associations with age, gender, and race/ethnicity are also reported in Table 3.

Among persons who initiated use at 18 years of age or older, the estimated adjusted association of ACE scores with age of opioid initiation was statistically significant ($b = -0.31, 95\%CI -0.51; -0.11, p = .003$) but somewhat attenuated when compared to the full sample.

4.0 Discussion

In this sample of persons with opioid use disorder entering a detoxification program, the number of ACE items endorsed was independently correlated with three landmarks in the trajectory of opioid use: age of initiation, ongoing IDU, and lifetime experience of overdose. Our study supports the findings from the two previous studies examining the ACE items in general populations in which higher ACE scores correlated with recent illicit drug use,

parenteral drug use, and an earlier age of initiation of “street” drug use (Allem et al., 2015; Dube et al., 2003) using novel developmental landmarks. Our findings demonstrate that adverse experiences of childhood are associated with each opioid-related behavioral marker in a graded, dose-response manner.

The robust relationships found between ACE score and opioid-related risk behaviors in this sample may be explained by numerous intersecting environmental and biological influences. For example, parental substance use (and mental health) problems may contribute to children’s drug use risk through genetic heritability, through direct modeling of parental behaviors (e.g., drug use to cope with negative affect states), and also by exacerbating environmental stressors (e.g., abuse, neglect, poverty, parental criminal justice involvement) that, in effect, drain critical resources, disrupt social learning, and inhibit skills acquisition in children (Lake et al., 2015). Negative childhood experiences are associated with impaired cognitive, emotional, and social development, including maladaptive coping mechanisms that may include substance misuse (Repetti et al., 2002; SAMHSA, 2015). Adverse childhood experiences may lead to neural changes, such as memory, attention allocation, perceptual cognitive processing, and cortical development impairment (Bick and Nelson, 2016; Gould et al., 2012; Matz et al., 2010; Teicher et al., 1997). Also, Gerra et al. (2014) identified a significant relationship between childhood neglect, arousal reaction, impaired hypothalamus-pituitary-adrenal axis response, and addiction severity. Although higher ACE scores may thus signify greater early epigenetic change and hence greater behavioral risk, studies point to the need for longitudinal research to support causal effects (see Vinkers et al., 2012 for review).

The graded association that emerged between number of ACEs and opioid risk outcomes is consistent with prior studies examining drug use (Allem et al., 2015; Dube et al., 2003) and a range of health risk behaviors (for review see Kalmakis and Chandler, 2014). This cumulative effect of ACE scores may be particularly important when studying opioid dependent persons who are susceptible to histories of multifaceted childhood trauma and adversity (Hayaki et al., 2005; Sansone et al., 2009). In the current study, participants reported a substantially higher mean ACE score than general population studies; for instance, nearly half of the respondents in this sample versus 15.5% in Dube et al.’s (2003) community-based study reported 4 or more of the 10 ACE consequences.

As has been documented in existing research, men in this sample reported earlier age of onset (Evans et al., 2015; Kelly et al., 2009) and were more likely to report recent IDU (Tetrault et al., 2008; Trenz et al., 2012) and lifetime overdose (Clausen et al., 2008) than women. However, women reported more ACEs overall and were nearly four times more likely to report childhood sexual abuse than men, consistent with prior research (Cavanaugh et al., 2015; Finkelhor et al., 2014). Given that women represent a growing segment of opioid dependent users (Cicero et al., 2008) and show more rapid progression from opioid initiation to dependence as well as greater vulnerability to opioid-related consequences than males (Hernandez-Avila et al., 2004), future research should further investigate the relationships between ACEs and opioid-related risk among women despite women’s lower overall opioid use patterns relative to men.

Limitations of this study include the fallibility of participants' retrospective recall of adverse experiences in childhood (Femina et al., 1990). Also, participants answered questions in-person with interviewers, which may have led to response bias and underreported ACE history and drug use behaviors. Third, our data came from opioid users entering a single detoxification program in the northeastern United States who were primarily White and male; therefore, these findings may not be representative of opioid users in other regions, not undergoing detoxification, those in medication-assisted treatment or samples that might consist primarily of women. Fourth, the ACE measure represents a particular set of ten experiences, and does not capture all childhood challenges. Fifth, although the vast majority of participants were detoxifying from heroin when recruited for this study, we did not ask about heroin use onset or age of first opioid injection. Finally, it is possible that participants' reported landmarks occurred prior to reported adverse events.

4.1 Conclusions

By demonstrating a significant additive negative impact of experiencing multiple adverse events during childhood, these findings have implications for community-based screening and clinical care of opioid users. Early prevention strategies could use high ACE scores as a marker for adolescents at risk for early opioid initiation. Including the ACE measure in assessment batteries for patients seeking treatment of opioid use disorders may provide a standardized way to identify patients at heightened risk for injection and overdose.

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Highlights

- Adverse Childhood Experiences (ACE) were associated with earlier age of initiating opioid use.
- ACE were associated with recent injection drug use and lifetime overdose.
- About half of respondents experienced four or more of the ten assessed ACE.

Table 1

Descriptive Statistics (n = 457).

	n (%)	Mean (SD)	Median	Range
Age		32.2 (\pm 8.64)	30	18 – 64
Sex (Male)	326 (71.3%)			
Hispanic Ethnicity	40 (8.8%)			
Race				
White	397 (86.9%)			
Black	25 (5.5%)			
Other	35 (7.7%)			
Age Initiated Opioid Use		21.7 (\pm 7.12)	20	Dec-54
ACE Score		3.63 (\pm 2.75)	3	0 – 10
IDU Past 30-Days	314 (68.7%)			
Ever Overdose	178 (39.0%)			

Table 2

Endorsement of Individual ACE Items by Sex. Cells give % endorsing and (95% confidence interval estimate). Respondents were asked, “While you were growing up, during your first 18 years of life,” then were asked the following questions.

	SEX			χ^2 (p =)
	Sample (n = 457)	Female (n = 131)	Male (n = 326)	
1. Did a parent or other adult in the household often swear at you, insult you, put you down, or humiliate you? Or did they act in a way that made you afraid that you might be physically hurt?	47.70%	53.80%	45.40%	2.67
	(43.1; 52.5)	(44.9; 62.6)	(39.9; 51.0)	-0.102
2. Did a parent or other adult in the household often push, grab, slap, or throw something at you? Or did they ever hit you so hard that you had marks or were injured?	36.20%	40.80%	34.50%	1.6
	(31.8; 40.8)	(32.2; 49.7)	(29.3; 39.9)	-0.206
3. Did an adult or person at least 5 years older than you ever touch or fondle you or have you touch their body in a sexual way? Or did they try to actually have oral, anal or vaginal sex with you?	19.60%	41.50%	10.80%	55.87
	(16.0; 23.5)	(33.0; 50.5)	(7.6; 14.7)	(<.001)
4. Did you often feel that no one in your family loved you or thought you were important or special? Or your family didn't look out for each other, feel close to each other, or support each other?	38.80%	48.10%	35.10%	6.66 (.010)
	(34.3; 43.4)	(39.3; 57.0)	(29.9; 40.5)	
5. Did you often feel that you didn't have enough to eat, had to wear dirty clothes, and had no one to protect you? Or your parents were too drunk or high to take care of you or take you to the doctor if you needed it?	16.50%	19.80%	15.10%	1.51
	(13.2; 20.2)	(13.4; 27.2)	(11.4; 19.5)	-0.219
6. Were your parents ever separated or divorced?	59.80%	58.80%	60.20%	0.08 (.782)
	(55.1; 64.3)	(49.8; 67.3)	(54.6; 65.6)	
7. Was your mother or stepmother Often pushed, grabbed, slapped or had something thrown at her? Or sometimes or often kicked, bitten, hit with a fist, or hit with something hard? Or ever repeatedly hit over at least a few minutes or threatened with a gun or knife?	28.80%	36.60%	25.60%	5.53
	(24.7; 33.2)	(28.4; 45.5)	(21.0; 30.7)	-0.019
8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?	51.30%	58.80%	48.30%	4.1
	(46.6; 56.0)	(49.8; 67.3)	(42.7; 53.9)	-0.043
9. Was a household member depressed or mentally ill or did a household member attempt suicide?	34.40%	45.00%	30.00%	9.31
	(30.0; 38.9)	(36.3; 54.0)	(25.1; 35.4)	-0.002
10. Did a household member go to prison?	20.30%	34.60%	28.60%	1.6
	(26.1; 34.8)	(26.5; 43.4)	(23.7; 33.8)	-0.206

Table 3

Adjusted Associations of Age of Initiating Opioid Use, Recent Injection Drug Use, and Lifetime History of Overdose with Demographic Characteristics and the Adult Childhood Experiences Scale (n = 457)

	Age Opioid Use	Recent IDU	Lifetime Overdose
	b (95% CI)^a	OR (95% CI)^b	OR (95% CI)^b
Years Age	0.40 *** (0.30; 0.50)	1.00 (0.97; 1.03)	1.03 * (1.01; 1.06)
Gender (Male)	-2.14 *** (-3.38; -0.90)	1.91 ** (1.21; 3.03)	1.91 ** (1.20; 3.10)
Non-Hispanic White	-1.96 * (-3.49; -0.44)	2.16 ** (1.28; 3.64)	1.05 (0.61; 1.80)
ACE	-0.50 *** (-0.70; -0.29)	1.11 ** (1.02; 1.20)	1.10 ** (1.02; 1.20)

* p < .05,

** p < .01,

*** p < .001

^a Ordinary least squares regression model. Tests of significance and 95% confidence intervals estimated using the heteroskedastic robust Huber-White standard errors.

^b Adjusted odds-ratios for estimated by multivariate logistic regression.