



Early life adversity and increased antisocial and depressive tendencies in young adults with family histories of alcohol and other substance use disorders: Findings from the Family Health Patterns project

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ABSTRACT

Background: Individuals with a family history of alcohol and other substance use disorders (FH+) are several times more likely to develop alcohol problems compared to individuals with no such family histories (FH-). Here we sought to evaluate associations of early life adversity (ELA) with two key risk-related FH+ phenotypic characteristics: increased antisocial and depressive tendencies.

Methods: We examined data from 1187 FH+ and FH- young adults (average age 23.6 years old) with and without personal histories of substance use disorders. Antisocial tendencies were evaluated with the Socialization scale of the California Personality Inventory (CPI-So), while depressive tendencies were evaluated with the Beck Depression Inventory II (BDI).

Results: In general, being FH+, having a personal substance use disorder history, and experiencing greater levels of ELA were associated with lower CPI-So scores (indicating more antisocial tendencies) and higher BDI scores (indicating more depressive tendencies).

Conclusions: These results suggest that ELA is linked to increased antisocial and depressive tendencies observed in FH+ persons. Given that FH+ individuals are disproportionately exposed to ELA, this increased exposure may be a major contributor to these and other risk-related characteristics commonly present in FH+ individuals. Additional studies are needed to evaluate the impact of ELA on risk-related phenotypic characteristics, including prospective studies in early childhood and mechanistic studies evaluating pathways by which ELA exerts its effects on FH phenotypic characteristics.

1. Introduction

Individuals with a family history of alcohol and other substance use disorders (FH+) are approximately 4–7 times more likely to develop problem substance use compared to individuals with no such family histories (FH-; Cotton, 1979, Cloninger, Bohman, & Sigvardsson, 1981, Russell, 1990). This elevated risk appears to have similar heritable and environmental contributions (Verhulst, Neale, & Kendler, 2015), and the most robust known environmental contributor to risk for substance misuse is early life adversity (ELA) (Duffy, McLaughlin, & Green, 2018). ELA is common in individuals with family or personal histories of substance use disorders (Acheson, Vincent, Cohoon, & Lovallo, 2018, Konstenius et al., 2017), and ELA amplifies substance use disorder risk

(Fenton et al., 2013, Kendler et al., 2012). A better understanding of how ELA associates with risk-related characteristics in FH+ persons may provide insight into how ELA contributes to their increased risk for substance use.

Two of the most prominent risk-related characteristics commonly present in FH+ persons are increased antisocial and depressive tendencies (Tarter et al., 2003, Sher, Grekin, & Williams, 2004, Sher & Trull, 1994), both of which are major contributors to increased risk for substance misuse (Iacono, Malone, & McGue, 2008). Both antisocial and depressive tendencies are linked to increased ELA exposure (Vaughn et al., 2011, Biederman, Faraone, & Monuteaux, 2002, Eaves, Prom, & Silberg, 2010, Abry et al., 2017, Carver, Johnson, McCullough, Forster, & Joormann, 2014, Schroeder, Slopen, & Mittal, 2018), suggesting that

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ELA may be directly linked to the increases in these traits seen in FH+ persons.

Previously it was reported a large cohort of FH+ and FH- young adults tested on a battery of demographic, temperament and cognitive measures were most robustly distinguished by FH+ having increased exposure to ELA and having increased antisocial tendencies and depressive tendencies (Acheson et al., 2018). Here we sought to evaluate associations of ELA with increased antisocial and depressive tendencies in this same cohort. We examined potential interactions and main effects of ELA and family and personal histories of substance use disorders on antisocial and depressive tendencies. Given that ELA may synergistically amplify addiction risk (Fenton et al., 2013, Kendler et al., 2012), we hypothesized ELA associated increases in antisocial and depressive tendencies may be greater in persons with family or personal histories of substance use disorders.

2. Methods

2.1. Participants

The Family Health Patterns (FHP) project is a large-scale study aimed at characterizing risk-related phenotypic differences in FH+ and FH- young adults. The present analysis is based on 1187 volunteers who underwent screening for the project, and for whom complete data were available for this analysis (77% of total the screening sample). All participants were compensated for study participation. The Institutional Review Boards at the University of Oklahoma Health Sciences Center and the Veterans Affairs Medical Center in Oklahoma City, OK, the University of Texas Health Sciences Center, San Antonio, TX, and the University of Arkansas for Medical Sciences, Little Rock, AR approved all study procedures. A Certificate of Confidentiality was obtained from the U.S. Department of Health and Human Services for participant privacy protection.

Subjects were recruited using local newspaper advertisements, posted flyers, and internet advertisements including Craig's List. Subjects were screened by telephone for potential eligibility followed by a laboratory visit for further evaluation. Physical health was assessed through a medical history checklist. Psychiatric history was assessed by a trained interviewer supervised by a licensed clinical psychologist using the computerized version of the Diagnostic Interview Schedule updated for DSM-IV diagnoses (C-DIS-IV) (Blouin, Perez, & Blouin, 1988). All participants were required to be between 18 and 30 years old and to have maintained contact with at least one biological parent who raised them. Participants were excluded who reported suspected fetal alcohol or other drug exposure, had grandparents but not parents with substance use disorders, or were unable to credibly describe substance use patterns for their parents and grandparents.

2.2. Analytic variables

Family history of alcohol and other drug use disorders was classified using Family History Research Diagnostic Criteria (FH-RDC) (Andreasen, Endicott, Spitzer, & Winokur, 1977, Uher et al., 2014). FH+ participants had at least one biological parent who met FH-RDC alcohol or other drug use disorder criteria. FH- participants had no reported substance use disorders in their biological parents and grandparents.

Personal history of alcohol and other drug use disorders was assessed using the C-DIS-IV diagnostic interview modules for alcohol and substance use disorders. Absence of personal substance use disorder history (SUD-) was coded 0 and presence (SUD+) was coded 1.

Early life adversity. ELA scores were derived from the C-DIS-IV post-traumatic stress disorders module as previously described (Acheson, Vincent, Cohoon, & Lovallo, 2019, Acheson et al., 2018). The items assessed included sexual or physical adverse experiences (Have you ever been raped or sexually assaulted by a relative? Have you ever been raped or sexually assaulted by someone not related to you? Have you ever been

mugged or threatened with a weapon or ever experienced a break-in or robbery?) and separation from parents (Before you were 15, was there a time when you did not live with your biological father for at least 6 months? Before you were 15, was there a time when you did not live with your biological mother for at least 6 months? Possible ELA scores ranged from 0 (no adverse events) to 5. Due to relatively lower frequency of individuals reporting >2 ELA events, we groups together those reporting ≥ 2 ELA events for the analyses.

Antisocial Behaviors and Depression. Antisocial and depressive tendencies were measured with the Socialization Scale of the California Personality Inventory (CPI-So; Gough, 1994) and the Beck Depression Inventory II (BDI-II; Beck, Steer, Ball, & Ranieri, 1996), respectively. Previously we found that CPI-So and BDI-II scores robustly distinguish FH+ and FH- young adults and are linked to ELA exposure (Acheson, Vincent, Sorocco, & Lovallo, 2011, Lovallo et al., 2013, Sorocco, Carnes, Cohoon, Vincent, & Lovallo, 2015, Acheson et al., 2018). We refer to scores on these measures as antisocial and depressive tendencies, respectively, because the majority of our cohort does not meet diagnostic threshold for antisocial personality disorder or depression.

2.3. Statistical analysis

Separate 3-way ANCOVAs using general linear model (GLM) framework were performed to test effects of family history of substance use disorders (FH-0, FH+), personal history of substance use disorders (SUD-, SUD+), and ELA (0, 1, ≥ 2) on antisocial and depressive tendencies controlling for pertinent covariates. Significant three-way interactions were followed by separate two-way ANCOVAs. Tukey HSD tests were used for post hoc tests. All analyses set statistical significance at 0.05. All data analyses used SAS software, Version 9.4 of the SAS System for Windows.

3. Results

Table 1 shows participant demographic characteristics. More SUD+ participants were males and older. More FH+ participants were females and had lower childhood SES. Both SUD+ and FH+ participants tended to be less educated with lower estimated intelligence and more ELA. Participants who were excluded because of incomplete data were demographically similar to included subjects (data not shown).

Antisocial Tendencies. A three-way ANCOVA was conducted to examine the effects of family history of alcohol or other substance use disorders (FH-, FH+), personal history of alcohol or other substance use disorders (SUD-, SUD+), and ELA (experiencing 0, 1, or ≥ 2 ELA events) on CPI-So scores controlling for childhood SES, years of education, and estimated intelligence (mental age). The three-way interaction was significant, $F(2, 1184) = 3.8, p = .024$, semi-partial $\omega^2 = 0.003$ (Fig. 1). Overall our model explained 36% of the CPI-So score variability.

To interpret the 3-way interaction, separate two-way ANCOVAs were examined by family history status. Among FH- (Fig. 1, left side), associations of ELA events and antisocial tendencies differed between the SUD+ and SUD- groups (significant ELA \times SUD interaction, $F(2, 567) = 4.91, p = .0077$, semi-partial $\omega^2 = 0.01$). FH-/SUD- with 1 or ≥ 2 ELA events had lower CPI-So scores (more antisocial tendencies) than FH-/SUD- with 0 ELA events ($p = .013$ and 0.001 , respectively). However, in FH-/SUD+, there was no difference in CPI-So scores between those with 0 or 1 ELA events ($p = .685$), but those with 0 or 1 ELA events both had higher CPI-So scores (less antisocial tendencies) than those with ≥ 2 ELA events ($p = .0152$ and 0.0003 , respectively).

Among FH+ (Fig. 1, right side), there was no significant ELA \times SUD interaction on CPI-So scores ($F(2, 535) = 0.26, p = .7734$). CPI-So scores were significantly lower in FH+/SUD+ relative to FH+/SUD- ($F(2, 535) = 51.69, p < .0001$, semi-partial $\omega^2 = 0.064$). Additionally, overall FH+ with 2 or more adverse early life events had lower CPI-So scores than those with either 0 or 1 ELA events ($F(2, 535) = 28.53, p < .0001$, semi-partial $\omega^2 = 0.069$).

Table 1
Study sample demographics.

Variable	Total	SUD-	SUD+	<i>p</i>	FH-	FH+	<i>p</i>
N	1187	847	340		606	581	
Male [N (%)]	480 (40)	324 (38)	156 (46)	0.02	281 (46)	199 (34)	<0.0001
Non-Hispanic [N (%)]	1055 (89)	754 (89)	301 (89)	0.74	536 (89)	519 (90)	0.56
Race [N (%)]				0.72			0.37
White	880 (74)	626 (74)	254 (75)		450 (74)	430 (74)	
Black	132 (11)	98 (12)	34 (10)		61 (10)	71 (12)	
Other	175 (15)	123 (15)	52 (15)		95 (16)	80 (14)	
Age	23.6 (3.5)	23.3 (3.5)	24.3 (3.2)	<0.0001	23.5 (3.4)	23.7 (3.5)	0.26
Education, yrs (n = 1175)	15.2 (2.3)	15.3 (2.1)	14.7 (2.6)	<0.0001	15.7 (2.2)	14.6 (2.2)	<0.0001
Mental Age (n = 1179)	17.4 (1.5)	17.5 (1.5)	17.2 (1.6)	0.007	17.7 (1.4)	17.1 (1.6)	<0.0001
Childhood SES (n = 1139)	45.5 (13.0)	45.9 (13.0)	44.6 (13.0)	0.13	48.3 (12.0)	42.5 (13.3)	<0.0001
CPI-So	29.8 (6.0)	31.3 (5.2)	26.2 (6.1)	<0.0001	32.0 (5.1)	27.5 (6.0)	<0.0001
BDI	6.3 (6.7)	5.5 (6.3)	8.2 (7.2)	<0.0001	4.5 (5.1)	8.2 (7.5)	<0.0001
FH+ [N (%)]	581 (49)	361 (43)	220 (65)	<0.0001			<0.0001
Early life adversity [N (%)]				<0.0001			<0.0001
0	499 (42)	405 (48)	94 (28)		369 (61)	130 (22)	
1	379 (32)	264 (31)	115 (34)		171 (28)	208 (36)	
≥2	309 (26)	178 (21)	131 (39)		66 (11)	243 (42)	
Any Substance Use Disorder [N (%)]	340 (29)		344 (100)		120 (20)	220 (38)	<0.0001

SES = socioeconomic status (Hollingshead, 1975). CPI-So = Socialization scale from the California Personality Inventory. BDI = Beck Depression Inventory II. FH+ = family history of alcohol or other substance use disorder.

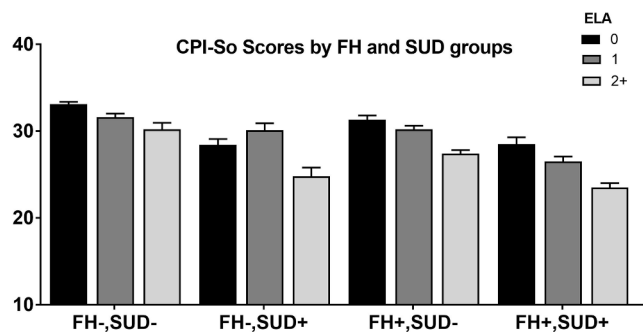


Fig. 1. Antisocial tendencies as indexed by decreased California Personality Inventory Socialization Scale (CPI-So) scores (adjusted means and SEM) in individuals with (FH+) and without (FH-) family histories of alcohol or other substance use disorders, with (SUD+) or without (SUD-) personal histories of substance use disorders, and experiencing 0, 1, or ≥2 early life adversity (ELA) events. There was a significant family history by SUD by ELA interaction and a significant SUD by ELA interaction among FH- participants (left side). Both interactions were driven by a lack of significant differences in CPI-So scores among FH-/SUD+ reporting 0 or 1 ELA events. Otherwise increased ELA was associated with decreased CPI-So scores for FH-/SUDs+ and FH-/SUDs- participants. For FH+ (right side), there were main effects of SUD status and ELA on decreasing CPI-So scores with no interactions. See Results and Table 2 for more details.

Depressive tendencies. A three-way ANCOVA was also used to test effects of family history of alcohol or other substance use disorders (FH-, FH+), personal history of alcohol or other substance use disorders (SUD-, SUD+), and ELA (0, 1, ≥2) on BDI scores controlling for childhood SES, years of education, and estimated intelligence (mental age). The 2- and 3-way interactions were not significant (all $p > .05$), thus they were removed from the model. All remaining main effects were significant and combined accounted for 12% of the variability in BDI scores (Fig. 2). BDI scores were higher (indicating greater depressive tendencies) in FH+ relative to FH- ($F(1, 112) = 28.53, p < .0001$, semi-partial $\omega^2 = 0.022$, in SUD+ relative to SUD- ($F(1, 1112) = 15.32, p < .0001$, semi-partial $\omega^2 = 0.011$, and in those with increasing levels of ELA ($F(2, 1112) = 7.57, p = .0005$, semi-partial $\omega^2 = 0.010$), see Table 2 for adjusted means and SEM.

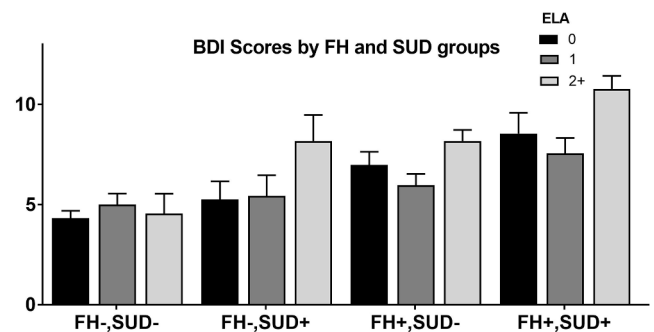


Fig. 2. Depressive tendencies as indicated by increased Beck Depression Inventory II (BDI) scores (adjusted means and SEM) in individuals with (FH+) and without (FH-) family histories of alcohol or other substance use disorders, with (SUD+) or without (SUD-) personal histories of substance use disorders, and experiencing 0, 1, or ≥2 early life adversity (ELA) events. There were significant main effects of family history, SUD status, and ELA on increasing BDI scores, however there were significant main effects (see results and Table 2).

4. Discussion

Here we examined associations of personal and family histories of alcohol and other substance use disorders and ELA on antisocial and depressive tendencies. In general, being FH+, SUD+, and experiencing greater levels of ELA were all associated with lower CPI-So scores (indicating more antisocial tendencies) and higher BDI scores (indicating more depressive tendencies). Collectively, these results suggest that ELA is linked to increased antisocial and depressive tendencies and that ELA may make prominent contributions to these addiction risk-related behavioral phenotypes.

These results build on findings published in this same cohort comparing FH+ and FH- young adults on a battery of demographic, temperament, and cognitive measures (Acheson et al., 2018). FH+ were most robustly distinguished from FH- by having increased exposure to ELA (Cohen's $d = 0.91$) and having increased antisocial tendencies (decreased CPI-So scores, Cohen's $d = -0.77$) and depressive tendencies (increased BDI scores, Cohen's $d = 0.58$). Here we found that increased ELA is linked to increased expression of antisocial and depressive tendencies in both FH+ and FH- with and without SUDs. The large sample size allowed us to compare influences of ELA across FH+ and FH-, which is difficult in smaller datasets due to lower frequency of ELA in FH-

Table 2
Adjusted Means (SEM) for Study Outcomes.

		SUD-	SUD+	Row Mean
CPI-So				
FH-	ELA 0	33.5 (0.26)	28.8 (0.65)	31.1 (0.35)
	ELA 1	31.9 (0.40)	30.3 (0.76)	31.1 (0.43)
	ELA ≥ 2	30.4 (0.72)	25.1 (0.95)	27.7 (0.60)
	Mean	31.9 (0.29)	28.1 (0.46)	29.7 (0.29)
FH+	ELA 0	30.8 (0.53)	28.0 (0.82)	29.4 (0.49)
	ELA 1	29.8 (0.45)	26.3 (0.61)	28.0 (0.38)
	ELA ≥ 2	27.1 (0.44)	23.3 (0.52)	25.2 (0.34)
	Mean	29.2 (0.27)	25.9 (0.38)	27.9 (0.23)
Column Mean	30.6 (0.20)	27.0 (0.30)	29.9 (0.14)	
BDI				
FH-	ELA 0	4.3 (0.37)	5.3 (0.90)	4.5 (0.40)
	ELA 1	5.0 (0.55)	5.4 (1.04)	5.0 (0.48)
	ELA ≥ 2	4.6 (0.99)	8.2 (1.30)	6.3 (0.67)
	Mean	4.4 (0.32)	6.1 (0.52)	5.7 (0.31)
FH+	ELA 0	7.0 (0.66)	8.6 (1.03)	8.1 (0.72)
	ELA 1	6.0 (0.56)	7.6 (0.76)	7.1 (0.55)
	ELA ≥ 2	8.2 (0.56)	10.8 (0.66)	9.6 (0.50)
	Mean	7.3 (0.40)	9.2 (0.55)	8.0 (0.28)
Column Mean	6.0 (0.23)	7.7 (0.36)	6.3 (0.19)	

CPI-So = Socialization scale from the California Personality Inventory. FH- = no family history of alcohol or other substance use disorders. FH+ = family history of alcohol or other substance use disorder. SUD- = no personal history of alcohol or other substance use disorder. SUD+ = personal history of alcohol or other substance use disorder. BDI = Beck Depression Inventory II. FH+ = family history of alcohol or other substance use disorder.

individuals. Given that FH+ individuals are disproportionately exposed to ELA, this increased exposure may be a major contributor to two of the most prominent risk-related characteristics commonly present in FH+ individuals.

These results parallel findings with delay discounting and ELA in this same study cohort (Acheson et al., 2018, Acheson et al., 2019). In the Acheson et al. (2018) study noted above, the most robust cognitive phenotype distinguishing FH+ and FH- was increased discounting of delayed rewards in FH+ (Cohen's $d = 0.30$). This analysis was followed by examining associations of delay discounting with family and personal histories of substance use disorders and ELA (Acheson et al., 2019). Similar to the present findings, ELA was linked to increased delay discounting in both FH+ and FH-. Additionally, in preliminary gene \times environment interaction analyses, antisocial and depressive tendencies and delay discounting appear to be more affected by ELA in individuals with specific genotypes associated with addiction and other psychopathology risk (Lovallo, Cohoon, Sorocco, et al., 2019, Lovallo et al., 2017, Lovallo et al., 2016).

Our findings tie into a growing body of literature that links ELA to increased risk for addiction, among other poor health outcomes (Lijffijt, Hu, & Swann, 2014, Bick & Nelson, 2016, Oshri, Kogan, Kwon, Wickrama, Vanderbroek, Palmer, & MacKillop, 2017). Increased ELA exposure is also linked to the blunted stress reactivity observed in FH+ (Lovallo, Cohoon, Acheson, et al., 2019) consistent with other studies linking blunted stress reactivity to substance abuse disorder vulnerability (Buchanan & Lovallo, 2018). The altered glucocorticoid functioning in FH+ may impair regulation of immunoreactivity and inflammatory processes while vulnerable frontal brain circuits are maturing, potentially contributing to the decreased grey matter volumes, decreased frontal white matter integrity, and altered brain activity in FH+ (Acheson, Wijtenburg, Rowland, Winkler, et al., 2014, Acheson, Wijtenburg, Rowland, Bray, et al., 2014, Acheson et al., 2015, Acheson, Franklin, et al., 2014, Acheson, Robinson, Glahn, Lovallo, & Fox, 2009, Hill et al., 2013, Hill et al., 2011, Hill & Sharma, 2019). These neural changes may result in impaired communication to and from the prefrontal cortex that contribute to the increased antisocial and depressive tendencies and poorer decision-making in FH+, thereby increasing risk for problem alcohol and other drug use. In essence, ELA

together with inherited vulnerabilities may be biologically predisposing FH+ individuals to be at greater risk for alcohol and other drug problems as well as other psychopathology, perpetuating increased addiction risk across generations.

This study has several strengths and limitations. We used a large, well-characterized sample of FH+ and FH- young adults with and without personal substance use disorder histories. The increased representation of FH+ individuals helped facilitate our analyses, but this may have limited how well these findings may generalize. Participants were excluded for reported fetal alcohol or other drug exposure, which may have limited participation of individuals with maternal substance use disorder histories and thus may have further limited how well our results may generalize. While we were able to identify ELA associations with antisocial and depressive tendencies, we were not able to determine causal relationships because we used cross-sectional data. The ELA measure was derived from a psychiatric screen, and specific ages when adverse events occurred was not collected. It is possible that some adverse events reported may have happened after age 18. The Childhood Trauma Questionnaire was collected on a portion of the cohort ($n = 460$) and there was a moderate Pearson r correlation with the ELA measure and the CTQ overall score ($r = 0.601$, $p < .0001$), suggesting the ELA measure does primarily reflect events occurring in childhood. ELA was potentially subject to recall biases because it was retrospectively reported, although the magnitude and severity of events assessed makes that unlikely. Finally, it is unclear how much ELA is directly associated with increased antisocial and depressive tendencies versus being a corollary of heritable parental characteristics. Children with parents who have greater antisocial or depressive tendencies often have more ELA experiences.

Collectively these results suggest that ELA may strongly contribute to the increased antisocial and depressive tendencies observed in FH+ persons. Additional studies evaluating the impact of ELA on risk-related phenotypic characteristics are needed, including prospective studies in early childhood and mechanistic studies evaluating pathways by which ELA exerts its effects on FH phenotypic characteristics.

CRediT authorship contribution statement

Ashley Acheson: Investigation, Conceptualization, Writing – original draft. **Andrea S. Vincent:** Formal analysis. **Andrew J. Cohoon:** Data curation. **William R. Lovallo:** Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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