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Family history, childhood maltreatment, and adolescent binge drinking exert synergistic effects on delay discounting and future alcohol use

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ABSTRACT

Background: The transition to college is associated with a sharp increase in alcohol binge drinking. Family history (FH) of alcohol use disorder (AUD), childhood maltreatment (CM), and adolescent binge drinking are each associated with heightened impulsivity and greater alcohol misuse.
Objectives: We hypothesized that FH, CM, and adolescent binge drinking synergistically increase impulsivity and lead to binge drinking increases over the first year of college.
Methods: Overall, 329 first-semester college students (18–19 years old, 70% female) with varying degrees of FH (Family History Assessment Module), CM (Childhood Trauma Questionnaire), and adolescent binge drinking (Carolina Alcohol Use and Patterns Questionnaire) completed an online study that included a computerized delay discounting task and surveys. Binge drinking was surveyed retrospectively to measure adolescent binge drinking, in addition to baseline and one-year follow-up measures. Linear regression analyses tested the interacting effects of FH, CM, and adolescent binge drinking on delay discounting as well as changes in binge drinking severity between baseline and one-year follow-up. A moderated mediation tested whether delay discounting mediated future binge drinking.
Results: Greater levels of FH, CM, and adolescent binge drinking interacted to reduce the selection of delayed rewards (β=-0.12, SE = 0.06), indicating increased impulsivity. There was a similar interaction effect on increased binge drinking over the one-year follow-up period (β = 0.37, SE = 0.13). Although FH, CM, and adolescent binge drinking influenced individual paths, the moderated mediation analysis was not significant.
Conclusions: Heritable and environmental risk factors for AUD predicted impulsivity and prospectively predicted college binge drinking. Interventions targeting delay discounting processes may represent an effective strategy to reduce harmful drinking specifically for certain high-risk college students.

Introduction

Alcohol Use Disorder (AUD) is a pattern of maladaptive behavior brought about by repeated use of alcohol. The increased drinking common in the transition to college thus has important implications for future alcohol misuse (1). In particular, this transition is characterized by increases in binge drinking in which large amounts of alcohol are consumed in a single drinking episode (1). Alcohol misuse in college not only affects academic success but of the 9% of full-time college students between the ages of 18 to 24 meeting criteria for AUD, 1,519 die annually from alcohol-related injuries (2). These data highlight the need to better understand the factors that contribute to AUD during this critical period.

Several individual-level risk factors for the development of AUD have been identified and broadly fall into heritable, environmental, and neurotoxicological categories. Family history (FH) of AUD represents a proxy for heritable risk for AUD (3,4) but is also associated with environmental risk through physical and intrapersonal consequences of familial alcohol use (5). Environmental risk is typically measured as childhood stress or adversity, including forms of childhood maltreatment (CM), which are associated with future AUD (6). Additionally, early alcohol use is a marker of risk for developing an AUD in adulthood (7), with adolescent binge drinking being of particular concern (8). Although adolescent binge drinking is related to environmental and heritable risk factors (9), it is also likely a neurotoxic risk factor, due to the effects of alcohol on the developing brain (8), including downstream neurocognitive effects (10).

Thus, although each of these variables influences AUD, they are not fully independent. Due to the overlapping influences of different forms of risk factors, studies that

account for each of these factors are crucial for resolving their unique and combined effects. Indeed, childhood adversity and FH interact to predict AUD, indicating that they have synergistic effects (4,11). In particular, the risk associated with FH in a well-powered sample was significant only if there was also CM (11). Thus, assessing multiple risk factors together may yield a powerful approach for disentangling their independent and/or synergistic roles in AUD risk.

Additionally, the behavioral mechanisms mediating the effects of AUD risk factors on increased alcohol-related problems remain undetermined. One mechanism through which these risk factors may influence the AUD development is through increased behavioral impulsivity (5,12). Impulsivity consists of many facets, including impulsive decision-making (12). Impulsive decision-making has been evaluated extensively using delay discounting tasks that quantify an individual's tendency to select either smaller, immediate monetary rewards over larger, delayed rewards (13). This trait translates readily to AUD, as individuals who are more impulsive with alcohol tend to prefer the short-term rewards of intoxication over the long-term effects of good health (14). Longitudinal studies suggest that heightened impulsivity precedes alcohol use (15–17). Thus, risk factors that promote impulsivity would be predicted to increase the risk for AUD.

The risk factors of interest in this study have previously been examined in relation to impulsivity. The degree of early life stress experienced in adolescence is correlated with steeper discounting of delayed rewards in young adulthood (18,19). FH is also associated with multiple impulsivity measures (12,20), including more impulsive choices on delay discounting tasks (18,21,22). Although FH effects may be partly accounted for by childhood adversity (18,19,22), effects of FH on delay discounting persist when controlling for environmental effects (18,22), consistent with evidence that delay discounting behavior is highly heritable (22,23). The association between FH and greater impulsivity in delay discounting tasks is apparent even in childhood (24), suggesting these effects precede alcohol use. Furthermore, in a cross-sectional study of heavy drinking college students, delay discounting mediated the relationship between FH and alcohol-related problems (25). Additionally, non-heavy drinkers who reported a first-degree relative to AUD show greater bias toward immediate rewards than non-heavy drinking adults without FH, supporting the notion that delay discounting represents a so-called "intermediate phenotype" for AUD (26). Greater decision-making impulsivity is also associated with adolescent binge drinking. In a longitudinal study of adolescents who were alcohol-naïve at baseline (aged 10–17 years), there was a significant association between alcohol misuse and greater impulsive choice (measured with a delay discounting task) assessed prospectively (27). However, results further indicated interacting influences of FH, such that adolescent binge drinking increased impulsivity only in FH-positive individuals. Thus, impulsivity is not only associated with early alcohol use but there is evidence that alcohol use itself can also further increase impulsivity, especially in the presence of FH.

Although many studies have examined FH, CM, and adolescent binge drinking effects separately, the strength of their independent or combined influence on delay discounting and AUD is less clear. Furthermore, although these risk factors are each associated with delay discounting, it is unclear whether delay discounting is a behavioral mechanism by which these risk factors lead to alcohol misuse. In this study, we examined how these risk factors for AUD contribute to impulsive behavior and the development of alcohol misuse in college students. To do so, we tested 18–19-year-old students entering their first year of college on a computerized delay discounting task, and we prospectively examined their binge drinking over the following one-year period. Building on previous studies that demonstrate the effects of these risk factors independently, we hypothesized these risk factors would synergistically increase delay discounting behavior, leading to greater college binge drinking.

Methods

Subjects

This study tested the effects of risk factors on impulsivity and binge alcohol use. To achieve a sufficient representation of at-risk subjects to test the hypothesis, students with FH and CM backgrounds were recruited with targeted. Overall, 329 first-year college students (18–19 years old) reporting varying degrees of FH, CM, and adolescent binge drinking were enrolled. The subjects were in their first semester at a four-year college/university in the United States or Canada ($n = 4$). Enrollment of this demographic was designed to capture the sharp rise in drinking during this period (1). We recruited online through Facebook and Instagram advertisements ($n = 195$), as well as from the University of North Carolina at Chapel Hill psychology participant pool ($n = 134$). Subjects completed the study online, including a delay discounting task and self-report surveys. Interested subjects followed a link in the advertisement to a brief screener in REDCap, which included a check-box consent for the screening followed by

questions assessing age, college attendance, and year in college. Subjects meeting the inclusion criteria (i.e., 18–19-year-old first-year college students) were offered a full online informed consent to participate in the study. Baseline data collection occurred during the Fall 2020 semester and follow-up data was collected during the Fall 2021 semester. Subjects received $25 or psychology research participation credit for the baseline study procedures and all subjects received $15 for the follow-up. Monetary compensation was sent via Venmo or a mailed Visa gift card. All study procedures were approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Self-report Questionnaires

The Childhood Trauma Questionnaire (CTQ) measures forms of child abuse and neglect in five subscales including physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect (28). We calculated a total CTQ score for each subject for use in statistical analyses.

FH was assessed with the Family History Assessment Module. Alcohol use problems were defined based on responses to the screening question: "Has drinking ever caused your [mother/father/etc.] to have problems with health, family, job, or police?" A response of "Yes" or a response of "Unsure" with more than two categories of DSM-5-related symptoms reported from the follow-up questions was considered as having alcohol use problems. Family history density is a composite of calculations related to first- and second-degree relatives and their experiences with alcohol use disorder based on genetic relatedness (29). FH density score was calculated based on subject-reported alcohol use problems among parents (weight = 0.5), grandparents (weight = 0.25), aunts (weight = 0.25), and uncles (weight = 0.25). Higher scores denote more drinking-related problems among the participants' relatives. Even in the absence of parental AUD, those with a high FH density are more likely to develop an AUD (30).

adolescent binge drinking was measured at baseline using our in-house Carolina Alcohol Use and Patterns Questionnaire which includes a question surveying the number of binge episodes (4+ drinks in 2 h for females, 5+ drinks in 2 h for males) prior to age 18 (31): "Before the age of 18, how often did you have 5 or more drinks (4 or more if you are female) containing any kind of alcohol within a two-hour period?" Because response options for this question were binned (e.g., Never, 1–3 times, 4–6 times, etc.), we converted this measure to discrete values (e.g., 0, 2, 5) corresponding to the total estimated number of binge drinking episodes, as

previously published (31). The test–retest reliability when comparing retrospective reports at baseline to retrospective reports 1 year later was moderate (Spearman's rho = 0.57).

For recent alcohol misuse, three questions from the Alcohol Use Questionnaire were included on the Carolina Alcohol Use and Patterns Questionnaire to calculate a "binge score," as previously published (32). These questions ask subjects to reflect on their typical drinking, referencing the prior 6 months, and quantify the rate and frequency of drinking to assess the frequency and severity of hazardous alcohol misuse (i.e., 1. "When you drink, how fast do you drink?;" 2. "How many times have you been drunk in the last 6 months? By 'drunk' we mean loss of coordination, nausea, and/or inability to speak clearly.;" 3. "What percentage of the times that you drink do you get drunk?"). Binge scores correlated with the number of binge episodes (four or more drinks for females or five or more drinks for males within an occasion) in the past year (Spearman's rho = 0.65) as reported on the Customary Drinking and Drug Use Record (CDDR) (33), attesting to its construct validity as a measure of alcohol misuse. Binge scores were collected at the baseline (first semester of college, 18–19 years of age) and 1 year later (fall semester, year 2 of college, 19–20 years of age). A total of 154 (47%) of subjects had binge drinking scores available from the follow-up survey. Subjects also reported on the CDDR whether they ever used cannabis (yes/no) or tobacco (yes/no). Alcohol Use Disorders Identification Test (AUDIT) (34) scores were collected for supplemental analyses. AUDIT scores and binge scores were log-transformed to approximate a normal distribution prior to their use as dependent variables in statistical analyses.

Behavioral task

Delay discounting, which indexes decision-making impulsivity, was assessed with a task administered on the Pavlovia.org online server. Subjects were offered 40 hypothetical choices between a larger amount of money ($100 or $1000) offered after a delay or a smaller amount of money, which was adjusted throughout the task based on previous choices and was offered "Today." Delays included 1 week, 1 month, 6 months, and 2 years. Eight objective choice trials were included in which subjects indicated the sooner delay or the larger monetary amount. Trials were presented in a pseudorandomized order. The task was self-paced. Data were excluded for subjects answering less than three of the objective trials incorrectly ($n = 14$), and behavioral data was missing for additional 35 subjects, leaving 280 subjects with valid behavioral data.

To measure delay discounting, we calculated the area under the curve (AUC) of preferred choices across delays for both the $100 trials and $1000 trials, with smaller AUC values indicating steeper discounting of delayed rewards. Individual estimates of delay discounting were calculated by first transforming AUC values across subjects into z-scores, separately for $100 and $1000, and then z-scores for $100 and $1000 were averaged for each subject to provide a single value of delay discounting.

Statistical analyses

Two separate regression analyses tested the primary hypothesis of three-way interacting effects of FH, CM, and adolescent binge drinking on 1) binge scores at one-year follow-up ($n = 154$ subjects) and 2) delay discounting ($n = 280$ subjects). Models included baseline binge scores, sex, cannabis use, and tobacco use as covariates. Cannabis and tobacco use were included as covariates due to potential associations with risk factors, DD, and future alcohol use, and thus they were included to remove the variance related to these potential confounding effects (35). Because we adjusted for baseline binge scores, follow-up binge scores reflect one-year residualized changes in alcohol misuse.

Preliminary regression diagnostics in SAS PROC REG indicated the presence of many high leverage data points. To provide more stable results, we tested all regression models using robust regression with the SAS PROC ROBUSTREG procedure. We used the MM estimation technique as this option accounts for both outliers and high leverage points. Note that the robust regression test statistic follows an x distribution.

Additional robust regression analyses examined the main effects of FH, CM, and adolescent binge drinking, as well as lower-order interactions (i.e., FH×CM, FH×ABD, CM×ABD) to further explore the strength of relationships for individual or combined risk factors in a stepwise fashion. These models also included baseline binge scores, sex, cannabis use, and tobacco use as covariates.

Supplemental analyses examined the effects without including cannabis and tobacco covariates and also tested AUDIT scores in place of binge scores as the outcome variable.

Finally, to examine whether delay discounting mediates the effect of risk factors on alcohol use at follow-up, we tested a moderated mediation model using the PROCESS toolbox in R (PROCESS Model 73). This method tests for moderated mediation by comparing differences in the indirect effects (i.e., a path multiplied by b path) across levels of the moderators, as recommended (32).

Specifically, we examined whether the effect of FH on future alcohol misuse was mediated by delay discounting and whether this mediation effect was influenced by CM (moderator 1) and further influenced by adolescent binge drinking (moderator 2; Figure 3). We conceptualize CM and adolescent binge drinking as moderating FH following a diathesis-stress model, as FH is a preexisting risk factor that may be further influenced by experiences. There is also strong evidence for FH to influence delay discounting as a potential behavioral mechanism of AUD (24,25). We denote CM as moderator 1, since CM is known to interact with FH to predict AUD (4,11), but note that the order of the two moderators does not affect the statistical results. Although PROCESS cannot incorporate weights for robust estimates, we excluded subjects for which their weights in the robust regressions were <0.7 in order to provide a more stable and accurate result while also maintaining a large sample size for analysis ($n = 282$). The PROCESS toolbox does not include subjects with missing data, and, as indicated above, many subjects in this study were missing either valid delay discounting behavioral data (36) or follow-up drinking data (172). Therefore, in order to combine these data to obtain estimates of the mediation effect, we conducted multiple imputations with *mice()* in R to replace the missing behavioral or follow-up drinking data using five iterations of predictive mean matching. Imputed data values were restricted to fall within the range of observed values. The mediation analysis included baseline binge scores, sex, cannabis use, and tobacco use as covariates. The significance was based on 95% confidence intervals derived from 5,000 bootstrap iterations.

Results

Sample characteristics, including CTQ scores, FH density, alcohol use, and delay discounting task performance are reported in Table 1. Table 2 presents the pairwise correlations between FH, CM, adolescent binge drinking, delay discounting, baseline binge scores, and follow-up binge scores. There were no significant differences between subjects who responded to the follow-up survey versus those who did not respond on FH ($t(327) = -0.45$, $p = .65$), CM ($t(327) = 0.77$, $p = .44$), adolescent binge drinking ($t(327) = 1.09$, $p = .28$), delay discounting ($t(279) = -0.85$, $p = .40$), baseline binge scores ($t(327) = 0.84$, $p = .40$), sex (X^2 (1) $= 3.13$, $p = .08$), cannabis use (X^2 (1) $= 2.66$, $p = .10$), or tobacco use (X^2 (1) $= 1.05$, $p = .31$).

We assessed whether risk factors predicted changes in binge drinking from baseline to follow-up. The majority of subjects (86.1%, Table 1) reported having tried alcohol by the one-year follow-up. There was a significant 3-way

Table 1. Sample characteristics.

	Mean (or %)	Std. Deviation	Min. Value	Max. Value
Sex (Females)	230 (70%)			
Race (%):				
Asian	18%			
African American or Black	5%			
Native American	<1%			
White	73%			
More than one	4%			
Ethnicity (% Hispanic/Latino)	11%			
Delay Discounting				
Delay Discounting AUC $100	402.1	176.5	19.1	718.6
Delay Discounting AUC $1000	465.2	170.2	26.8	715.5
Mean Response Time Decision Trials (s)	1.9	0.9	0.3	8.6
# Correct Control Trials (n/8)	6.8	1.6	2	8
Family History Density	0.3	0.4	0	1.75
Childhood Trauma Questionnaire				
Total	42.8	15.9	25	102
Physical Abuse	6.9	3.1	5	24
Emotional Abuse	11.5	5.5	5	25
Sexual Abuse	6	3.2	5	25
Physical Neglect	7.5	3.2	5	23
Emotional Neglect	11	5	5	25
Estimated # Binge Episodes before Age 18	5.5	18.6	0	156
Age at First Drink	15.6	2.2	1	19
Binge Score Baseline	14.8	18.8	0	92
Binge Score Follow-up	14.7	19.3	0	128
AUDIT Baseline	3.7	4.6	0	26
AUDIT Follow-up	4.4	4.7	0	21
Alcohol Use Baseline (%)	75.3%			
Alcohol Use Follow-up (%)	86.1%			
Cannabis Use Baseline (%)	44.4%			
Cannabis Use Follow-up (%)	50.8%			
Tobacco Use Baseline (%)	30.8%			
Tobacco Use Follow-up (%)	30.1%			

Estimated binge episodes before age 18 and binge scores were determined from the Carolina Alcohol Use and Patterns Questionnaire. Age at first drink as well as cannabis and tobacco use were assessed with the Customary Drinking and Drug Use Record. AUC, area under the curve of delay discounting choices; AUDIT, Alcohol Use Disorders Identification Test.

Table 2. Pairwise Pearson correlations between risk variables, delay discounting, and binge drinking.

	FH	CM	ABD	DD	Binge Score Baseline
FH	–				
CM	**0.31**				
	<.0001	–			
ABD	**0.18**	**0.15**			
	0.001	*0.01*	–		
DD	−0.09	−0.04	−0.08		
	0.10	*0.43*	*0.20*	–	
Binge Score Baseline	**0.16**	**0.15**	**0.53**	−0.10	
	0.003	*0.005*	*<.0001*	*0.11*	–
Binge Score Follow-up	0.07	0.11	**0.31**	−0.05	**0.63**
	0.41	*0.18*	*<.0001*	*0.53*	*<.0001*

Bolded values indicate significant correlations. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. DD values were estimated from a computerized task. FH, family history; CM, childhood maltreatment; ABD, adolescent binge drinking; DD, delay discounting.

interaction of FH, CM, and adolescent binge drinking on binge scores at one-year follow-up (X^2 (1) = 8.24, Standardized β Estimate = 0.37, Standard Error = 0.13, p = .004, Cramer's V = 0.23; Figure 1), indicating increased alcohol misuse associated with the combination of risk factors. This mirrored findings for AUDIT scores at one-year follow-up (X^2 (1) = 16.45, Standardized β Estimate = 0.56, Standard Error = 0.14, $p < .001$, Cramer's V = 0.33; Supplemental Table 1). There was similarly a significant 3-way interaction of FH, CM, and adolescent binge drinking on delay discounting (AUC) collected at baseline (X^2 (1) = 3.86, p = .049, Standardized βEstimate = −0.12, Standard Error = 0.06, Cramer's V = 0.12; Figure 2), indicating more impulsive decision-making associated with the combination of risk factors. There were no significant main effects or interactions of these risk factors in the reduced models testing these effects. Results for each of the robust regression models tested are reported in Table 3,

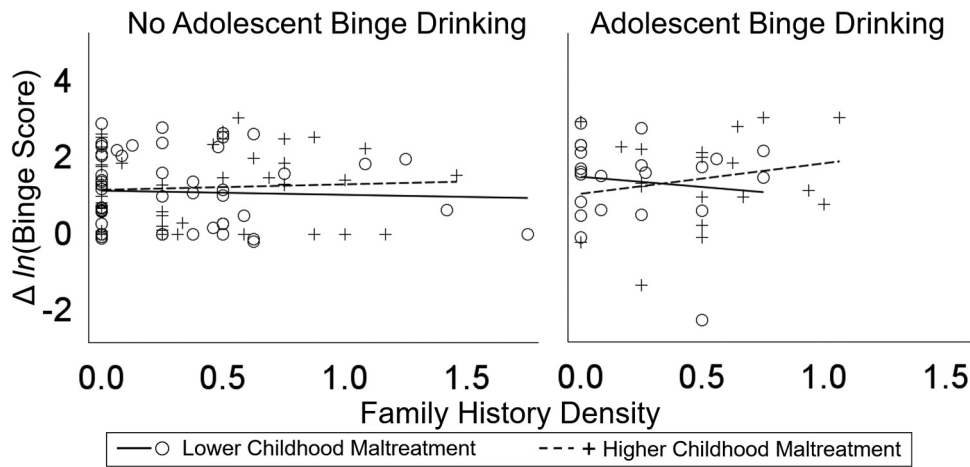## No Adolescent Binge Drinking / Adolescent Binge Drinking

Figure 1. Scatter plot demonstrating a significant three-way interaction of family history (FH), childhood maltreatment (CM), and adolescent alcohol binge drinking on binge drinking at 1-year follow-up. Subjects with higher levels of both CM and adolescent binge drinking (dashed line, right panel) showed the greatest effects of FH density on future binge drinking. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. Y-axis values are adjusted for baseline binge scores and thus represent change in binge drinking over one year. Groups were defined for visualization purposes based on a median split of CM and adolescent binge drinking values. Data points for subjects for which their weight in the robust regression analysis was < 0.7 were omitted from this scatterplot.
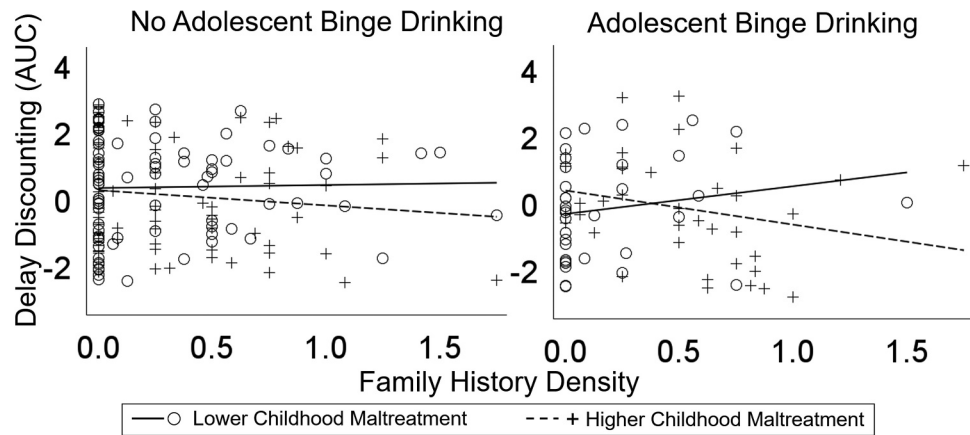

Figure 2. Scatter plot demonstrating a significant three-way interaction of family history (FH), childhood maltreatment (CM), and adolescent alcohol binge drinking on delay discounting. Subjects with higher levels of both CM and adolescent binge drinking (dashed line, right panel) showed greater effects of FH density on impulsive behavior. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. Delay discounting was measured with a computerized task. Y-axis values represent the mean area under the curve for discounting of $100 and $1000 following z-score transformation; Lower values correspond with greater impulsivity. Groups were defined for visualization purposes based on a median split of CM and adolescent binge drinking values. Data points for subjects for which their weight in the robust regression analysis was < 0.7 were omitted from this scatterplot.

indicating the strength of the statistical associations between main effects and interactions. Additional results without tobacco and cannabis use as covariates are included in Supplemental Table 2. Adjusted R^2 values are also included for each model.

A mediation analysis tested for potential moderated mediation based on differences in the indirect effects across levels of the moderators (Figure 3, Table 4).

Indirect effect estimates are provided at low (16th percentile), median, and high (84th percentile) values of FH and CM in Table 4 and plotted in Figure 4 to assist interpretation of results (25,37). These values would correspond with one standard deviation above or below the mean for normally distributed data, but we use percentiles here due to skewed distributions. As the median number of adolescent binge drinking episodes was 0, estimates are only provided
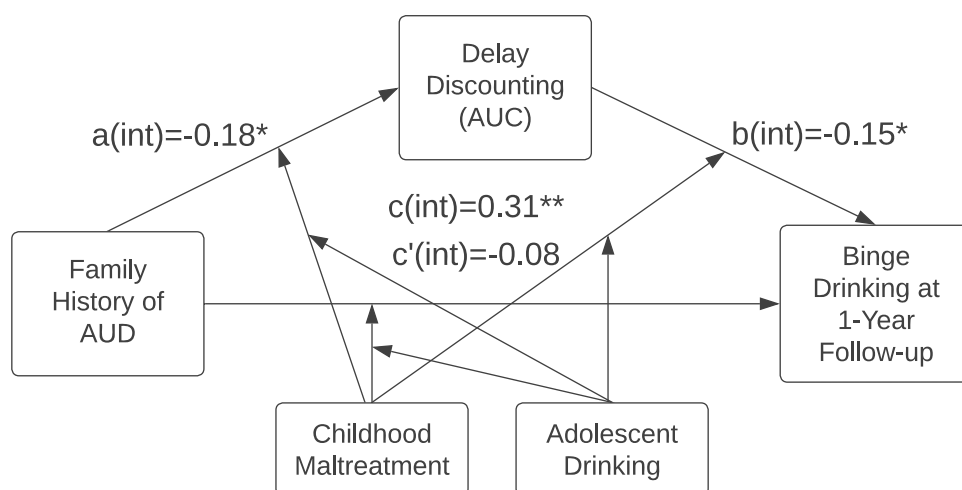
Figure 3. A moderated mediation in which delay discounting mediates the risk for future binge drinking associated with family history (FH), childhood maltreatment (CM), and adolescent alcohol binge drinking. Moderating effects of CM and adolescent binge drinking were tested on all three paths. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. Delay discounting was measured with a computerized task. Reported path coefficients (a, b, c, c′) represent three-way interaction effects (int). *$p < .05$, **$p < .0001$.

Table 3. Results of full and reduced linear regression models testing effects of risk factors on delay discounting and binge drinking.

Delay Discounting (Area Under the Curve)

Full Model			Reduced Model 1			Reduced Model 2		
$R^2_{adj} = 0.023$	Standardized Estimate	p	$R^2_{adj} = 0.010$	Standardized Estimate	p	$R^2_{adj} = 0.012$	Standardized Estimate	p
Binge Score Baseline	−0.02	.82	Binge Score Baseline	−0.01	.90	Binge Score Baseline	−0.02	.83
Sex	0.03	.63	Sex	0.05	.51	Sex	0.05	.45
Cannabis	−0.02	.84	Cannabis	−0.02	.85	Cannabis	−0.03	.78
Tobacco	−0.16	.07	Tobacco	−0.15	.09	Tobacco	−0.14	.11
FH	−0.04	.62	FH	−0.04	.59	FH	−0.03	.67
CM	0.02	.82	CM	0.02	.83	CM	−0.01	.88
ABD	0.03	.83	ABD	−0.07	.58	ABD	−0.08	.45
FH×CM	−0.09	.23	FH×CM	−0.10	.18			
FH×ABD	−0.03	.74	FH×ABD	−0.09	.38			
CM×ABD	0.20	.05	CM×ABD	0.08	.31			
FH×CM×ABD	−0.12	.05						

Binge Score Follow-up

Full Model			Reduced Model 1			Reduced Model 2		
$R^2_{adj} = 0.296$	Standardized Estimate	p	$R^2_{adj} = 0.297$	Standardized Estimate	p	$R^2_{adj} = 0.309$	Standardized Estimate	p
Binge Score Baseline	0.51	<.001	Binge Score Baseline	0.49	<.001	Binge Score Baseline	0.48	<.001
Sex	−0.02	.84	Sex	−0.02	.76	Sex	−0.02	.77
Cannabis	0.29	<.001	Cannabis	0.3	<.001	Cannabis	0.30	<.001
Tobacco	0.04	.70	Tobacco	0.01	.91	Tobacco	0.01	.94
FH	−0.13	.25	FH	0.1	.26	FH	0.09	.26
CM	0.01	.51	CM	−0.02	.81	CM	−0.02	.82
ABD	−0.61	<.001	ABD	−0.1	.62	ABD	−0.03	.75
FH×CM	0.1	.27	FH×CM	0.01	.94			
FH×ABD	−0.8	.01	FH×ABD	0.05	.72			
CM×ABD	0.06	.14	CM×ABD	−0.01	.95			
FH×CM×ABD	0.37	.004						

Standardized estimates and p-values are reported for each independent variable. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. FH, family history; CM, childhood maltreatment; ABD, adolescent binge drinking. Lower-order effects are not interpreted for significance.

Table 4. Indirect effect estimates of the mediation of family history and future binge drinking by delay discounting at values of the moderators: Childhood maltreatment and adolescent binge drinking.

Values of CM	Values of ABD	Indirect Effect	95% CI
Low	Low/Median	−0.003	−0.029, 0.022
Low	High	−0.000	−0.026, 0.030
Median	Low/Median	−0.000	−0.010, 0.011
Median	High	−0.000	−0.010, 0.009
High	Low/Median	−0.003	−0.031, 0.021
High	High	0.009	−0.023, 0.044

Values of childhood maltreatment (CM): Low = 28, Median = 38, and High = 59; Values of adolescent binge drinking (ABD): Low/Median = 0, and High = 2; CI, confidence interval.

for low/median (0 binge episodes) and high (2 binge episodes) values. The indirect effect estimates did not differ from each other or from 0 at any of the levels of the risk factors based on 95% confidence intervals.

Johnson-Neyman significance values were estimated in PROCESS for the moderated mediation model. The Johnson-Neyman technique estimates the range of values for which the effect of a moderator in significant interaction transitions from insignificant to significant.

The estimated number of adolescent binge episodes for the interaction of FH and CM to significantly affect delay discounting (i.e., path *a*) was estimated at 1.4, representing 33% of the current sample. The estimated number of adolescent binge episodes for CM to significantly affect the path between delay discounting and binge drinking at 1-year follow-up (i.e., path *b*) was estimated at 10.3, representing 7% of the current sample.

Discussion

By testing FH, CM, and adolescent binge drinking together, we show that these three risk factors for AUD interacted to predict both increased delay discounting and increased college binge drinking. However, the results did not demonstrate evidence that delay discounting mediated the AUD risk-associated changes in alcohol misuse over the first year of college. Nonetheless, the individual paths for the mediation indicated that those individuals that maintained higher cognitive control
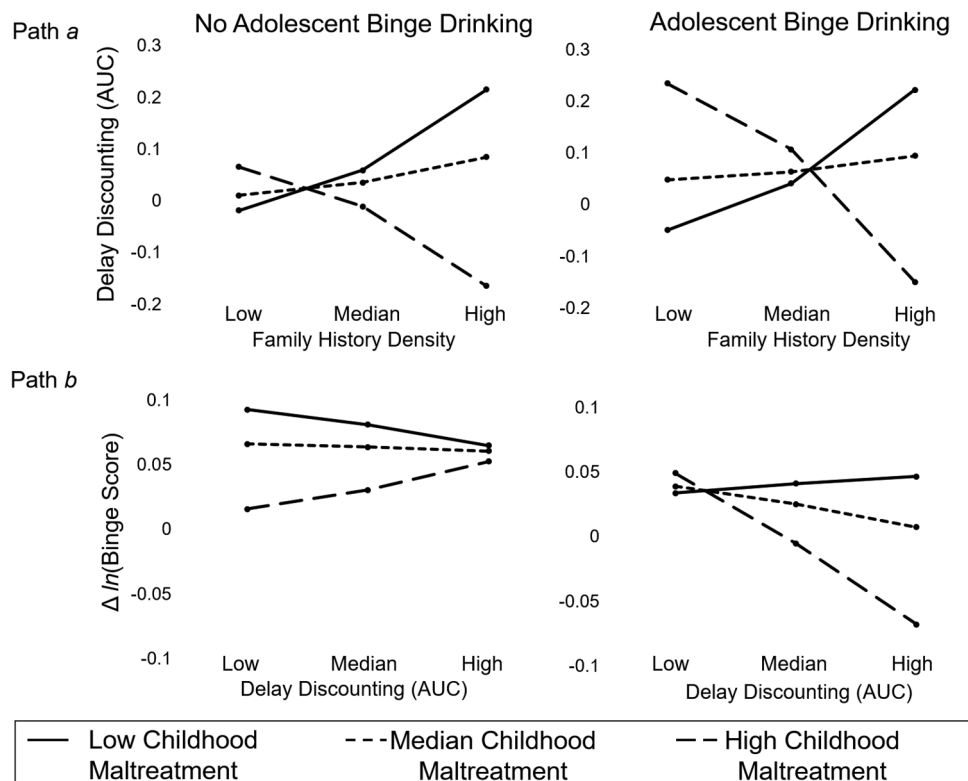

Figure 4. Plots of the effects of family history (FH), childhood maltreatment (CM), and adolescent alcohol binge drinking from the moderated mediation analysis. Effects of path *a* (upper panel) demonstrate significant three-way interaction effects of FH (x-axis), CM, and adolescent binge drinking on delay discounting, expressed as the area under the curve, where lower values represent greater impulsivity. Effects of path *b* (lower panel) demonstrate significant three-way interaction effects of delay discounting (x-axis), CM, and adolescent binge drinking on future binge drinking. FH, CM, and adolescent binge drinking were measured via self-report surveys using the Family History Assessment Module, Childhood Trauma Questionnaire, and Carolina Alcohol Use and Patterns Questionnaire, respectively. Delay discounting was measured with a computerized task.

despite having these risk factors may be protected from escalations in binge drinking.

Figure 3 suggests that FH effects on steeper delay discounting are increased in the presence of environmental risk factors, CM and adolescent binge drinking. In fact, Johnson-Neyman significance values for path *a* of the mediation analysis indicated that the interaction of FH and CM was only significant in those who engaged in any adolescent binge drinking, approximately one-third of this sample. In other words, even 1–2 adolescent binge episodes may alter behavioral impulsivity in at-risk individuals. Early adolescent exposure to alcohol induces neurotoxic effects within cortical brain regions, which could exacerbate susceptibility to other risk factors (38). However, an alternative explanation is that individuals with higher FH and CM who abstained from alcohol throughout adolescence could have been more resilient and thus exhibited lower levels of delay discounting compared to those who initiated alcohol binge drinking sooner. This interpretation does not seem to be supported by the current data (Figure 2 and 4), which actually indicates that students who engaged in adolescent binge drinking demonstrate relatively low discounting even compared to those without adolescent binge drinking, except when they have higher CM and FH. Nonetheless, recent evidence suggests that delay discounting in adolescence predicts future alcohol use better than alcohol use predicts changes in delay discounting (39), though, of note, drinking levels in that sample were low. A multitude of preclinical studies support the theory that adolescent binge drinking exposure can lead to increased impulsivity (10). Future work to examine the extent to which adolescent binge drinking leads to increased delay discounting or *vice versa* is warranted. Social factors such as easy access, family culture, and living on a college campus can also enhance the potential for adolescents and emerging adults to binge drink (40), representing potentially important points of intervention and education for high-risk individuals (i.e., those with FH, adolescent binge drinking, and CM histories).

Furthermore, path *b* between delay discounting and future alcohol misuse was moderated by CM and adolescent binge drinking, indicating that these risk factors influenced the effects of delay discounting on future alcohol misuse. Greater delay discounting related to greater future alcohol misuse, with the steepest slopes in individuals with higher CM and adolescent binge drinking (Figure 4). However, the data actually suggest an interesting relationship in which future binge drinking was not generally greater in subjects with both higher CM and adolescent binge drinking and steeper discounting compared with other subgroups; rather, those subjects reporting higher CM and adolescent binge drinking but lesser delay discounting demonstrate *lower* future alcohol misuse. Thus, the data suggest that enhanced cognitive control (i.e., reduced delay discounting) in at-risk individuals – despite these same individuals being more likely to have steeper discounting – may protect them from escalations in alcohol misuse. These relationships help explain why we detected significant effects for both path *a* and path *b*, yet there was no evidence for a moderated mediation. These findings may also explain inconsistent reports of the relationship between impulsivity and alcohol use across the literature, as these effects may differ depending on the presence of risk factors.

The current results add to a growing literature indicating that heritable and environmental risk factors relate to AUD through increased delay discounting. For example, previous work has indicated that FH and previous alcohol use interact to increase delay discounting (18). Moreover, early-life stress related to physical, emotional, and sexual trauma (18,19), as well as socio-economic status (22), is associated with steeper delay discounting. Heritable effects on delay discounting have also been detected even when controlling for environmental effects (18,22). Furthermore, self-reported impulsivity (as a subfacet of neuroticism) mediates the link between CTQ scores and AUD (41). Other work has shown that the additive effects of multiple environmental and heritable risk factors predicted future alcohol use in adolescents, with an indirect effect through delay discounting (42). Our data uniquely demonstrate that heritable, environmental, and toxicological risk factors synergistically increase delay discounting, although they did not provide evidence for delay discounting as mediator of these risk factors on future alcohol misuse.

Delay discounting is underpinned by brain regions associated with both cognitive control and those involved in reward (43,44). The regions involved in intertemporal choice also correspond with the frontal and subcortical brain regions impacted by FH (45), CM (46) and adolescent binge drinking (10), suggesting potential neural mechanisms of risk. For example, individuals with early life stress histories display altered neural processing of rewards (47). FH is also associated with altered neural processing of rewards (48), though with qualitative differences in the implicated brain regions relative to early life stress. Future studies should consider the interacting effects of these risk factors on the brain to examine whether they target common or interacting brain networks.

Pearson correlations between risk factors and outcome variables mostly exhibited expected relationships. The significant positive correlations among the three risk factors in Table 4 are consistent with the notion that each of these variables do not represent independent heritable, environmental, and toxicological effects. Furthermore, this overlap underlines the importance of considering each of these variables in statistical models that seek to measure the effect of any single risk factor. Surprisingly, the individual risk factors each significantly correlated with baseline binge scores, but they were weaker predictors of follow-up scores. One explanation for this finding is that baseline scores largely reflect drinking immediately prior to entering college, as these data were reported in their first semester, whereas the follow-up scores reflect drinking while enrolled in college. The somewhat weaker associations with college drinking could relate to the added influence of college drinking norms that could partially wash out the signal of risk factors *i. e.*, many students engage in college binge drinking regardless of risk factors. Nonetheless, linear regression results support the influence of these risk factors – when combined – on increases in college drinking.

Limitations

Several study limitations should be considered. The data was collected within the first 2 years of the COVID-19 pandemic, which may have affected the relationships between risk factors and alcohol use. Due to the focus on college students, the results may not generalize to a broader population. Moreover, impulsivity is a vast construct with measures beyond delay discounting. It is possible other aspects of impulsivity may mediate the effects of risk factors on alcohol misuse. Importantly, because delay discounting was assessed after adolescent binge drinking, the direction of the relationship between delay discounting and adolescent binge drinking cannot be definitively determined. Finally, it is likely that some subjects underreported their alcohol use in the surveys, which could have led to bias in the results (49).

Conclusions

The reported findings have implications for health care that is catered toward individuals that have both genetic and environmental predispositions to AUD. Interventions targeting delay discounting-related processes may not necessarily represent an effective strategy for reducing harm in at-risk college students. Strategies at the level of public health to reduce exposure to multiple forms of risk and their compounding effects may offer an avenue to lessen the burden of alcohol use disorder on individuals and their communities.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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