

Early Life Adversity Contributes to Impaired Cognition and Impulsive Behavior: Studies from the Oklahoma Family Health Patterns Project

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Background: Stressful early life experience may have adverse consequences in adulthood and may contribute to behavioral characteristics that increase vulnerability to alcoholism. We examined early life adverse experience in relation to cognitive deficits and impulsive behaviors with a reference to risk factors for alcoholism.

Methods: We tested 386 healthy young adults (18 to 30 years of age; 224 women; 171 family history positive for alcoholism) using a composite measure of adverse life experience (low socioeconomic status plus personally experienced adverse events including physical and sexual abuse and separation from parents) as a predictor of performance on the Shipley Institute of Living scale, the Stroop color-word task, and a delay discounting task assessing preference for smaller immediate rewards in favor of larger delayed rewards. Body mass index (BMI) was examined as an early indicator of altered health behavior.

Results: Greater levels of adversity predicted higher Stroop interference scores ($F = 3.07$, $p = 0.048$), faster discounting of delayed rewards ($F = 3.79$, $p = 0.024$), lower Shipley mental age scores ($F = 4.01$, $p = 0.019$), and higher BMIs in those with a family history of alcoholism ($F = 3.40$, $p = 0.035$). These effects were not explained by age, sex, race, education, or depression.

Conclusions: The results indicate a long-term impact of stressful life experience on cognitive function, impulsive behaviors, and early health indicators that may contribute to risk in persons with a family history of alcoholism.

Key Words: Lifetime Adversity, Alcoholism, Cognition, Delay Discounting, Health Behavior.

THIS STUDY EXAMINED the impact of lifetime adversity on cognitive performance, impulsive decision-making, and body mass index (BMI) in persons with (FH+) and without (FH-) a family history of alcoholism. FH+ persons have a genetic risk of future alcoholism (Cloninger, 1987), and they display a tendency toward impulsive and

risky behaviors (Sher, 1991) that may contribute additionally to their level of risk (Tarter et al., 2004). In addition to genotype, environmental factors may contribute to cognitive and emotional response biases that may enhance risk in FH+ persons (Cloninger, 1987). Ellis and Boyce (2008) have called attention to the impact of social adversity on behavioral characteristics and stress reactivity in children. Such work is in accord with the effects of childhood maltreatment and its impact on psychological and behavioral characteristics in adulthood, with special reference to genetic vulnerabilities, as illustrated in the studies by Caspi and colleagues (2002). These studies are in broad agreement that exposure to moderate and severe childhood stress can result in long-term behavioral and psychological outcomes in adolescence and early adulthood. We have recently shown that adverse life events before age 15 predicted blunted cortisol and heart rate reactivity to psychosocial stress in this sample of healthy young adults (Lovallo et al., 2012). Basal cortisol secretion and heart rate were unaffected, pointing to an impact of early adversity on brain mechanisms that determine physiological responses to psychological stressors (Lovallo and Gerin, 2003). The present paper explores the impact of adverse life experience on cognitive tasks implicated in the functioning of these higher brain systems.

Early stress exposure can result in altered patterns of connectivity within the prefrontal cortex and between the

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prefrontal cortex and limbic system structures, particularly the amygdala, the bed nuclei of the stria terminalis, and the ventromedial prefrontal cortex (Fox et al., 2010). Others have shown that the presumed stress of low social standing may also impact both structure and function in these same brain areas (Gianaros et al., 2011). Low socioeconomic status (SES) and personally experienced adverse events are more likely to occur to FH+ persons due to poor parenting and long-term family disruption. In turn early life adversity may leave a “biological residue” (Miller et al., 2009) because of a “biological sensitivity to context” (Ellis and Boyce, 2008) that can affect health and behavior throughout life.

Accordingly, we examined cognitive function and behavioral tendencies in FH+ and FH– persons of lower SES who were exposed to adverse experiences including physical or sexual abuse or exposure to other violence or separation from either parent prior to age 15. We predicted that FH+ persons experiencing more lifetime adversity would have poorer cognitive function and display more impulsive decision-making and have higher BMI compared to FH– persons.

MATERIALS AND METHODS

Overview

The Oklahoma Family Health Patterns Project is a study of healthy young adults who are FH+ or FH– with the goal of characterizing differences between these risk groups that may bear on risk for alcoholism. In preliminary analyses, FH of alcoholism scores were significantly correlated with adversity scores ($r = 0.351$, $p < 0.0001$, $R^2 = 0.123$, suggesting a moderate effect size). We recently reported that lifetime adversity predicts blunted stress reactivity (Lovallo et al., 2012), which in turn may be a marker of risk for alcoholism (Sorocco et al., 2006). We therefore examined the effect of lifetime adversity on the cognitive and behavioral variables of interest with reference to possible risk for alcoholism.

Subjects

The present sample includes 386 persons (224 women, 162 men) recruited through community advertisement. Each subject signed a consent form approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center and the Veterans Affairs Medical Center, Oklahoma City, OK, and received financial compensation for participating.

Inclusion and Exclusion Criteria

Prospective volunteers were excluded if they had a history of alcohol or drug dependence; met criteria for substance abuse within the past 2 months; failed a urine drug screen or a breath-alcohol test on days of testing; had a history of any Axis I disorder other than past depression (>60 days prior), as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (American Psychiatric Association, 1994). The potential influence of past depression was accounted for in the analyses. Women were required to have a negative urine pregnancy test on each day of testing. All participants were in good physical health, had a BMI < 30, were not taking prescription medications, and had no reported history of serious medical disorder. Smoking and smokeless tobacco use were not exclusionary.

Subject Background and Psychological Assessments

A telephone screening for conformity with inclusion criteria was followed by a laboratory visit for detailed screening, including a psychiatric history assessed using the computerized version of the Diagnostic Interview Schedule-IV (C-DIS-IV; Blouin et al., 1988), conducted by a trained assistant under the supervision of a licensed clinical psychologist. Subjects visited the laboratory twice more for behavioral and psychophysiological testing.

Personally experienced forms of adversity were based on C-DIS-IV items derived from the posttraumatic stress disorder (PTSD) scale and are closely similar to the life events assessed retrospectively in the studies by Caspi and colleagues (2002) as follows: Physical or Sexual Adversity (Have you ever been mugged or threatened with a weapon? Have you ever experienced a break-in or robbery? 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?) and Emotional Adversity (Before you were 15, was there a time when you did not live with your biological mother for at least 6 months? Before you were 15, was there a time when you did not live with your biological father for at least 6 months?). PTSD reports have a very high degree of test-retest reliability and inter-instrument reliability (Foa and Tolin, 2000). Each person was assigned an adversity score ranging from 0 (no adverse events) to a maximum of 5. SES was estimated using Hollingshead and Redlich's system and was defined as the highest education and occupational level of the head of household in which the subject grew up, with occupation level categorized from 1 (lowest) to 9 (highest) \times 5 plus years of education \times 3 (Hollingshead, 1975). For this sample, the scores ranged from 13 (unskilled labor or menial worker) to 68 (professional or major business owner or executive) with a mean of 46 (minor business owner or technical worker). SES tended to be lower for subjects experiencing more adversity, with those reporting 0 adverse events having $SES \geq 56$ (major business owner, professional), 1 event, 40 to 55 (medium business, minor professional, technical), and 2 or more events having $SES < 40$ (skilled craftsmen to unskilled laborers). The composite adversity score used here was constructed as the sum of adverse events (0 to 5) and placement in the upper, middle, and lower third of the SES distribution (0, 1, and 2) for our subject population and ranged from 0 to 7. As few subjects had scores of 5 to 7, we collapsed the scale to reflect low, medium, and higher levels of composite adversity based on composite scores of 0, 1 to 2, and 3+ ($Ns = 70$, 206, and 110, respectively).

FH classification was established using the Family History Research Diagnostic Criteria (FH-RDC; Andreasen et al., 1977). The FH-RDC has a high degree of interrater reliability (0.95) for reports of substance use disorders (Andreasen et al., 1977). All FH+ participants reported that at least 1 biological parent met at least 2 of the possible 6 criteria for alcohol or substance abuse. FH– participants reported no alcohol or substance use disorders in their biological parents and grandparents. Eleven subjects had a parent who used alcohol and other drugs, and 2 subjects were included who reported an FH of substance abuse without a history of alcohol abuse. The participant's FH-RDC was confirmed by parent interview in all possible cases (79% of these participants) and parents confirmed the subject's report of FH status in 89% of these cases. FH status could confidently be reassigned in 3% of the cases and 6% were dropped for inconsistent or insufficient information. Accordingly, for the 21% of participants with no parent interview, we assume that 89% are also correctly classified, leaving an estimated 3% with an unknown classification and a final estimate that 97% of the total included sample is correctly classified. Participants were excluded if either they or the parent reported possible fetal exposure to alcohol or other drugs.

Study Design and Procedure

Working memory was assessed using Dordill's version of the Stroop color-word task (Salinsky et al., 2002) consisting of 176 repetitions of the color words "red, orange, green, and blue," each printed in a discrepant ink color. The subject reads the list aloud 2 times, first reading the printed words while the time is recorded to the nearest second and next reciting the ink colors while that time is recorded. The interference score is the difference in seconds between the time to read the ink colors and the time to read the words. Stroop performance calls for attentional focus on the ink color and correct response selection calling for suppression of the dominant response; both processes are considered core elements of working memory (Smith and Jonides, 1999).

Impulsive decision-making was assessed using a delay discounting questionnaire (Kirby, 2009) consisting of 27 choices between smaller, immediate, and larger, delayed amounts of money such as "Would you prefer (a) \$34 today or (b) \$50 in 30 days?" Nine of the 27 choices offered small amounts of delayed money (\$25 to \$35), 9 offered medium amounts of delayed money (\$50 to \$60), and 9 offered large amounts of delayed money (\$75 to \$85). Discount rate estimates (k) based on the hyperbolic discounting function of Mazur (1987) were calculated for each participant based on the pattern of choices made across all 27 questions. Possible values of k for each money size category ranged from 0.00016 (choosing all 9 delayed options in a given category) to 0.25 (choosing all 9 immediate options in a given category).

Global cognitive functioning was measured using the Shipley Institute of Living scale (Zachary et al., 1985) consisting of vocabulary and abstraction subscales and yielding a mental age estimate in years ranging up to 22 years, representing full adult level of intellectual function.

BMI in kg of body weight divided by height in m² (kg/m²) was used as a measure of health behavior.

Data Analysis

Analysis of covariance (ANCOVA) was used to examine the effect of composite adversity score and FH status on the dependent variables with age, sex, years of education, depression history, and race used as covariates. In a preliminary examination of the data, we noted that the FH scores (0 to 6 affected parents and grandparents) and the adversity scores (0 to 7) were positively correlated ($r = 0.35$). We tested for multicollinearity in the models for each of the dependent variables and determined that the variance inflation factors were minimal (<1.2 in all cases), and multicollinearity was not considered a factor in the results (Kutner et al., 2004). Effect sizes are reported as partial eta squared. Data were analyzed using SAS software, Ver. 9.2 for Windows (SAS Institute Inc., Cary, NC).

RESULTS

Demographics are shown in Table 1. Composite adverse personal experience is grouped as 0, 1, or 3+. Persons with more composite lifetime adverse experience were moderately older in this sample, and the women had less education. FH+ persons were disproportionately represented in the groups with 3+ composite adversity scores among both men (61% FH+) and women (79% FH+), and the unequal distribution of FH+ across the composite adversity groups was highly significant, $\chi^2 = 61.8$, $p < 0.0001$. There was no impact of adversity on alcohol intake or risky drinking practices as measured by the Alcohol Use Disorders Identification Test in this sample. Smoking showed a nonsignificantly higher

percentage of smokers to occur in the 3+ adversity groups. As reported elsewhere, compared to men, women experienced more total adversity, $\chi^2 = 8.87$, $p = 0.03$, more emotional adversity, $\chi^2 = 6.09$, $p < 0.047$, and more physical and sexual abuse, $\chi^2 = 11.44$, $p = 0.006$ (Lovallo et al., 2012).

Stroop Interference

Stroop interference scores are shown in Table 2. Stroop interference was greater in persons with more adverse life events ($F = 3.07$, $p = 0.048$, $\eta^2 = 0.02$; Fig. 1A). This suggests that adversity and FH+ contribute to poorer Stroop performance and that FH+ in the highest adversity group had the highest interference scores (100 seconds). These results were not affected by years of education, race, age, or history of depression.

Shipley Mental Age

The Shipley mental age scores are shown in Table 2. Composite adversity predicted lower mental age scores ($F = 4.01$, $p = 0.019$, $\eta^2 = 0.021$), as did FH ($F = 11.51$, $p = 0.0008$, $\eta^2 = 0.03$), although the FH \times adversity interaction was nonsignificant (Fig. 1B). These results were not affected by years of education, race, age, or history of depression.

Delay Discounting

We then examined the delay discounting parameter, k , to assess the effect of lifetime adversity and FH on a tendency to prefer smaller, immediate rewards in favor of larger future rewards (Table 2). Preliminary analysis showed the distribution of k values to be skewed, and so the data were log-transformed to normalize the distribution. The ANCOVA showed that persons with higher composite adversity scores were likely to discount rewards at a faster rate ($F = 3.79$, $p = 0.024$, $\eta^2 = 0.02$), with FH and the FH \times adversity interaction terms being nonsignificant (Fig. 1C). These results were not affected by years of education, race, age, or history of depression.

Body Mass Index

We tested the impact of adversity and FH of alcoholism on BMI as a marker of long-term health outcomes (Table 2). We found that FH+ persons experiencing greater adversity had higher BMI than the other groups as reflected in the FH \times adversity interaction ($F = 3.40$, $p = 0.035$, $\eta^2 = 0.03$; Fig. 1D). These results were not affected by years of education, race, age, or history of depression.

DISCUSSION

The present analysis examined volunteers for interactions between their composite lifetime adversity score and an FH of alcoholism to identify potential risk-associated behavioral

Table 1. Subject Demographic and Biometric Characteristics

	Males				Females			
	0	1 to 2	3+	<i>p</i>	0	1 to 2	3+	<i>p</i>
<i>N</i>	31	98	33		39	108	77	
Age (years)	23.1 (0.5)	24.0 (0.3)	23.5 (0.6)	0.3	22.8 (0.4)	23.5 (0.3)	24.0 (0.4)	0.1
Education (years)	15.5 (0.3)	15.8 (0.2)	14.4 (0.4)	0.002	16.1 (0.3)	15.7 (0.2)	15.0 (0.2)	0.004
Race (% White)	97	88	85	0.3	90	97	74	0.0001
Smokers (%) (<i>n</i>)	16 (5)	8 (8)	21 (7)	0.1	11 (12)	10 (4)	14 (11)	0.8
AUDIT	3.65 (0.5)	4.34 (0.4)	3.61 (0.6)	0.4	3.9 (0.5)	3.4 (0.3)	3.1 (0.3)	0.4
QFI	42 (5.2)	55 (4.2)	46 (7.9)	0.2	52 (6.7)	42 (2.9)	44 (4.6)	0.3
Height	71.13 (0.5)	71.11 (0.3)	70.61 (0.9)	0.8	65.27 (0.5)	65.36 (0.3)	64.92 (0.5)	0.7
Weight	171 (6.3)	177 (3.3)	180 (6.8)	0.6	135 (3.6)	141 (2.4)	147 (3.8)	0.1
FH score (<i>n</i> of 6)	1.67 (0.3)	1.44 (0.1)	1.6 (0.2)	0.6	1.86 (0.3)	1.90 (0.2)	2.09 (0.1)	0.6
FH+ (%)	19	35	61	0.0022	39	18	79	0.0001

SES, Hollingshead socioeconomic status index; AUDIT, Alcohol Use Disorders Identification Test; QFI, Quantity Frequency Index; FH, family history. Entries show *M* (SEM) or % of total. *p*-Values are based on *F*-tests or χ^2 .

Table 2. Dependent Variables by Family History of Alcoholism and Composite Lifetime Adversity Scores

<i>N</i>	Family history	
	FH+	FH-
	170	216
Lifetime adversity	Stroop interference score (seconds)	
0	83 (7.78)	81 (3.64)
1 to 2	98 (3.93)	88 (2.52)
3+	100 (4.00)	97 (6.51)
	ShIPLEY mental age score	
0	17.9 (0.19)	17.9 (0.16)
1 to 2	17.9 (0.12)	17.8 (0.12)
3+	17.3 (0.14)	17.7 (0.23)
	Delay discounting (log <i>k</i>)	
0	-4.73 (0.44)	-5.07 (0.19)
1 to 2	-4.27 (0.12)	-4.52 (0.12)
3+	-4.27 (0.13)	-3.99 (0.21)
	Body mass index (kg/m ²)	
0	21.7 (1.24)	23.1 (0.43)
1 to 2	24.3 (0.55)	23.7 (0.33)
3+	24.9 (0.57)	23.6 (0.70)

tendencies. Our working hypothesis was that adversity could potentially have a greater impact on FH+ compared to FH- persons. The results showed that persons with greater adversity in childhood and adolescence had poorer working memory performance, a lower Shipley mental age, had a preference for immediate over delayed rewards, and had a higher BMI. An FH of alcoholism was predictive of significantly lower Shipley mental ages, and a significant interaction of FH and adversity was seen in BMI. The results were independent of years of education, race, age, or history of depression. In a prior paper from this sample, we showed that persons with more adverse life events had smaller stress responses with no additional impact of being FH+ (Lovallo et al., 2012). These collective findings point to a relatively pervasive impact of adverse life experience on cognition, behavior, and stress axis reactivity. Although the direct contribution of FH to these results was minimal, the greater

prevalence of adverse experience in FH+ persons presents a picture that has the long-term potential to play into a tendency for FH+ persons to engage in risky drinking practices.

Delay Discounting

A preference for immediate rewards, seen in more rapid rates of discounting value over time, is consistent with an attraction to rewards and a reduced ability to resist temptations such as alcohol, tobacco, drugs, and food (de Wit, 2009). We previously reported higher rates of delay discounting in these FH+ when they had lower SES and Shipley mental ages and more symptoms of depression ($F = 5.95$, $p < 0.0001$; Acheson et al., 2011). Therefore, the impact of FH+ on rates discounting is enhanced by contributory variables, some of which are also risk factors for alcoholism. The present analysis takes this a step further and indicates that when composite lifetime adversity is taken into account, the FH effect becomes nonsignificant in favor of adversity as an explanatory variable. We now see that the apparent effect of FH+ on faster delay discounting is accounted for by greater adversity in the FH+ group. We provisionally conclude that the experience of stress during childhood and adolescence may bias individuals to settle for smaller immediate rewards in favor of delayed rewards as a possible adaptation to their past experience with the environment. Adversity tends to concentrate in FH+ families, and a potential result is that an orientation to immediate gratification may contribute additively to behavioral characteristics that can put FH+ at risk.

Other research indicates that a tendency toward immediate gratification may predict risk for substance use disorder, including the Stanford Marshmallow Experiment that tested delay of gratification in 4- to 6-year-olds (Mischel et al., 1972). Children who delayed taking a single marshmallow in favor of having 2 at the end of a 15-minute delay period had higher Scholastic Aptitude Test (SAT) scores in high school, and their parents described them as more self-controlled and less distractible and subject to frustration (Shoda et al., 1990). In their 40s, the high delayers had superior perfor-

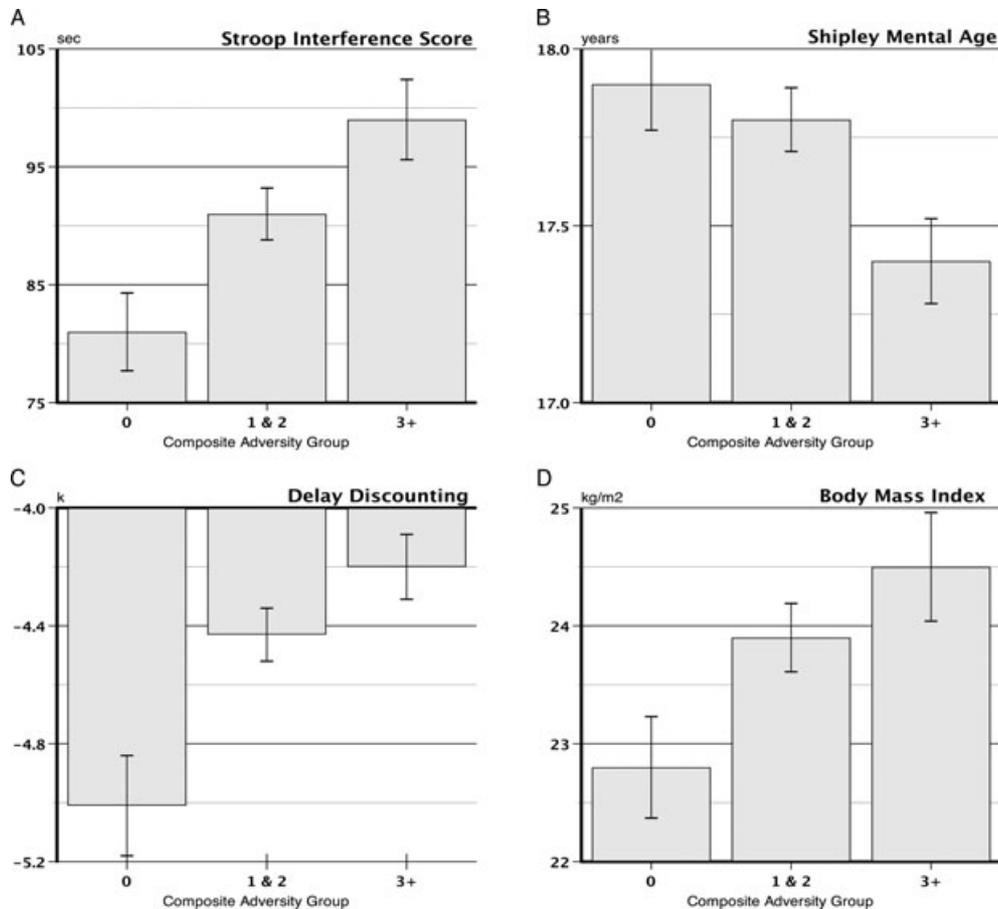


Fig. 1. The impact of early life adverse experience on: (A) Stroop interference scores; (B) Shipley mental age; (C) delay discounting rate; and (D) body mass index. Adversity groups were based on composite adversity scores of 0 (low adversity), 1 or 2 (moderate adversity), or 3+ (high adversity).

mance on an emotional Go-NoGo reaction time task while low delayers made impulsive false-alarm errors (Casey et al., 2011). During neuroimaging, the long delayers were more effective at recruiting activity in the right inferior frontal gyrus while inhibiting false alarms. In contrast, short delayers had greater ventral striatal activation. The predictive value of self-control measured at age 4.5 over the subsequent 40 years indicates that delay discounting tendencies are indicative of a life-long ability for self-regulation.

Stroop

The present analysis also indicated additive effects of FH+ and adversity on the Stroop interference effect, suggesting that the consequences of adversity may bear on risk-related characteristics in FH+ persons. The Stroop task is considered a prototypical working memory task (Smith and Jonides, 1999); good performance requires attentional focus on the relevant stimulus cue (word color) and suppressing interference from the dominant response (word reading). These working memory processes depend on the integrity of the prefrontal cortex including the ventrolateral prefrontal cortex (D'Esposito et al., 1999) and the anterior cingulate gyrus (Carter and van Veen, 2007), an area active when choosing

between response alternatives. Stroop interference scores are greater in persons with prefrontal functional deficits involving impulse control including: attention-deficit hyperactivity disorder (Rapport et al., 2001), alcoholism (Dao-Castellana et al., 1998), pathological gambling (Potenza et al., 2003), and psychopathic tendencies (Vitale et al., 2005). Interference scores are also greater in obese persons (Verdejo-Garcia et al., 2010; Waldstein and Katzel, 2006), and in obesity with disinhibited eating (Maayan et al., 2011). Stroop interference scores are also greater among healthy FH+ persons who display a disinhibited temperament (Lovallo et al., 2006). The foregoing findings indicate that adverse experiences early in life appear to have a negative impact on working memory functions involved in self-regulation with implications for alcoholism risk.

Shipley Mental Age

The present analysis shows that persons exposed to early life adverse events have lower Shipley Mental Age scores. Scores on the Shipley Institute of Living scale are considered useful indicators of full-scale IQ (Dennis, 1973), and IQ tests in turn are heavily weighted toward tasks relying on working memory and processing speed (Coyle et al., 2011). The Ship-

ley abstraction scale that forms half of the mental age score is a particularly challenging test of problem solving and depends heavily on abstraction ability and working memory. In the present data, lower mental age scores are correlated significantly with higher Stroop interference scores ($r = -0.322$, $p = 0.0001$) and with faster delay discounting rates ($r = -0.195$, $p = 0.0001$). The negative correlation between the Stroop and Shipley Mental Age scores offers converging evidence of impaired working memory in the high adversity groups using different tasks of working memory, response inhibition, and abstract thinking. Shipley scores are lower in substance abusing patients with childhood conduct disorder (Stevens et al., 2001). The present data are suggestive of a negative impact of early life adversity cognitive functions reflected in the Shipley mental age scores.

BMI and Impulsivity

Although the present sample does not show a relationship between adversity and drinking behaviors, we did observe an impact of adversity on BMI. We note that our sample was selected to be within the normal range for BMI, and this may have attenuated its relationships with other variables. Nonetheless, FH+ persons experiencing the most adversity had the highest BMIs in this sample. Table 1 shows that the impact of adversity on BMI is due to higher body weights in both men and women. Other work shows that BMI may be related to self-reported impulsivity (van den Berg et al., 2011), poorer executive function (Waldstein and Katzel, 2006), greater delay discounting and reward responsiveness (Fields et al., 2011), greater attention-deficit hyperactivity disorder (Ptacek et al., 2009), impulsive and varied reaction times on a Go-NoGo task (Pauli-Pott et al., 2010), and poorer performance on the Stroop and the Iowa Gambling Task (Verdejo-Garcia et al., 2010). In the present study, BMI was positively correlated with Stroop interference scores ($r = 0.209$). Accordingly, BMI appears to be a health-relevant behavioral outcome of early adverse experience that is accompanied by impulsivity and reward dependence with the greatest impact in the FH+ group.

Relevance to Stress Axis Reactivity

We and others have recently reported that early life adversity is associated with diminished cortisol and autonomic responses to psychosocial stress (Carpenter et al., 2011; Lovallo et al., 2012). At a clinical level, blunted cortisol and autonomic responses to stress are associated with externalizing disorders and impulsive tendencies and earlier initiation of sexual activity in men and women (Raine, 1996). Low stress reactivity may therefore be associated with reduced responses to external threats, consistent with a model under which early life events program biological and behavioral adaptations that may have implications for health and behavior. Small cortisol stress responses are associated with earlier age of first drink (Evans et al., 2012), a known risk factor for

alcoholism (Sartor et al., 2007). The present findings along with our report of lower stress axis responsivity in the same sample points to a pervasive impact of adverse experience during childhood and adolescent development that shapes stress reactivity as well as behavioral tendencies and intellectual functioning, all with implications for risk for alcoholism.

Relationship Between Adversity and FH+

Our prediction that adversity and its related behavioral characteristics would cluster in FH+ persons was supported. Persons coming from alcoholic families were more likely to have encountered adverse life experiences. When testing models containing adversity, FH, and their interaction as predictors, adversity accounted for a greater proportion of the variance than FH or the interaction. This indicates that adverse events themselves have a significant impact on behavior in both FH+ and FH- persons, and it also suggests that the greater occurrence of adversity in FH+ may contribute additively to maladaptive behaviors that may increase risk for alcoholism. The phenotypic combination of poorer working memory, faster delay discounting, and higher BMI form a pattern of disinhibition that may enhance familial risk of alcoholism. Finally, we note that our FH+ subjects exposed to greater adversity do not report drinking more alcohol or engaging in risky drinking practices. This should be viewed in context of the original intent of this project, which was to study young adults whose functioning was not affected by severe abuse of alcohol or drugs. As a result, possible relationships at the high end of the drinking continuum may have been attenuated by these selection procedures.

The effect of adversity on both stress reactivity and impulsivity and cognitive function leads to a consideration of brain mechanisms that may be associated with both sets of outcomes. A substantial literature in animal models shows that both nurturing and stressful events in early life can have permanent effects on brain systems controlling cortisol reactivity as well as behavioral responsivity (Byrne and Suomi, 1999; Gutman and Nemeroff, 2003). Work in primates by Suomi and colleagues has repeatedly shown that early life stress, such as maternal separation and/or peer conflict, can alter brain morphology and increase behavioral impulsivity and that this relationship can be enhanced in the presence of genetic variants influencing central serotonergic and dopaminergic function (Newman et al., 2009; Spinelli et al., 2009). There is also a growing human literature showing an impact of early life adversity on brain morphology and function. In this case, young adults from a low-SES background had reduced overall activation in the anterior cingulate gyrus and dorsomedial prefrontal cortex during reward processing and also less functional connectivity between these areas and the ventral striatum (Gianaros and Manuck, 2010). The neural and behavioral effects of early life stress in primates are associated with tendencies toward alcohol self-administration and preference (Barr et al., 2004; Newman et al., 2009).

One strength of the present study is its relatively large sample size. In developing the Oklahoma Family Health Patterns study, it was our intention to study persons with and without an FH of alcoholism who were healthy, nonobese, free of psychiatric comorbidities, and had no significant evidence of a substance use disorder. These sample characteristics allow us to generalize the present findings to a broad segment of the general population. A question arises as to the interpretation of studies in FH+ versus FH– young adults when the persons in question are unaffected by the disorder under study, in this case alcohol and other substance use disorders. Cloninger has addressed this question in discussing his studies of cross-fostered FH+ and FH– Scandinavian twin pairs: "...alcohol abuse itself is not a sensitive criterion of genetic susceptibility" (Cloninger et al., 1981, p. 867, 1988). In the general case of persons at high risk based on presumed liability to diseases of polygenetic origin, Falconer (1965) has noted that the presence of disease in the high-risk probands is not a requirement for meaningful comparisons between the risk groups as the study of risk factors does not require the presence of the disease itself. In the case of the present findings, we believe that the results draw significant meaning because they emerge from an otherwise healthy, normative sample.

However, these inclusion criteria may also have attenuated the strength of the relationships we report here. The severity and types of adversity covered in our interview are commonly encountered; 55% of the present sample reported 1 or more adverse life events. As such, the present results may represent many persons in the general population, but they may be less generalizable to groups that have been severely traumatized or that meet diagnostic criteria for PTSD. A weakness of the present methodology is shared by most studies of the effects of adverse life experience when the data are derived from retrospective self-report. We believe that this concern is mitigated by the relatively low likelihood that the cortisol and heart rate reactivity differences we saw resulted from systematic bias in how the subjects reported on life events. Instead, poor recall alone would be more likely to cause null findings in a study such as this. In addition, the demonstrated reliability of our subjects' reports of FH of alcoholism suggests this is a reliable sample of informants from whom other forms of report are likely to be accurate.

These findings suggest that the experience of adverse events during childhood and adolescence is associated with behavioral impulsivity, impaired cognitive function, and greater BMI along with our report of attenuated stress axis reactivity (Lovallo et al., 2012). Collectively, these findings indicate that exposure to adversity appears to be a meaningful source of individual differences in reactivity to psychological stress and to behavioral impulsivity and poor cognitive control. Adverse life events and ensuing impulsive behavioral characteristics may cluster in FH+ persons and by doing so, contribute to increased risk of alcoholism. The results were found in an otherwise normative, healthy sample of young adults free of psychiatric comorbidities. This finding points to the role of personal experience in shaping the response charac-

teristics of the human stress axis and cognition and decision-making in relation to risk for alcoholism in FH+ individuals.

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AUTHOR CONTRIBUTIONS

WRL designed the study and details of the protocol. NHF, AJC, and ASV maintained the data set and analyzed the data. KHS oversaw the assessment procedures and psychiatric interviews. AA provided input on the interpretation of impulsive behavioral tendencies in persons with greater adversity. All authors contributed to writing the paper and approve of its content.

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