Adolescent Behavioral Characteristics Mediate Familial Effects on Alcohol Use and Problems in College-Bound Students

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ABSTRACT

BACKGROUND: Studies suggest a broad spectrum of behaviors associated with drinking. Consequently, it is unclear whether patterns of familial risk for psychopathology are directly or indirectly related to patterns of alcohol use and problems in late adolescence or mediated by behavioral characteristics, such as temperament, mood.

OBJECTIVES: We examined direct and indirect effects of perceived family history of psychopathology on pre-collegiate alcohol use and problems via the Transmissible Liability Index (TLI).

METHODS: Participants (N = 302; 29.6% male) provided self-report data on age of onset of drinking, past 90-day frequency of alcohol use and problems (AUP), family history of internalizing and alcohol and illicit substance use, and TLI.

RESULTS: Approximately 21% of participants reported having at least one relative with a history of regular and/or problematic alcohol use, compared to 12% for illicit substance use, and ~55% for internalizing problems. Higher TLI scores were associated with increased family history of substance use, alcohol use, and internalizing problems, as well as earlier age of onset of drinking. Family history of internalizing problems was the most robust indicator of AUP ($β=0.20$, [95% CI = 0.04-0.36], $P= .01$). Path analyses suggested that the individual-level behaviors that comprise TLI mediate the effects of family history on age of initiation and regular alcohol consumption.

CONCLUSIONS: Family history of internalizing, drinking, and illicit substance use reflect generalized risk for a broad set of behaviors associated with risk for alcohol initiation and use during the transition from high school to college.

KEYWORDS: Transmissible Liability Index, alcohol, family history, adolescent health, college

Introduction

Underage alcohol consumption is a persistent societal problem that contributes to high healthcare costs, lost productivity, and criminal activity.1 Problematic alcohol use is prevalent in the United States and affects 10.7% of young adults (ie, individuals between 18 to 25 years; http://samhsa.gov). Among young adults, college students are particularly at risk for heavy alcohol consumption and other patterns of disordered alcohol use.2 College students show significantly heavier drinking patterns than their non-college attending peers and are more likely to receive a diagnosis of DSM-IV alcohol abuse.3 It has been hypothesized that college may represent a unique environmental context (eg, high stress, demands for academic success, and peer influence) that might account for the relatively higher rates of alcohol misuse on campuses.4 Studies show that students reporting higher stress and depressed mood consume more alcohol5 and that the transition to college is associated with greater frequency of binge drinking.6

Family history of drug use and/or psychopathology is a robust determinant of adolescent drug and alcohol misuse. For example, college students with a family history (FH) of alcohol and substance problems have previously been shown to exhibit higher levels of impulsivity, as well as (1) an increased risk for initiating alcohol use during college, (2) higher levels of alcohol consumption, and (3) a greater number of endorsed alcohol use disorder (AUD) criteria.7 Likewise, a family history of internalizing problems (FH-IP) has also been shown to be a transmissible component of liability to substance use disorders (SUDs). Several cross-sectional and longitudinal studies have reported associations between FH of depression,8 anxiety,9 and AUDs10 with the presence of the same pathological outcome in the offspring. Furthermore, FH of AUDs and anxiety disorders have been shown to influence the risk of developing either condition.11 Given the relationship between FH of AUDs and dimensions of internalizing problems, it is imperative to investigate the unique contribution of each construct on the drug and alcohol misuse, as well as childhood
and adolescent behaviors and traits that often predate the onset of drug initiation.

While drug and alcohol use behaviors are often assessed in isolation, it is understood that multiple processes (genetic and environmental) contribute to the use and misuse of one or multiple substances. These factors include childhood and adolescent behavioral and developmental problems that are also known to be under moderate to strong genetic influence. The transmissible liability index of substance use disorders (TLI) is a quantitative index of the common variance among predictors of early substance use. The TLI originally comprised 45 items and was indicated by symptoms that reflected disruptive behavior disorders, sleep disruption, appetite, and suicidality, to name a few. As a behavior genetic construct, pre-adolescent and adolescent TLI has been tested and shown to be positively associated with substance use behaviors and emotional disturbances. To date, a single study has examined the TLI to understand potential mechanisms through which college students develop AUP.

The present study examined individual and familial factors in discerning individual differences in the frequency of past 90-day frequency of alcohol use and alcohol-related problems among students at the start of college. Given the complexity of liability to substance use behaviors, we examined generalized versus specific effects of FH of substance involvement relative to internalizing problems to better understand their mechanism of action in relation to TLI. We hypothesized that FH of alcohol (FH-AU) and illicit substance use (FH-SU), and FH of broad internalizing problems (FH-IP), would be partly mediated by individual factors, captured by TLI (ie, broadly related to emotional disturbances and behavioral under-control), in their effects on both the initiation of drinking and pre-collegiate alcohol use and problems.

**Methods**

**Sample**

Participants were randomly recruited from 2 east-coast college campuses that are part of a single institution serving over 5000 undergraduates (N = 303; 29.6% male; M_{age} = 18.58 [SD = 0.39]). The sample was comprised of first-year students from a large incoming class with a racial representation of 38% Caucasian, 24% Asian, 11% Hispanic, 7% African American, 4% multi-racial/ethnic groups; 16% self-identified as Non-US citizens rather than a racial category. Recruitment was open to all demographic groups and occurred during the first 6 weeks of the fall semester using web-based surveys (M_{week} = 3.17 [1.78]). Students were made aware of the study using flyers and invitations at campus events and classrooms specific to first-year students. Students were directed to an online survey where they reviewed and completed a local IRB-approved consent form to receive their individual pin to complete the survey. Participants then completed the online 60-minute survey and subsequently received a $15 compensation and an additional $5 for providing salivary DNA.

**Measures**

**Family history reports**

The Family History Screen (FHS) was used to assess the perceived density of psychiatric symptoms and suicidal behavior among the respondent’s blood relatives (ie, fathers, mothers, aunts/uncles, brothers, sisters, grandparents, and cousins). The FHS has demonstrated validity, reliability, and utility in cases where family members are not available for direct interview; as such, family history (FH) effects described herein are perceived by the student as other relatives were not contacted for confirmation. Respondents indicated whether there was any perceived family history of psychopathology and which family member was being referenced. FH-AU was assessed using responses to the survey item, “Have any of your blood relatives ever had a period in his or her life when they drank a lot?” Similarly, FH-SU was assessed using responses to the question, “Have any of your blood relatives ever had a period in his or her life when they used illegal drugs regularly?” FH-IP was assessed using 5 items that tapped into anxiety and depression. For example, participants were asked, “Have any of your blood relatives ever had a period during which they felt sad, blue, or depressed that lasted for 2 weeks or more?” or, “[. . .] ever worry almost every day for 6 months or more about things that other people wouldn’t have worried about that much?” Additionally, participants reported on their family members’ experience of emotional breakdowns, frequency and duration of worries, suicidality, and sleep problems. Information across these internalizing dimensions were summed to create a broad FH-IP score.

FH-AU/SU/IP were derived (respectively) by selecting the dichotomous yes/no item responses to the screener question (ie, “Have any of your blood/biological relatives ever had a serious mental illness, emotional problem, or nervous breakdown”). If the participant responded yes, they were then asked to identify which family member(s) had experienced that given problem. As such, participant scores were weighted by familial load (ie, average genetic similarity between the reporter and their reported relative: mother and/or father [0.5], brother and/or sister [0.5], aunts and/or uncles [0.25], grandparent [0.25], and cousin [0.125]). In doing so, we created a weighted summary score where higher scores indicated an aggregate of “known family history” of each trait. Notably, this score was sensitive to the fact that individuals had the opportunity to opt out of identifying a family member. Specifically, participants received a score of 0 if they reported no family history, a score of 1 if they endorsed having a family history but opted not to identify any particular family member, and a weighted score which was defined as 1 + the sum of degree of genetic similarity with identified relatives. Of note, participants could achieve similar scores via different combinations of relative information, such as indicating only a parent (ie, 1 + 0.5) versus aunts/uncles & grandparents (ie, 1 + 0.25 + 0.25). In doing so, the score captures the degree of phenotypic and genetic concurrence within each participant’s family. Our initial examination of the data identified...
only 8 participants who did not identify a specific relative when answering internalizing problems questions. The analyses described below were conducted before and after including these individuals; no differences in the pattern of results or effect size estimates were observed.

Transmissible Liability Index

Behavioral and temperamental characteristics associated with SUDs was inferred for each participant using responses on a personal history (lifetime) survey that mirrored the Transmissible Liability Index (TLI) items studied by the Center for Education and Drug Abuse Research CEDAR.18 Participants were asked yes/no questions, such as “Have you ever had a strong fear or avoidance of being in a crowd or standing in a line?” or, “Did you get into a lot of fights that you started?” The current study employed 24 items that captured TLI behaviors, such as disruptive shoplifting, typically manifest in childhood and adolescence.22,23 Therefore, the general/full model posited that family history factors directly influence TLI behaviors, the age of onset of alcohol use, and alcohol use and problems. Further, since younger age of onset for substance use among family history positive individuals is generally associated with more severe problem drinking, we examined its direct effects on both outcomes. Overall, the model allowed for the examination of the direct effect of each family history measure on both outcomes, as well as their indirect effects via TLI and age of onset of drinking. Direct and indirect effects were tested by examining the change in model fit using Wald Chi-square tests in which path loadings were fixed at zero (ie, submodels I-VII). Model fit was assessed using the TLI, CFI, and RMSEA.24

Results

Descriptive statistics

Sample descriptive statistics are provided in Table 2. Approximately 63% of students report having tried alcohol. Alcohol users reported initiating at an average of approximately 16 years. Additionally, males and females endorsed a similar frequency of past 3-month alcohol use, however, males endorsed a greater amount of alcohol problems. TLI scores were invariant across sexes and campuses.

Approximately 21% of participants reported having at least one relative with a history of regular and/or problematic alcohol use. Roughly, 12% of the sample reported a family history of illicit substance use, and nearly 55% reported internalizing problems; most individuals endorsed a parent or aunt/uncle (Table 3). Both sexes also had similar mean levels of family history of alcohol and illicit substance use/problems, but females reported higher levels of internalizing issues in their families, on average.

Indicators of frequency of alcohol use and problems

Table 4 summarizes the regression model examining the effects of family history and TLI on age of initiation and recent alcohol use and problems. Individuals who joined the study later in the semester had a later age of onset of drinking. Likewise, larger
TLI scores were associated with a greater likelihood of alcohol initiation (Odds-ratio = 1.71 [1.20, 2.45]). Both higher TLI scores and family history of illicit substance use were associated with alcohol initiation at an earlier age. None of the 3 family history indicators were associated with frequency of drinking in the past 3 months, suggesting that a positive family history for these traits may not confer specific risk for drinking more overall at this developmental time-point. Among drinkers, the model predicting alcohol problems performed well, accounting for 14% of the variation in symptomology, with FH-IP positively associated over and above all other indicators.

Figures 1 and 2 summarize the path model results for alcohol use and problems (Table 5). Overall, the models explained 20% ($r^2 = 0.205$, standard error (SE) = 4.30, $P < .001$) of the variance in TLI, 8% of the variance in age of onset drinking ($r^2 = 0.084$, SE = 4.00, $P < .05$), 15% of the variance in frequency

### Table 1. Standardized TLI factor loadings.

| ITEM DESCRIPTION                                                                 | $\beta$ | SE  | $P$     |
|----------------------------------------------------------------------------------|---------|-----|---------|
| 1. In your entire life, have you ever had a time, lasting 2 wk, when you didn’t care about the things you usually care about, or you didn’t enjoy what you usually enjoy? | 0.738   | 0.046 | <.001   |
| 2. Have you ever had a time that lasted for at least 2 y when your mood was low, sad, or depressed most of the day, more than half of the time? | 0.651   | 0.059 | <.001   |
| 3. Have you ever had a strong fear or avoidance of being in a crowd or standing in a line? | 0.485   | 0.066 | <.001   |
| 4. Most of the time throughout your life, regardless of the situation or whom you were with, have you avoided jobs or tasks that dealt with a lot of people? | 0.515   | 0.068 | <.001   |
| 5. Do you often have to keep an eye out to keep people from using you, hurting you, or lying to you? | 0.741   | 0.046 | <.001   |
| 6. Do you spend a lot of time wondering if you can trust your friends or the people you work with? | 0.712   | 0.052 | <.001   |
| 7. Do you find that it is best not to let other people know much about you because they will use it against you? | 0.695   | 0.055 | <.001   |
| 8. Do you often get angry or lash out when someone criticizes you in some way? | 0.482   | 0.078 | <.001   |
| 9. Did you ever have a time in your life when you lied a lot or any time you lied to keep from being hurt? | 0.664   | 0.048 | <.001   |
| 10. Did you ever have a time in your life when you lied a lot, NOT counting any times you lied to keep from being hurt? | 0.650   | 0.060 | <.001   |
| 11. Did you ever get more than 3 traffic tickets for reckless or careless driving, speeding, or causing an accident? | N/A     | N/A  | N/A     |
| 12. Did you ever run away from home overnight at least twice when you were living at home, or run away and stay away for a longer time? | 0.688   | 0.104 | <.001   |
| 13. Did you ever destroy, break, or vandalize someone else’s property like their car, home, or other personal belongings? | 0.131   | 0.107 | .221    |
| 14. Did you ever fail to pay off your debts- like moving to avoid paying rent, not making payments on a loan or mortgage, failing to make alimony or child support payments or filing for bankruptcy? | N/A     | N/A  | N/A     |
| 15. Did you ever steal anything from someone or someplace when no one was around? | 0.573   | 0.069 | <.001   |
| 16. Did you ever shoplift? | 0.599   | 0.077 | <.001   |
| 17. Did you ever rob or mug someone or snatch a purse? | N/A     | N/A  | N/A     |
| 18. Did you ever get into a lot of fights that you started? | 0.922   | 0.068 | <.001   |
| 19. Did you ever get into a fight that came to swapping blows with someone like a husband, wife, girlfriend, or boyfriend? | N/A     | N/A  | N/A     |
| 20. Did you ever hit someone so hard that you injured them or they had to see a doctor? | 0.400   | 0.150 | .007    |
| 21. Did you ever physically hurt another person in any other way on purpose? | 0.418   | 0.096 | <.001   |
| 22. Did you ever harass, threaten, or blackmail someone? | 0.879   | 0.077 | <.001   |
| 23. Did you ever make money illegally like selling stolen property, or selling drugs? | 0.690   | 0.140 | <.001   |
| 24. Did you ever use a weapon like a stick, knife, or gun in a fight? | N/A     | N/A  | N/A     |

N/A, excluded from model due to low level of endorsement.
of alcohol use and AUP ($r^2 = 0.146, SE = 4.30, P < .01; and $r^2 = 0.155, SE = 6.40, P < .001$, respectively). Based on the full model, a denser family history of internalizing problems and heavy alcohol use were associated with elevated TLI scores, suggesting increased vulnerability to a range of mental behavioral health outcomes in adolescence. Notably, higher family history of internalizing problems was directly associated with initiating use at an earlier age. Likewise, higher TLI scores were associated with earlier onset of drinking. With respect to use, but not problem drinking, individuals who initiated drinking earlier in life used more frequently in the 3 months leading up to college. There was limited evidence of direct effects of family history or TLI on alcohol use. None of the family history measures nor TLI were directly associated with frequency of alcohol consumption. Based on the model comparisons the best fitting model for use, suggested full mediation of the family history and TLI effects. On the contrary, only family history of broad internalizing behaviors was associated with problem drinking.

**Discussion**

The current findings are aligned with recent studies that suggest an increased risk for alcohol consumption and problems among individuals with a family history of internalizing psychopathology, drinking, and illicit drug use. Moreover, we demonstrate how a family history for heavy drinking, illicit substance usage, or internalizing problems relates to a broad index of substance use disorder liability (TLI). Further, we demonstrate direct and indirect effects on initiation, post-secondary to early-collegiate alcohol consumption, and alcohol problems. The positive relationship between FH-AU and emerging adult alcohol initiation and use, suggests alcohol-specific familial risk (ie, genetic and/or shared family environmental factors). We also found support for internalizing familial risk for alcohol initiation, use, and problems via FH-IP. Notably, the relationship of all the family history variables on initiation and use, but not problems, reflects a broad set of under-control and internalizing behaviors that predispose emerging adults to use in college, but not necessarily to developing problematic use at this time-point.

Zero-order correlations suggest FH-AU is associated with AUP, but this effect is confounded with other inherited risk indices, FH-drug and FH-IP. This is consistent with prior studies, suggesting a common genetic liability for a FH of alcohol use,7 substance use,27 and internalizing problems.10 Results from comparisons between FH variables and AUP demonstrated that FH-IP has both unique and shared effects with FH-AU on AUPs. One possible interpretation is that the stronger association between FH-IP and AUP is an artifact of measurement differences; FH-IP was assessed using 5 items and has more variance, whereas FH of substance and alcohol use and AUP ($r^2 = 0.146, SE = 4.30, P < .01$; and $r^2 = 0.155, SE = 6.40, P < .001$, respectively). Based on the full model, a denser family history of internalizing problems and heavy alcohol use were associated with elevated TLI scores, suggesting increased vulnerability to a range of mental behavioral health outcomes in adolescence. Notably, higher family history of internalizing problems was directly associated with initiating use at an earlier age. Likewise, higher TLI scores were associated with earlier onset of drinking. With respect to use, but not problem drinking, individuals who initiated drinking earlier in life used more frequently in the 3 months leading up to college. There was limited evidence of direct effects of family history or TLI on alcohol use. None of the family history measures nor TLI were directly associated with frequency of alcohol consumption. Based on the model comparisons the best fitting model for use, suggested full mediation of the family history and TLI effects. On the contrary, only family history of broad internalizing behaviors was associated with problem drinking.

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| TABLE 2. Descriptive statistics by sex. |
|----------------------------------------|
| **VARIABLE**                            | **OVERALL** | **FEMALES** | **MALES** |
|                                        | N           | MEAN (SD)/N (%) | N           | MEAN (SD)/N (%) | N           | MEAN (SD)/N (%) |
| Demographic information                |             |               |             |               |             |               |
| Sex (female [1] versus male [0]), n (%)| 300         | 89 (30%)      | 211         | N/A           | 89          | N/A           |
| Age                                    | 302         | 18.58 (0.39)* | 211         | 18.55 (0.39)  | 89          | 18.65 (0.38)  |
| Week of assessment completion          | 302         | 3.17 (1.79)   | 211         | 3.16 (1.75)   | 89          | 3.18 (1.90)   |
| Campus (metro [1] versus suburb [0]), n (%)| 302         | 192 (64%)     | 211         | 130 (62%)     | 89          | 62 (70%)      |
| Family history                         |             |               |             |               |             |               |
| Family history of alcohol use          | 301         | 0.63 (1.23)   | 210         | 0.65 (1.24)   | 89          | 0.61 (1.21)   |
| Family history of substance use        | 300         | 0.35 (0.97)   | 210         | 0.39 (1.02)   | 89          | 0.27 (0.85)   |
| Family history of internalizing problems| 290         | 2.18 (2.63)** | 206         | 2.50 (2.77)   | 82          | 1.44 (2.07)   |
| Individual transmissible risk          |             |               |             |               |             |               |
| TLI                                    | 302         | 0.06 (0.83)   | 211         | 0.11 (0.84)   | 89          | –0.07 (0.78)  |
| Alcohol involvement                    |             |               |             |               |             |               |
| Alcohol initiation (lifetime; yes [1] versus no [0]) | 300         | 189 (48%)     | 210         | 138 (66%)     | 88          | 50 (57%)      |
| Age first used alcohol                 | 186         | 16.42 (2.06)  | 136         | 16.47 (2.10)  | 50          | 16.30 (1.95)  |
| Frequency of alcohol use in past 3mo   | 186         | 2.54 (1.35)   | 137         | 2.46 (1.31)   | 49          | 2.76 (1.44)   |
| Alcohol use problems (log$_{10}$[x+1] transformed) | 168         | 0.39 (0.39)** | 123         | 0.33 (0.37)   | 45          | 0.53 (0.38)   |

*Indicates significant sex difference at $P < .05$. **indicates significant sex difference at $P < .01$. 

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use were assessed using one item, respectively. Nevertheless, our finding that FH-IP is the most robust indicator of risk is supported by previous work highlighting the transmissibility of AUDs and internalizing problems as well as the influence that each has on the subsequent development of the other.\textsuperscript{11} Specifically, having a FH of anxiety and depression has been shown to be associated with an increased risk of presenting with an AUD and vice-versa.\textsuperscript{10,11} Research has also suggested that elevation in anxiety-sensitivity (ie, fear of arousal-related sensations) is a risk factor for presenting with alcohol-related disorders,\textsuperscript{28} particularly as a negatively reinforced coping mechanism (ie, tension reduction) among college students.\textsuperscript{29} Furthermore, a FH-IP may increase an individual's sensitivity to peer influences, particularly in relation to alcohol consumption\textsuperscript{7} suggesting that a genetic liability for internalizing problems may interact with environmental influences to increase the risk for developing AUP. Additionally, there is substantial evidence to suggest that there is a shared genetic liability between internalizing problems and alcohol use. Several genome-wide association studies have found a genetic correlation between alcohol use scores and major depressive disorder using validated symptom criteria,\textsuperscript{30-32} including finding significant gene associations between co-occurring alcohol dependence and major depression.\textsuperscript{33}

Though tentative and in need of replication, TLI's meditational properties were observed through path analyses. This suggests that the TLI reflects familial liability for alcohol involvement irrespective of the individual's current pattern of use. Further, the TLI shows potential value as a possible proxy for measuring the effects of FH on subsequent alcohol use in a sample of college students. This is consistent with contemporary literature which has shown the TLI to be an effective predictor of risk for developing a substance use disorder,\textsuperscript{18,34,35} as well as being a proxy for FH effects of substance use\textsuperscript{18} and FH of externalizing problems.\textsuperscript{14}

This study should be interpreted in light of several considerations. First, we employed version of the TLI that was based on a subset of questions from the more expansive measure that has been previously used in the literature.\textsuperscript{36} Nevertheless, the present data are largely consistent with prior studies that have examined the effect of TLI in youth and young adults. Second, this study analyzed a subset of DSM-5 problems assessed by the ASSIST. Consequently, the lack of replication of family history of alcohol and illicit substance use on AUP may be partly due to the fact that the ASSIST provides an incomplete view of symptom severity; care should be taken when attempting to generalize these findings to future studies that might include the full complement of symptoms. Third, the observed effects of perceived family history are limited to our assessment of internalizing and drug use behaviors that are a focus of the Family History Screen. Additional research is needed to confirm whether the observed trends generalize to other externalizing behavior pathways that are associated with adolescent

| FAMILY HISTORY VARIABLE | ANY RELATIVE | SPECIFIC RELATIVE |
|-------------------------|-------------|-------------------|
| Family history of alcohol use | 66 (21.4) | 36 (12.3) |
| Family history of substance use | 38 (12.3) | 118 (38.3%) |
| Family history of internalizing problems | 169 (54.5) | 118 (38.3%) |
| Relative with a breakdown, n = 298 | 116 (39.2%) | 116 (39.2%) |
| Relative with depression, n = 299 | 108 (35.1%) | 108 (35.1%) |
| Relative with excessive sleep, n = 302 | 117 (38.9%) | 117 (38.9%) |
| Relative with suicidality, n = 300 | 29 (9.4%) | 29 (9.4%) |
| Relative with excessive Worry, n = 301 | 57 (18.5%) | 57 (18.5%) |

Respondents could endorse more than one relative.
Table 4. Multiple regression results (β [95% CI]) for alcohol initiation, age of first use, and past 90 day use and problems.

| PREDICTOR                              | INITIATION   | AGE OF FIRST USE | FREQUENCY OF USE | PROBLEMS   |
|----------------------------------------|--------------|------------------|------------------|------------|
| TLI                                    | 0.23 [0.08, 0.37]** | −0.21 [−0.37, −0.06]** | −0.03 [−0.19, 0.13] | 0.13 [−0.03, 0.29] |
| Family history of alcohol use          | −0.06 [−0.21, 0.10] | 0.06 [−0.10, 0.23] | 0.03 [−0.14, 0.20] | 0.07 [−0.10, 0.24] |
| Family history of substance use        | 0.14 [−0.05, 0.32] | −0.20 [−0.37, −0.04]* | 0.08 [−0.09, 0.26] | 0.02 [−0.15, 0.19] |
| Family history of internalizing problems | 0.07 [−0.09, 0.24] | 0.05 [−0.12, 0.21] | 0.06 [−0.11, 0.23] | 0.19 [0.02, 0.35]* |
| Age                                    | 0.03 [−0.10, 0.16] | −0.05 [−0.19, 0.10] | 0.05 [−0.09, 0.20] | 0.02 [−0.12, 0.17] |
| Sex                                    | −0.06 [−0.19, 0.07] | −0.07 [−0.22, 0.08] | 0.13 [−0.01, 0.28] | 0.28 [0.14, 0.42]* |
| Week of study completion               | 0.15 [0.01, 0.28]* | −0.03 [−0.17, 0.11] | 0.12 [−0.03, 0.26] | 0.04 [−0.10, 0.19] |
| Campus                                 | 0.07 [−0.06, 0.21] | −0.08 [−0.22, 0.08] | −0.02 [−0.16, 0.13] | 0.04 [−0.11, 0.18] |
| R-square (SE)                          | 0.13 (0.05)* | 0.09 (0.04)* | 0.05 (0.033) | 0.14 (0.05)** |

Abbreviations: TLI, Transmissible liability index. Notations used to indicate statistically significant regression estimate effects at *P < .05. **P < .01. ***P < .001.

Figure 1. Path model of family history and TLI effects on age of initiation of drinking and past-90 day frequency of alcohol use (ie, past 90-day alcohol use). Path analysis showing direct and indirect effects on past 90 day frequency of alcohol use. Darker lines indicate significant standardized path loadings along with their respective 95% confidence intervals; gray lines indicate paths that were non-significant.

Figure 2. Path model of family history and TLI effects on age of initiation of drinking and number of past-90 day alcohol problems. Path analysis showing direct and indirect effects on past 90 day frequency of alcohol problems. Darker lines indicate significant standardized path loadings along with their respective 95% confidence intervals; gray lines indicate paths that were non-significant.
drinking and problems.37 Fourth, while the present study provides novel insight into alcohol behavior in the summer months preceding college, it is unclear whether the observed effects will persist throughout college.38 There are several aspects of interpersonal development (ie, identity exploration, group affiliation) that occur during college that could contribute to an increased likelihood of individuals engaging in risky drinking behaviors within the context of peer influences or as an attempt at stress reduction.4 Given that young adults often attribute the initiation of their drinking behaviors to social motives and peer influences,39 the observed increase in alcohol consumption during the transition to college represents an important, albeit understudied, time period to better examine the initiation of these approaches.

Model comparisons are made in relation to the fit of the full model for alcohol use ($\chi^2 = 4.24, df = 4, P = .374, \text{RMSEA} = 0.015, \text{TLI} = 0.997, \text{CFI} = 0.984$) and problems ($\chi^2 = 4.24, df = 4, P = .374, \text{RMSEA} = 0.015, \text{TLI} = 0.997, \text{CFI} = 0.983$).

### Table 5. Model fitting results for alcohol use and problems.

| MODEL | FIT COMPARISON RELATIVE TO BASELINE | $\Delta \chi^2$ | $\Delta DF$ | $P$ |
|-------|-------------------------------------|----------------|------------|-----|
| Alcohol use | Submodel I | 73.59 | 3 | <.001 |
| | Submodel II | 14.42 | 4 | .01 |
| | Submodel III | 87.99 | 3 | <.001 |
| | Submodel IV | 5.72 | 3 | .13 |
| | Submodel V | 2.12 | 3 | .55 |
| | Submodel VI | 1.61 | 1 | .21 |
| | Submodel VII | 8.47 | 7 | .29 |
| Alcohol problems | Submodel I | 73.59 | 3 | <.001 |
| | Submodel II | 14.42 | 4 | .01 |
| | Submodel III | 88.01 | 3 | <.001 |
| | Submodel IV | 5.72 | 3 | .13 |
| | Submodel V | 7.59 | 3 | .06 |
| | Submodel VI | 1.59 | 1 | .21 |
| | Submodel VII | 19.96 | 7 | .01 |

Model comparisons are made in relation to the fit of the full model for alcohol use and problems. The findings from this study have potential implications for preventative care. Someone with a family history of internalizing problems may benefit from assessment and reduction of modifiable risk factors, in particular females who may be more sensitive to the perception of internalizing problems.40 On college campuses, fraternities and sororities have higher rates of substance use, including binge drinking, and suffer greater substance-related negative consequences when compared to non-members.41-44 Avoidance of high-risk situations and minimization of negative peer influences can help to promote positive changes that decrease the likelihood of substance use progression. Students also often overestimate the degree of substance use in their peers,45,46 which can lead to a more normative view of peer substance use and a greater likelihood of personal alcohol use.47 Increased knowledge about accurate drinking behaviors can help correct misconceptions and possible justification of one’s own excessive use.

The current results also suggest that regular substance use screening before and during college might serve as a valuable opportunity for early intervention and education. Our observed associations between familial, temperamental, and behavioral measures with alcohol consumption in the months leading up to college support the inclusion of antecedents known to be associated with drug use in college screeners. Having familial and behavioral information about a student prior to the start of college provides insight into first-year drinking patterns.15,48 Unfortunately, the use of individual-level screening instruments that assess family history does not appear to be widespread outside of the clinical setting.49 Still, a number of available programs assist college campuses in mitigating pre-existing risk factors for substance use in young adults that include screening scales. Notably, CollegeAim, a program developed by the National Institute on Alcohol Abuse and Alcoholism, helps schools identify effective alcohol intervention strategies that focus on the individual and the environment.50 Individual-centered strategies work to reduce drinking behaviors by changing a student’s level of knowledge and attitudes around drinking. In doing so, these strategies reduce TLI behaviors that are positively associated with drinking (eg, risk taking). The Brief Alcohol Screening and Intervention for College Students (BASICS) program integrates motivational interviewing and cognitive behavioral therapy skills to reduce alcohol consumption among college students who are at risk for alcohol-related problems and has been implemented by schools.51 The College Drinker’s Check-up (CDCU), a computer-based brief intervention, has demonstrated effectiveness in reducing heavy alcohol use in college students.52 In addition to brief interventions, referral to treatment should be offered to anyone with active substance use problems or high-risk substance use behaviors. Further data is necessary to understand whether or not the incorporation of TLI and/or perceived or actual assessments of FH may improve the effectiveness of these approaches.

In conclusion, the current study contributes to growing evidence that FH of alcohol and illicit substance problems and mood are important tools for clinicians, researchers, and higher education officials. As shown, family history measures contribute additional information that is likely to prove useful in designing
investigations based on a youth’s liability for alcohol use problems, for developing individualized treatment needs, or to identify cohorts of youth who might benefit from a much broader preventative measures targeted at behavioral and temperamental characteristics that drive SUDs. Yoon et al. pointed out that family history, and therefore to an extent the broad indices of vulnerability to addiction (TLI), may not be able to distinguish between youth at high and moderate risk for alcohol use problems. While results need to be replicated, the current study suggests that combining these pieces of information will help to identify young adults at-risk so they may receive targeted interventions, such as empowering them with that information that might help to motivate meaningful changes in their behavior.

**Data Availability**
The data that support the findings of this study are available on request from the corresponding author, RHP. The data are not publicly available due to privacy restrictions and a use agreement.

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**Author Contributions**
AB and RE designed the study under the direction of RHP. AB prepared and analyzed the data under the supervision of RHC. AB and RE co-wrote the first draft of the manuscript that was subsequently reviewed and edited by RHP, CEB, and JWW. All authors have read and approved the final manuscript.

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**REFERENCES**
1. Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. 2010 national and state costs of excessive alcohol consumption. *Am J Prev Med.* 2015;49:e73-e79.
2. Arria AM, Caldeira KM, Allen HK, Vincent KB, Bugbee BA, O’Grady KE. Drinking like an adult? Trajectories of alcohol use patterns before and after college graduation. *Alcohol Clin Exp Res.* 2016;40:583-590.
3. Shults WS. Alcohol use disorders among US college students and their non-college-attending peers. *Arch Gen Psychol.* 2005;62:321-327.
4. Merrill JE, Carey KB. Drinking over the lifespan: focus on college ages. *Alcohol Res.* 2016;38:103-114.
5. Camatta CD, Nagoshi CT. Stress, depression, irrational beliefs, and alcohol use and problems in a college student sample. *Alcohol Clin Exp Res.* 1995;19:142-146.
6. Bewick BM, Mulhern B, Barkham M, Trusler K, Hill AJ, Stiles WB. Changes in undergraduate student alcohol consumption as they progress through university. *BMC Public Health.* 2008;8:163.
7. Kendall KS, Edwards A, Myers J, Cho SB, Adkins A, Dick D. The predictive power of family history measures of alcohol and drug problems and internalizing disorders in a college population. *Am J Med Genet B Neuropsychiatr Genet.* 2015;168B:337-346.
8. Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. *Am J Psychiatry.* 2000;157:1552-1562.
9. Manassis K, Hood J. Individual and familial predictors of impairment in childhood anxiety disorders. *J Acad Child Adolesc Psychiatry.* 1998;37:428-434.
10. Milne BJ, Caspi A, Harrington HL, Poulton R, Rutter M, Moffitt TE. Predictive value of family history on severity of illness: the case for depression, anxiety, alcohol dependence, and drug disorder. *Arch Gen Psychiatry.* 2009;66:738-747.
11. Moreau ME, Corbin WR, Sinha R, O’Malley SS. Parental history of anxiety and alcohol-use disorders and alcohol expectancies as predictors of alcohol-related problems. *J Stud Alcohol Drugs.* 2009;70:227-236.
12. Leyton M, Stewart S. Substance Abuse in Canada: Childhood and Adolescent Pathways to Substance Use Disorders. Canadian Centre on Substance Abuse; 2014.
13. Vanyukov MM, Kirisci L, Tarter RE, et al. Liability to substance use disorders: 2. A measurement approach. *Neurosci Biobehav Rev.* 2003;27:517-526.
14. Kirisci L, Tarter R, Ridener T, Reynolds M, Horner M, Vanyukov M. Externalizing behavior and emotion dysregulation are indicators of transmissible risk for substance use disorder. *Addict Behav.* 2015;42:57-62.
15. Arras AM, Vincent KB, Caldeira KM. Measuring liability for substance use disorder among college students: implications for screening and early intervention. *Am J Drug Alcohol Abuse.* 2009;35:233-241.
16. Cornelius JR, Kirisci L, Reynolds M, Vanyukov M, Tarter R. Does the transmissible liability index (TLI) assessed in late childhood predict suicidal symptoms among young adulthood? *Am J Drug Alcohol Abuse.* 2015;41:264-268.
17. Milne BJ, Caspi A, Crump R, et al. The validity of the family history screen for assessing family history of mental disorders. *Am J Med Genet B Neuropsychiatr Genet.* 2009;150B:41-49.
18. Ridener TA, Kirisci L, Tarter RE, Vanyukov MM. Could a continuous measure of individual transmissible risk be useful in clinical assessment of substance use disorders? Findings from the national epidemiological survey on alcohol and related conditions. *Drug Alcohol Depend.* 2011;119:10-47.
19. Humenik R, Ali R, Babor TF, et al. Validation of the alcohol, smoking and substance involvement screening test (ASSIST). *Addiction.* 2008;103:1039-1047.
20. SPSS. IBM SPSS Statistics for Windows, Version 25.0. IBM Corp.; 2017.
21. Muthen LK, Muthen BO. *Mplus User’s Guide: Statistical Analysis with Latent Variables.* 7th ed. Muthen & Muthen; 1998-2012.
22. Vanyukov M, Kim K, Irons D, et al. Genetic relationship between the addiction diagnosis in adults and their childhood measure of addiction liability. *Behav Genet.* 2015;45:1-11.
23. Hicks BM, Schaler BD, Malone SM, Iacono WG, McGue M. Psychometric and genetic architecture of substance use disorder and behavioral disinhibition measures for gene association studies. *Behav Genet.* 2011;41:459-475.
24. MacCallum RC, Browne MW, Sugawara HM. Power analysis and determination of sample size for covariance structure modeling. *Psychol Methods.* 1996;1:30-149.
25. Merikangas KR, Dierker L, Fenton B. Familial factors and substance abuse: implications for prevention. *NIDA Res Monogr.* 1998;177:12-41.
26. Elliott JC, Carey KB, Bonafide KE. Does family history of alcohol problems influence college and university drinking or drinking use? A meta-analytical review. *Addiction.* 2012;107:774-785.
27. Hicks BM, Iacono WG, McGue M. Index of the transmissible common liability to addiction: heritability and prospective associations with substance abuse and related outcomes. *Drug Alcohol Depend.* 2012;123:S18-S23.
28. Schmidt NB, Buckner JD, Keough ME. Anxiety use as a prospective predictor of alcohol use disorders. *Behav MODIF.* 2007;31:262-269.
29. Lawyer SR, Karg RS, Murphy JG, Dudley-McGlynn FD. Heavy drinking among college students is influenced by anxiety sensitivity, gender, and contexts for alcohol use. *J Anxiety Disord.* 2002;16:165-173.
30. Kranzler HR, Zhou H, Kember RL, et al. Genome-wide association study of alcohol consumption and use disorder in 274,424 individuals from multiple populations. *Nat Commun.* 2019;10:1499.
31. Edwards AC, Aliev F, Bierut LJ, et al. Polygenic scores for major depression: 2. A measurement approach. *JAMA Psychiatry.* 2014;71:1153-1160.
32. Zhou H, Polimanti R, Yang BZ, et al. Genetic risk variants associated with comorbid alcohol dependence and major depression. *JAMA Psychiatry.* 2017;74:1234-1241.
35. Kirisci L, Tarter R, Mezzich A, Ridenour T, Reynolds M, Vanyukov M. Prediction of cannabis use disorder between boyhood and young adulthood: clarifying the phenotype and environment. *Am J Addict*. 2009;18:36-47.

36. Vanyukov MM, Kirisci L, Moss L, et al. Measurement of the risk for substance use disorders: phenotypic and genetic analysis of an index of common liability. *Behav Genet*. 2009;39:233-244.

37. Abu-Shakra M, Cox S. The externalizing developmental pathway to substance use disorders. In: Leyton M, Stewart S, eds. *Substance Abuse in Canada: Childhood and Adolescent Pathways to Substance Use Disorders*. Canadian Centre on Substance Abuse; 2014: 24.

38. Fromme K, Corbin WR, Kruse MI. Behavioral risks during the transition from high school to college. *Dev Psychol*. 2008;44:1497-1504.

39. Kuntsche E, Knibbe R, Gmel G, Engels R. Why do young people drink? A review of drinking motives. *Clin Psychol Rev*. 2005;25:841-861.

40. Fischer AH, Kret ME, Broekens J. Gender differences in emotion perception and self-reported emotional intelligence: a test of the emotion sensitivity hypothesis. *PLoS One*. 2018;13:e0190712.

41. Cheney MK, Harris LW, Gowin MJ, Huber J. Smoking and membership in a fraternity or sorority: a systematic review of the literature. *J Am Coll Health*. 2014;62:264-276.

42. LaBrie JW, Kenney SR, Mirza T, Lac A. Identifying factors that increase the likelihood of driving after drinking among college students. *Accid Anal Prev*. 2011;43:1371-1377.

43. Scott-Shepherd LA, Carey KB, Carey MP. Health behavior and college students: does Greek affiliation matter? *J Behav Med*. 2008;31:61-70.

44. Soule EK, Barnett TE, Moorhouse MD. Protective behavioral strategies and negative alcohol-related consequences among US college fraternity and sorority members. *J Subst Use*. 2015;20:16-21.

45. ACHA. *National College Health Assessment II: Reference Group Undergraduate Student Reference Group Executive Summary Fall 2017*. American College Health Association; 2018.

46. Sanders A, Stogner JM, Miller BL. Perception vs. reality: an investigation of the misperceptions concerning the extent of peer novel drug use. *J Drug Educ*. 2013;43:97-120.

47. Borsari B, Carey KB. Peer influences on college drinking: a review of the research. *J Subst Abuse*. 2001;13:391-424.

48. Hoepner BB, Barnett NP, Jackson KM, et al. Daily college student drinking patterns across the first year of college. *J Stud Alcohol Drugs*. 2012;73:613-624.

49. USDaHs. *Facing Addiction in America: The Surgeon General’s Report on Alcohol, Drugs, and Health*. U.S. Department of Health and Human Services (HHS), Office of the Surgeon General; November 2016.

50. Cronce JM, Toomey TL, Lenk K, Nelson TF, Kilmer JR, Larimer ME. NIAAA’s College alcohol intervention matrix. *Alcohol Res*. 2018;39:43-47.

51. Dimoff LA, Baer JS, Kivlahan DR, Marlatt GA. *Brief Alcohol Screening and Intervention for College Students (BASICS): A Harm Reduction Approach*. Guilford Press; 1999.

52. Hester RK, Delaney HD, Campbell W. The college drinker’s check-up: outcomes of two randomized clinical trials of a computer-delivered intervention. *Psychol Addict Behav*. 2012;26:1-12.

53. Yoon PW, Scheiner MT, Peterson-Oehlke KL, Gwinn M, Faucett A, Khoury MJ. Can family history be used as a tool for public health and preventive medicine? *Genet Med*. 2002;4:304-310.

54. Marteau TM, Lerman C. Knowledge of genetic risk may not change behaviour. *BMJ*. 2001;322.