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Psychology of Addictive Behaviors

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Associations Between Childhood Adversity, Adult Stressful Life Events, and Past-Year Drug Use Disorders in the National Epidemiological Study of Alcohol and Related Conditions (NESARC)

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Stress sensitization, whereby CA lowers tolerance to later stressors, has been proposed as a potential mechanism explaining the association between exposure to childhood adversities (CA) and drug use disorders in adulthood. However, this mechanism remains untested. This paper begins to address this gap through exploring associations between CA exposure and stressful events in adulthood for predicting drug use disorders. We used data drawn from Wave 2 of the U.S. National Epidemiological Survey of Alcohol and Related Conditions (n = 34,653) to explore whether the association between past-year stressful life events and the 12-month prevalence of disordered cannabis, stimulant, and opiate use varied by the number of types of CA that an individual was exposed to. Past-year stressful life events were associated with an increased risk of cannabis, stimulant, and opiate use disorders among men and women. Exposure to CA was associated with increased risk for disordered cannabis use among men and women and opiate use among men only. Finally, we found significant associations between exposure to CA and past-year stressful life events in predicting disordered drug use, but only for women in relation to disordered stimulant and opiate use. Findings are suggestive of possible stress sensitization effects in predicting disordered stimulant and opiate use among women. Implications of these findings for the prevention and treatment of drug use disorders and for future research are discussed.

Keywords: childhood adversity, stressful life events, drug use disorders, NESARC

The prevalence of drug use disorders is high in the general population, with an estimated 2–3% of the U.S. population meeting the *Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition* (*DSM–IV*) criteria for 12-month drug abuse or dependence (Grucza, Abbacchi, Przybeck, & Gfroerer, 2007). One strategy for reducing the prevalence of these disorders is to identify and intervene with individuals who are at high risk for drug-related problems. Previous research, conducted across multiple contexts and populations, has shown significant associations between exposure to childhood adversities (CAs) and drug use disorders in adolescence and adulthood (Cuijpers et al., 2011; Douglas et al., 2010; Dube et al., 2003). Specifically, exposure to CAs such as domestic violence (Dube et al., 2003; Fagan & Wright, 2011); physical, emotional and sexual abuse (Douglas et al., 2010; Shin, Hong, & Hazen, 2010); neglect (Dube et al., 2003; Shin, Miller, & Teicher, 2013); and parental dysfunction due to alcohol or drug use (Douglas et al., 2010) increase propensity for drug use disorders across the life span (Clark, Caldwell, Power, & Stansfeld, 2010). In addition, the effects of CA appear cumulative, with greater exposure to CAs associated with heightened risk for drug use disorders (Dube et al., 2003; Pérez-Fuentes et al., 2013; Sugaya et al., 2012). Together, these findings suggest that exposure to CA may act as a diathesis for drug use disorders.

The diathesis-stress model of psychopathology offers a possible explanation for the association between CA and drug use disorders. According to this model, psychopathology arises from the interaction between a diathesis, such as CA, and stress (Hammen,

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Henry, & Daley, 2000). However, most diathesis-stress models of psychopathology do not consider the nature of the interaction between the diathesis and stress (Hammen et al., 2000). One version of the diathesis-stress model, known as the stress sensitization hypothesis, provides an explanation for how exposure to CA augments liability for drug use disorders within the context of stress (Hammen et al., 2000). According to this hypothesis, exposure to CA may permanently alter the stress response system, thereby physiologically and psychologically sensitizing individuals to later stress, which triggers the onset of psychopathology. Specifically, individuals exposed to the diathesis are more likely to develop psychopathology following lower levels of stress than individuals with no exposure to the diathesis (Hammen et al., 2000).

Prior studies support the claim that exposure to CA lowers tolerance for future stressful events such that even relatively minor stressors elicit heightened reactions and difficulties in regulating negative emotions (Hammen et al., 2000; McLaughlin & Hatzenbuehler, 2009; McLaughlin, Conron, Koenen, & Gilman, 2010). As minor life events occur much more frequently than the major life events that typically precede the onset of psychopathology (Hammen, 2005), people with exposure to CA are more likely to develop psychopathology in the context of stress than those without this diathesis.

Although the pathways through which CA exposure lowers tolerance for future stress are not entirely clear, this may occur through neurobiological mechanisms such as increased autonomic nervous system reactivity (Heim & Nemeroff, 2001), alterations to dopamine and other neurotransmitter regulation (Anderson, Teicher, Polcari, & Renshaw, 2002; Andersen & Teicher, 2009), dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (Andersen & Teicher, 2009), and changes to the prefrontal cortex that alter the threat-appraisal response system (Andersen & Teicher, 2009; Loman & Gunnar, 2010).

Stress sensitization effects have been documented primarily in predicting mood and anxiety disorders (Espejo et al., 2007; Harkness, Bruce, & Lumley, 2006; Kendler, Kuhn, & Prescott, 2004; McLaughlin et al., 2010); however, emerging evidence suggests that the stress sensitization hypothesis may have utility in predicting externalizing behaviors, including intimate partner violence (Roberts, McLaughlin, Conron, & Koenen, 2011), binge drinking (Keyes et al., 2012), and alcohol use and dependence (Young-Wolff, Kendler, & Prescott, 2012). In addition, evidence of associations between stressful life events and drug use (Covault et al., 2007; Slopen et al., 2011), affective dysregulation following both stressors and the onset of drug use (Cheetham, Allen, Yucel, & Lubman, 2010), and evidence that dysregulation of neurobiological stress systems play a role in drug use (Anderson et al., 2002) support the possibility of a stress sensitization effect in the development of drug use disorders. Yet, no studies have tested whether the stress sensitization hypothesis has utility in predicting drug use disorders.

As a preliminary step to addressing this gap in the literature, we use the National Epidemiologic Study of Alcohol and Related Conditions (NESARC) to examine whether exposure to stressful events in adulthood is associated with past-year cannabis, opiate, and stimulant use disorders among individuals with varying levels of exposure to CA. Given substantial gender differences in the prevalence of drug use disorders (Cotto et al., 2010) and stress reactivity (Stroud, Salovey, & Epel, 2002), we also examined whether gender differences were present in these associations.

Method

Sample

Data are drawn from NESARC, a nationally representative psychiatric epidemiological study of the U.S. adult population. NESARC targeted civilians aged 18 years and older residing in households or group living facilities. In 2001–2002, 43,093 respondents completed face-to-face interviews in Wave 1 of data collection, representing an 81% response rate. From 2004 to 2005, respondents from Wave 1 were followed up with, and 34,653 respondents completed a second interview, representing an 86.7% response rate. The cumulative response rate for both waves was 70.2%. Blacks, Hispanics, and young adults between 18 and 24 years of age were oversampled. Data were adjusted for the oversampling of these groups and household- and person-level nonresponse. The weighted data were then adjusted to represent the U.S. population for several sociodemographic variables (see Grant & Kaplan, 2005 for a detailed description of the methods). For this paper, the analyses are based on Wave 2 data, which assessed CAs and stressful life events (Ruan et al., 2008).

Measures

Drug use disorders. The presence of *DSM–IV* past-year drug use disorders was assessed with the Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM–IV* version (AUDADIS-IV; Grant, Dawson, & Hasin, 2001). As the number of respondents meeting criteria for past-year cannabis, opiate, amphetamine, and cocaine abuse and dependence was low, we created a single category of drug use disorder for each class of drug that included respondents who met criteria for abuse, dependence, or abuse and dependence. Further, as the prevalence of past-year amphetamine or cocaine use disorder was low, we combined these variables to create a variable examining the presence of past-year stimulant use disorder.

Childhood adversity (CA). Respondents completed a series of questions relating to CAs experienced before the age of 18. Emotional and physical abuse and exposure to domestic violence were assessed using questions from the Conflict Tactics Scale (Straus, 1979). Emotional abuse was measured by three items that assessed the frequency that caretakers insulted or swore at, said hurtful things, and threatened respondents with violence. Physical abuse was measured by two items that examined the frequency with which caregivers pushed, hit, or bruised the respondent. Domestic violence exposure was assessed through four questions examining the frequency with which violent behavior was directed at the respondent's female caregiver.

Neglect was assessed using items from the Childhood Trauma Questionnaire (Bernstein, Fink, Hondelsman, Foote, & Lovejoy, 1994). These five items examined the frequency with which respondents were left unsupervised when they were too young to be alone, went without things they needed, and were not provided with regular meals or necessary medical treatment. An endangerment item that assessed whether respondents were made to do chores that were dangerous for someone their age was included.

Sexual abuse was assessed using four previously validated questions (Wyatt, 1985) about unwanted sexual experiences that involved an adult or that occurred when the respondent was too young to know what was happening. In addition, an item was included from the posttraumatic stress disorder trauma section of the NESARC questionnaire that assessed whether respondents had been sexually assaulted, raped, or experienced unwanted sexual contact before the age of 18.

Respondents reported the frequency of exposure to these CAs (with the exception of sexual assault before the age of 18, which had *yes*/*no* response option) on a scale ranging from 1 (*never*) to 5 (*very often*). Physical or sexual abuse, endangerment, and exposure to domestic violence were coded as present if respondents endorsed any exposure to these adversities. Emotional abuse and neglect was coded as present if respondents reported that they occurred sometimes, fairly often, or very often. These types of CA were coded differently as physical and sexual abuse and domestic violence are extreme experiences, and exposure to any degree of such violence is sufficient to qualify as the presence of CA. In contrast, emotional abuse and neglect are dimensional in nature and the threshold is higher for these experiences to qualify as CA. This approach to coding is standard for studies of CA (see Walker et al., 1999).

Three types of CA related to parental dysfunction due to serious mental illness, incarceration, or alcohol and drug abuse were also examined. Parental dysfunction due to serious mental illness was assessed by three items examining the presence or absence of parental hospitalization for mental illness, suicide attempt, or suicide completion. Parental dysfunction due to substance abuse was assessed by two items examining the presence or absence of parental alcohol abuse or drug abuse. Parental dysfunction due to incarceration was assessed by one item examining the presence or absence of a parent ever having been sent to prison.

The scores for all CAs were then summed to create a composite variable that assessed the number of types of CAs to which respondents had been exposed before the age of 18. This variable was treated as a categorical variable, with responses coded as no CA exposure, exposure to one to two types of CA, or exposure to $\geq$3 types of CA. We created a categorical variable for exposure to adversity as we were interested in examining interaction models and because the distribution of exposure to CA was skewed.

Adulthood stressful life events. The AUDADIS-IV was used to assess for the presence of major stressful life events occurring in the 12 months preceding the interview (Ruan et al., 2008). Fourteen events were classified as major life events, including being fired or laid off; being unemployed and looking for work for more than 1 month; marital separation, divorce, or the breakup of a steady relationship; serious financial crisis or bankruptcy; unexpected death of a family member or close friend; war exposure; having a life-threatening illness or accident; natural disaster exposure; sexual assault; being the victim of interpersonal violence; being kidnapped or held hostage; being stalked; witnessing someone being seriously injured or killed; and being (or someone close being) the victim of a terrorist attack.

In addition, the NESARC questionnaire assesses for the presence of minor stressful life events occurring in the 12 months preceding the interview (McLaughlin et al., 2010). Eleven events were classified as minor stressors, including moving or living with someone new; interpersonal problems at work; changes in work responsibilities; interpersonal problems with a neighbor, friend, or relative; legal problems; being the victim of theft; intentional damage to one's property; being mugged; having a family member or close friend being mugged or assaulted; expected death of a family member or close friend; and legal problems of family member or close friend.

Positively endorsed major and minor stressful life events were summed to create two variables that assessed degree of exposure to minor stressful life events and degree of exposure to major stressful life events in the 12 months preceding the interview. These variables were treated as categorical variables in all analyses, with responses coded as no exposure (0), low exposure (one to two events), or high exposure (three or more stressors). We created categorical variables for exposure to stressful life events so that we could examine the interaction between CA, stressful events and drug use disorders, and also because the distribution of these variables was skewed.

Axis I mood and anxiety disorders. The AUDADIS-IV was used to assess for the presence of 12-month mood disorders (including major depression, dysthymia, and bipolar) and anxiety disorders including generalized anxiety disorder, specific phobia, panic disorder, and posttraumatic stress disorder. AUDADIS-IV diagnoses have been found to be reliable in a number of general population and clinical reappraisal studies (Ruan et al., 2008).

Control variables. Individual-level control variables included age, sex, race/ethnicity, income, and nativity (United States or elsewhere). We controlled for these variables in the analyses given that studies have consistently found associations between these variables and disordered drug use (Ortega, Rosenheck, Alegria, & Desai, 2000; Wu, Woody, Yang, Pan, & Blazer, 2011).

Analyses

To examine the relationship between stress in adulthood, past-year drug use disorders and exposure to CA, we conducted six logistic regression analyses: two for each class of drug use disorder, while examining exposure to major and minor stressors in separate regression models. CA, past-year exposure to minor/major stress, and the interaction between CA and minor/major stress exposure were entered into each model, while adjusting for covariates significantly associated with the drug use disorder. In these models, significant interactions between exposure to CA and exposure to stressful events in adulthood would provide preliminary support for a relationship between CA and stress in adulthood in predicting drug use disorders. Risk differences (i.e., the difference between proportions of individuals with a drug use disorder at low or high levels of past-year stress exposure relative to no stress exposure) were estimated for each level of CA exposure. Analyses were conducted separately for male and female participants. Additionally, gender differences were tested through three-way interaction terms between exposure to CA, past-year stress exposure, and gender in predicting drug use disorders. Finally, given the potentially confounding effects of comorbid psychopathology on the relationship between CA and drug use (Afifi, Henriksen, Asmundson, & Sareen, 2012), we conducted a sensitivity analysis in which we tested the robustness of our findings by further

adjusting models for Axis I mood and anxiety disorders. Analyses were conducted using SUDAAN version 10.0 (Research Triangle Institute, 2008), which adjusts variance estimates for the complex sampling design. Statistical significance was evaluated using two-tailed tests, with alpha set at 0.05.

Results

Prevalence of CAs, Stressful Life Events, and Disordered Drug Use

Exposure to CA was widespread, with 28.3% of the sample reporting exposure to one to two types of CA and 15.4% reporting exposure to three or more types of CA. The prevalence of CA exposure was similar among male and female respondents (see Table 1).

Most respondents reported experiencing a minor stressful event in the year preceding the interview. Specifically, 50.1% experienced one to two and 13.4% experienced three or more minor stressful events. A smaller proportion of participants experienced major stressful events in the year preceding the interview, but these major events were still common, with 29.3% of the sample reporting one to two and 4.0% reporting three or more major events. There were no gender differences in the prevalence of minor or major stressful events (see Table 1).

For the overall sample, 0.5% reported disordered opiate use, 1.6% reported disordered cannabis use, and 0.4% reported disordered stimulant use in the past year. The prevalence of disordered opiate and stimulant use was similar among male and female respondents; however, the prevalence of disordered cannabis use was higher among males (2.4%) relative to females (0.6%; Table 1).

We also examined the relationship between potential confounders and disordered drug use (see Table 2). Nativity, age, and income was significantly associated with disordered opiate, cannabis, and stimulant use and was controlled for in all subsequent analyses. Race/ethnicity was significantly associated with disordered cannabis use only; we only controlled for race/ethnicity in analyses for this class of drug use (see Table 2).

Table 1
Demographic Characteristics of the NESARC Sample (2004–2005)

	Total sample		Women		Men	
	N Unweighted	% Weighted	*N* Unweighted	% Weighted	*N* Unweighted	% Weighted
Age (years)						
20–29	4,913	16.34	2,787	15.68	2,126	17.05
30–39	6,621	18.71	3,945	18.14	2,676	19.32
40–49	7,539	21.50	4,224	21.06	3,315	21.99
50–59	6,117	17.74	3,416	17.63	2,701	17.86
60–69	4,174	11.52	2,363	11.42	1,811	11.63
>70	5,289	14.19	3,354	16.07	1,935	12.15
Nativity						
U.S. born	29,287	86.14	17,010	86.56	12,277	85.67
Foreign born	5,363	13.86	3,076	13.44	2,287	14.33
Race/ethnicity						
White	20,161	70.91	11,308	70.62	8,853	71.22
Black	6,587	11.05	4,261	11.94	2,326	10.08
Native American	578	2.19	338	2.31	240	2.06
Asian and Pacific Islander	968	4.27	542	4.20	426	4.35
Hispanic	6,359	11.58	3,640	10.92	2,719	12.29
Income						
≤$19,999	15,189	42.19	10,938	55.36	4,251	27.87
$20,000–$34,999	8,087	23.11	4,512	21.82	3,575	24.52
$35,000–$69,999	8,180	24.29	3,706	18.12	4,474	31.00
≥$70,000	3,197	10.41	933	4.70	2,264	16.61
Disordered drug use (past year)						
Disordered opiate use	154	0.54	73	0.42	81	0.68
Disordered cannabis use	491	1.60	155	0.86	336	2.40
Disordered stimulant use	128	0.40	43	0.25	85	0.58
Childhood adversities (CA)						
None	18,919	56.25	11,013	56.76	7,906	55.69
1–2 types of CA	10,016	28.33	5,505	26.42	4,511	30.41
3 or more types of CA	5,718	15.42	3,571	16.82	2,147	13.90
Past-year minor stressors						
None	12,458	36.56	7,238	37.04	5,220	36.04
1 to 2	17,384	50.05	10,059	49.81	7,325	50.31
3 or more	4,781	13.39	2,772	13.15	2,009	13.66
Past-year major stressors						
None	22,745	66.75	13,142	67.09	9,603	66.38
1 to 2	10,405	29.29	6,061	29.02	4,344	29.57
3 or more	1,503	3.96	886	3.89	617	4.04

Table 2
Associations Among Age, Nativity, and Race/Ethnicity and 12-Month Disordered Drug Use

	Disordered opiate use			Disordered cannabis use			Disordered stimulant use		
	β	*p*	*OR* (95% CI)	β	*p*	*OR* (95% CI)	β	*p*	*OR* (95% CI)
Age (years)									
20–29[a]	—	—	—	—	—	—	—	—	—
30–39	−0.58	**.013**	0.56 (0.36, 0.88)	−0.98	**<.001**	0.37 (0.27, 0.52)	−0.91	**.002**	0.40 (0.23, 0.71)
40–49	−0.50	.068	0.61 (0.35, 1.04)	−1.25	**<.001**	0.29 (0.21, 0.39)	−0.89	**.005**	0.41 (0.23, 0.75)
50–59	−1.01	**.003**	0.36 (0.19, 0.71)	−1.88	**<.001**	0.15 (0.10, 0.24)	−1.65	**<.001**	0.19 (0.08, 0.46)
60–69	−2.62	**<.001**	0.07 (0.02, 0.30)	−3.04	**<.001**	0.05 (0.02, 0.11)	−3.59	**<.001**	0.03 (0.01, 0.10)
>70	−2.46	**<.001**	0.09 (0.03, 0.25)	[b]	[b]	[b]	[b]	[b]	[b]
Nativity									
U.S. born[a]	—	—	—	—	—	—	—	—	—
Foreign born	−1.88	**<.001**	0.15 (0.07, 0.35)	−0.95	**.001**	0.39 (0.22, 0.67)	−1.36	**.005**	0.26 (0.10, 0.65)
Race/ethnicity									
White[a]	—	—	—	—	—	—	—	—	—
Black	−0.62	.066	0.54 (0.28, 1.04)	0.26	.122	1.30 (0.93, 1.80)	−0.20	.465	0.81 (0.47, 1.42)
Native American	−0.23	.711	0.80 (0.24, 2.68)	0.76	**.013**	2.14 (1.18, 3.89)	−0.08	.924	0.93 (0.19, 4.54)
Asian and Pacific Islander	[b]	[b]	[b]	−0.39	.377	0.68 (0.28, 1.63)	[b]	[b]	[b]
Hispanic	−0.56	.081	0.57 (0.31, 1.07)	−0.41	**.023**	0.66 (0.47, 0.94)	−0.20	.489	1.22 (0.69, 2.13)
Income									
≤$19,999[a]	—	—	—	—	—	—	—	—	—
$20,000, $34,999	−0.10	.697	0.90 (0.54, 1.51)	−0.32	**.033**	0.73 (0.55, 0.97)	−0.37	.191	0.69 (0.39, 1.21)
$35,000, $69,999	−0.58	**.013**	0.56 (0.36, 0.88)	−0.58	**<.001**	0.56 (0.41, 0.78)	−0.86	**.003**	0.42 (0.24, 0.74)
≥$70,000	−0.63	.054	0.53 (0.28, 1.01)	−0.80	**.002**	0.45 (0.27, 0.73)	−1.97	**.008**	0.14 (0.03, 0.59)

Note. *OR* (95% CI) = odds ratios (95% CI). The *p* values in bold represent statistically significant associations.
[a] Reference category. [b] No one in the category has the corresponding drug use disorder.

Stressful Life Events, CAs, and Drug Use Disorders

We first examined the association between 12-month drug use disorders, past-year minor stressful events, and exposure to CA, while adjusting for potential confounders. Among men, the risk of having a past-year cannabis use disorder was greater among those with high (β = 1.93, $p < .001$) versus no exposure to past-year minor life events (see Table 3). In addition, high exposure to minor stressful events (relative to no exposure) was associated with increased risk for opiate (β = 3.10, $p = .006$) and stimulant use disorders (β = 2.62, $p = .003$) among men. When controlling for minor stressful life events, exposure to one to two types of CA was associated with increased risk of cannabis use disorders (β = 1.37, $p = .002$) and increased risk of opiate disorders (β = 2.76, $p = .015$; Table 3).

Similarly, among women, the risk of having a past-year cannabis use disorder was greater among those with exposure to three or more minor stressful events (β = 3.33, $p = .003$) relative to those with no exposure (see Table 3). Exposure to three or more minor stressful events relative to no exposure was also associated with increased risk for opiate use disorders among women (β = 3.32, $p = .003$). Women with low exposure to minor stressful life events were less likely to report past-year disordered stimulant use than those with high exposure to these stressful events (β = −1.77, $p = .019$; Table 3). When controlling for past-year exposure to minor stressful events, women who had been exposed to one to two types of CA (β = 2.83, $p = .014$) and three or more types of CA (β = 2.71, $p = .045$) had increased odds of having a cannabis use disorder relative to those with no exposure to CA. The prevalence of opiate and stimulant use disorders did not vary according to CA exposure (see Table 3).

Next, we examined the association between 12-month drug use disorders, past-year major stressful events, and exposure to CA (see Table 4). Among men, the risk of having a past-year cannabis use disorder was greater among those with high (β = 0.92, $p = .023$) relative to no exposure to major stressful life events (see Table 4). In addition, high exposure to major stressful events (relative to no exposure) was associated with increased risk for stimulant use disorders (β = 2.50, $p < .001$) but not opiate use disorders among men. When controlling for major stressful life events, exposure to one to two (β = 0.78, $p = .005$) or three or more types of CA (β = 1.24, $p < .001$) was associated with increased risk of cannabis use disorders, but not stimulant or opiate use disorders (see Table 4).

Similarly among women, the risk of having a past-year cannabis use disorder was greater among those with high (β = 2.50, $p = .002$) versus no exposure to major stressful events (see Table 4). Further, high exposure to major stressful events (β = 3.39, $p = .001$) was associated with greater odds of stimulant use disorders, but not opiate use disorders (see Table 4). When controlling for exposure to past-year major stressors, women who had been exposed to one to two (β = 2.34, $p < .001$) and three or more types of CA (β = 2.96, $p < .001$) had increased risk of a cannabis use disorder relative to those with no CA exposure (see Table 4). The prevalence of opiate and stimulant use disorders did not vary according to CA exposure (see Table 4).

Interaction Between CA Exposure, Past-Year Stressors, and Disordered Drug Use

We examined whether CA exposure modified the association between stressful events and drug use disorders. There was a significant interaction between exposure to CA and major stressful events in predicting stimulant use disorders among women ($\chi^2 = 94.41$, $p < .001$, but not among men (see Table 4). The risk difference of stimulant use disorders for women exposed to three

Table 3
Logistic Regression of 12-Month Disordered Drug Use by Level of Exposure to Past-Year Minor Stressors and Exposure to Childhood Adversity Among Men and Women

	Men			Women		
	β	*p*	*AOR* (95% CI)	β	*p*	*AOR* (95% CI)
Disordered opiate use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	2.76	**.015**	15.84 (1.72, 145.45)	2.16	.082	8.70 (0.76, 99.99)
3 or more types	2.97	**.015**	19.49 (1.82, 208.29)	[c]	[c]	[c]
Minor stressors						
None[a]	—	—	—	—	—	—
1–2	2.67	**.015**	14.41 (1.73, 120.45)	2.20	**.040**	9.03 (1.11, 73.55)
3 or more	3.10	**.006**	22.23 (2.57, 192.40)	3.32	**.003**	27.75 (3.22, 239.33)
χ^2_4 (*p* value)[b]	6.17	.187		79.29	**<.001**	
Disordered cannabis use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	0.65	.123	1.92 (0.83, 4.42)	2.83	**.014**	16.94 (1.82, 157.54)
3 or more types	1.22	**.043**	3.40 (1.04, 11.10)	2.71	**.045**	15.03 (1.07, 211.66)
Minor stressors						
None[a]	—	—	—	—	—	—
1–2	0.99	**.002**	2.68 (1.44, 5.00)	2.44	**.021**	11.46 (1.46, 90.21)
3 or more	1.93	**<.001**	6.87 (3.71, 12.75)	3.33	**.003**	27.84 (3.36, 230.32)
χ^2_4 (*p* value)[b]	1.62	.805		1.92	.751	
Disordered stimulant use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	−0.24	.828	0.79 (0.09, 6.90)	1.07	.082	2.92 (0.87, 9.78)
3 or more types	−1.08	.398	0.34 (0.03, 4.27)	0.47	.432	1.60 (0.49, 5.22)
Minor stressors						
None[a]	—	—	—	[c]	[c]	[c]
1–2	0.94	.297	2.57 (0.43, 15.42)	−1.77	**.019**	0.17 (0.04, 0.74)
3 or more	2.62	**.003**	13.78 (2.52, 75.35)	[a]	—	—
χ^2_4 (*p* value)[b]	10.03	**.040**		6.28	.179	

Note. The *p* values in bold represent statistically significant associations. *AOR* (95% CI) = adjusted odds ratios (95% CI), adjusted for age, race, nativity; CA = childhood adversities.
[a] Reference category. [b] χ^2 test of the interactions between CA and past-year stressors in models for 12-month disorders. [c] No one in this category has the corresponding drug use disorder.

or more major stressful events vs. no major stressful events was significantly higher among women exposed to one to two types of CA (16.2%, 95% confidence interval [CI] = 4.59–27.76) than among women with no exposure to CA (1.0%, $p = .049$), and the risk difference for women with exposure to one to two major stressful events versus no events was significantly higher among women exposed to one to two types of CA (14.3%) than no exposure to CA (0.1%, $p = .010$). We also found a significant interaction between CA exposure and minor stressful events ($\chi^2 = 10.03$, $p = .040$) in predicting stimulant use disorders among men but not among women (see Table 3). However, when we examined the risk difference of stimulant use disorders for men exposed to one to two or three or more minor stressful life events versus no events, they did not differ significantly by number of types of CA exposure.

There was a significant interaction between CA and minor stressful events in predicting opiate use disorders among women ($\chi^2 = 79.29$, $p < .001$; Table 3), but not among men (see Table 3). The risk difference of opiate use disorders for women with 3 or fewer minor stressful events versus no minor events was significantly higher among women with exposure to three or more types of CA (2.1%) than among women with exposure to one to two types of CA (0.8%, $p = .019$) or no CA exposure (0.5%, $p = .005$). There were no significant interactions between exposure to CA and past-year minor (see Table 3) or major stressful events (see Table 4) in predicting cannabis use disorder among men or women.

Gender Differences

There was a significant interaction between CA, minor stressors and gender in predicting opiate use disorders ($\chi^2_4 = 40.45$; $p < .001$). We found significant interactions between CA exposure and minor stressful events in predicting opiate use for women only. In addition, there was a significant interaction between CA, major life events and gender in predicting stimulant use disorders ($\chi^2_4 = 52.13$; $p < .001$). We found significant interactions between CA exposure and major stressful events in predicting stimulant use for women only. There was no evidence of possible stress sensitization effects for men.

Sensitivity Analyses

To evaluate whether mood and anxiety disorders impacted on associations between CA exposure, past-year stressful life events,

Table 4
Logistic Regression of 12-Month Disordered Drug Use by Level of Exposure to Past-Year Major Stressors and Exposure to Childhood Adversity Among Men and Women

	Men			Women		
	β	*p*	*AOR* (95% CI)	β	*p*	*AOR* (95% CI)
Disordered opiate use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	0.97	.183	2.63 (0.63, 11.01)	0.91	.114	2.48 (0.81, 7.71)
3 or more types	1.40	.083	4.04 (0.83, 19.67)	1.32	.063	3.75 (0.93, 15.16)
Major stressors						
None[a]	—	—	—	—	—	—
1–2	1.55	**.015**	4.73 (1.37, 16.36)	0.71	.244	2.04 (0.61, 6.84)
3 or more	1.35	.153	3.84 (0.60, 24.61)	1.31	.128	3.71 (0.68, 20.21)
χ^2_4 (*p* value)[b]	2.90	.575		0.59	.964	
Disordered cannabis use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	0.78	**.005**	2.17 (1.28, 3.69)	2.34	**<.001**	10.37 (4.03, 26.65)
3 or more types	1.24	**<.001**	3.45 (1.84, 6.49)	2.96	**<.001**	19.29 (6.04, 61.56)
Major stressors						
None[a]	—	—	—	—	—	—
1–2	1.00	**<.001**	2.72 (1.69, 4.37)	1.58	**.009**	4.83 (1.49, 15.66)
3 or more	0.92	**.023**	2.51 (1.14, 5.51)	2.50	**.002**	12.20 (2.71, 54.98)
χ^2_4 (*p* value)[b]	5.70	.223		2.91	.572	
Disordered stimulant use						
CA						
None[a]	—	—	—	—	—	—
1–2 types	1.00	.114	2.72 (0.78, 9.47)	[c]	[c]	[c]
3 or more types	1.45	.072	4.27 (0.88, 20.78)	1.24	.317	3.44 (0.30, 39.87)
Major stressors						
None[a]	—	—	—	—	—	—
1–2	1.74	**.004**	5.72 (1.77, 18.53)	1.38	.107	4.20 (0.74, 21.30)
3 or more	2.50	**<.001**	12.12 (3.00, 49.03)	3.39	**.001**	32.72 (4.17, 211.67)
χ^2_4 (*p* value)[b]	3.16	.531		94.41	**<.001**	

Note. The *p* values in bold represent statistically significant associations. *AOR* (95% CI) = adjusted odds ratios (95% CI), adjusted for age, race, nativity; CA = childhood adversities.
[a] Reference category. [b] χ^2 test of the interactions between CA and past year stressors in models for 12-month disorders.

and disordered drug use, we conducted sensitivity analyses in which logistic regression models were further adjusted for these disorders. Adjusting for these comorbid disorders did not change our originally observed pattern of results.

Discussion

In keeping with the stress sensitization hypothesis (Hammen et al., 2000), we anticipated finding significant associations between past-year stressors and disordered cannabis, stimulant, and opiate use among individuals exposed to CA but not among individuals without a history of CA. Our findings from a national sample of men and women provide only partial support for this hypothesis. Prior studies found that exposure to stressful life events (Keyes et al., 2012; Slopen, Williams, Fitzmaurice, & Gilman, 2011) and CA (Cuijpers et al., 2011; Dube et al., 2003) individually predict past-year prevalence of drug use disorders. Similarly, we found that high exposure to both minor and major stressful events in adulthood was associated with elevated risk of cannabis use disorders, greater exposure to minor and major stressors was associated with heightened odds of stimulant use disorders, and higher levels of exposure to minor stressors were associated with increased likelihood of opiate use disorders among women and men. In contrast to these earlier findings, we found that a history of CA was associated with only some types of past-year drug use disorders. Finally, we found significant associations between exposure to CA and experience of past-year stressful events in predicting risk for drug use disorders, but only for women in relation to stimulant and opiate use. This finding extends recent evidence documenting stress sensitization effects in predicting alcohol use problems, particularly binge drinking (Keyes et al., 2012), as well other externalizing behaviors such as perpetration of intimate partner violence (Roberts et al., 2011).

One plausible explanation for our findings of significant interactions between CA exposure and past-year stressful events in predicting stimulant and opiate use disorders lies in the effect that CA has on the development of the mesolimbic dopaminergic system (Andersen & Teicher, 2009). Preclinical studies show that CA increases extracellular dopamine in the nucleus accumbens, resulting in a baseline state of dysphoria and anhedonia (Matthews & Robbins, 2003; Rüedi-Bettschen et al., 2006). Individuals exposed to early adversity therefore may be predisposed to initiate drug use in an effort to normalize this baseline state. In addition,

preclinical and clinical studies have shown that early adversity disrupts the expression of dopamine D2 receptors, diminishing the availability of these receptors in the striatum and increasing the likelihood of drug use disorders (Lovic et al., 2013; Schellekens, Ellenbroek, DeJong, Buitelaar, & Verkes, 2006). Low striatal dopamine D2 receptor expression appears associated with impulsivity and poor inhibitory control (Volkow, Fowler, Wang, Baler, & Telang, 2009), and dopamine D2 receptor availability seems to modulate the extent to which opiates and particularly stimulants are experienced as reinforcing (Kenny, 2007; Volkow et al., 2009). Individuals exposed to CA may thus be more sensitive to the reinforcing effects of rewarding drugs such as opiates and stimulants, increasing the likelihood of compulsive drug use.

However, these interactions between CA exposure and stressful life events in predicting disordered drug use were observed for women only, potentially reflecting sex differences in neurobiological or psychological responses to CA and stress. Preclinical and clinical studies have demonstrated sex differences in the effects of exposure to stress on the structure and function of the HPA axis (Kudielka & Kirschbaum, 2005; Stroud et al., 2002) and in behavioral responses to stressful situations, with females appearing more sensitive to the effects of exposure to psychological stress than males (Iwasaki-Sekino, Mano-Otagiri, Ohata, Yamauchi, & Shibasaki, 2009; Kudielka & Kirschbaum, 2005; Shalev et al., 2009). This is partly because the function of the HPA axis is strongly influenced by female sex hormones (Kajantie & Phillips, 2006; Shalev et al., 2009; Trainor, 2011), which influence the functioning of glucocorticoid and mineralocorticoid receptors in the HPA and modulate dopaminergic function (Trainor, 2011). In addition, preclinical studies have documented sex differences in the functioning of the dopaminergic system after exposure to stress (Duchesne, Dufresne, & Sullivan, 2009). As dysregulation of the dopaminergic system contributes to the development of drug use disorders (Volkow, Baler, & Goldstein, 2011), sex differences in dopaminergic functioning after exposure to stress may partially account for the differences between males and females observed in this study.

While significant interactions between CA exposure and past-year stressors in predicting drug use disorders are suggestive of stress sensitization effects, several methodological limitations prevent us from making definitive statements about the role of stress sensitization effects in predicting drug use disorders. First, we were unable to determine whether the occurrence of past-year stressors preceded the onset or recurrence of the drug use disorder. For some respondents, it is possible that the onset of drug use disorders may have predated the occurrence of recent stressful events, especially as some of the acute interpersonal stressors examined in this study could have stemmed from drug use (Tate, McQuaid, & Brown, 2005). Second, the study used a checklist of stressful life events that did not explore the chronicity of these stressors. This may have limited our ability to detect relationships between stressors and drug use disorders, particularly as other studies have found associations between exposure to chronic stressors in adulthood and the onset of substance use disorders (Keyes et al., 2012; Stockdale et al., 2007). Third, exposure to CA was retrospectively self-reported. This could have led to recall bias and an underreporting of adverse events, which may have diminished our ability to detect relationships between CA, stressors, and disordered drug use. While possible, this limitation seems unlikely, given the high levels of CA exposure in this sample. Finally, we were unable to explore whether repeated exposure to a particular type of CA (such as sexual or physical abuse) impacted on the relationship between stress exposure and drug use disorders. These limitations suggest that our findings should be considered as a first step in exploring stress sensitization effects in the etiology of drug use disorders. Further prospective studies that establish the temporal associations between exposure to CA, exposure to acute and chronic stressors, and the onset of drug use disorders are needed. Specifically, future studies should examine whether severity of exposure to CA mediates the effects of exposure to stressful life events on risk for disordered drug use.

Despite these limitations, our findings still have implications for the prevention and treatment of drug use disorders. As findings suggest that exposure to CA creates a diathesis for drug use disorders among women, one strategy to prevent the onset of these disorders would be to identify young women exposed to CA and provide them with interventions that target the deleterious and lasting effects of exposure to CA. Second, as stressful conditions in adulthood seem associated with drug use disorders among women with histories of CA, early interventions that equip young women who have a history of CA with the cognitive and behavioral skills needed to cope with stressful life events may help prevent the onset of drug use disorders in adulthood. Third, as exposure to past-year life stressors was associated with greater propensity for drug use disorders among women and men and because stress has been associated with relapse to drug use (Danielson et al., 2009), it may be useful to equip people with strategies for coping with stress during the course of drug treatment. Marlatt's relapse prevention model, which teaches pragmatic strategies for dealing with stress-related triggers for drug use, may be a useful intervention approach (Marlatt & Donovan, 2007).

In conclusion, our findings add to a growing literature suggesting the sensitizing role of CA experiences to psychopathology in the context of stressful events in adulthood. Replicating these associations in prospective studies that allow the temporal associations between drug use disorders and stressors to be firmly established remains an important goal for future research.

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