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Characterizing the co-occurrence of alcohol experimentation and suicidal thoughts and behaviors in early adolescence

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Abstract

This study aims to investigate the roles of decision-making processes and genetics in the co-occurrence of alcohol use and suicidal thoughts/behaviors (STB) in adolescence. We used data from the ABCD® study (abcdstudy.org) and included behavioral (computerized tasks, self-report questionnaires) and genetic (polygenic scores [PGS]) measures related to cognitive (executive functions) and affective (delay-discounting, risk-taking, impulsivity) processes involved in decision-making. First, we evaluated the latent structure of decision-making in the full sample (N=11,868) using a split-half exploratory and confirmatory factor analysis. Second, we evaluated the association between alcohol experimentation (>1 sip) and STB in three genetically-defined ancestry groups: European (EUR, N=6,080), African (AFR, N=2,085), and the Americas (AMR, N=2,712). We used logistic regressions to examine which PGS and behavioral factors were related to STB and tested the mediational effect of behavioral processes. STB prevalence was between 0.85-4.17%. Decision-making was best represented by three latent factors: cognitive, emotional-impulsivity, and premeditation-perseverance. Regression analyses showed that alcohol experimentation was related to STB in EUR only (OR=1.44, 95%CI=1.10;1.89). Lower tendencies on the emotional-impulsivity factor were related to lower STB in all groups (ORs 0.69-0.77), and better premeditation-perseverance were associated with lower STB in EUR (OR=0.57) and AFR (OR=0.72). In EUR, the association between alcohol experimentation and STB was mediated by the emotional-impulsivity (15.33%) and premeditation-perseverance (22.60%) latent factors. The associations between PGS for externalizing behaviors and STB also acted through the emotional impulsivity and perseverance-premeditation factors (mediations 6.98-10.30%). These findings suggest that decision-making-related processes may contribute to the alcohol use-STB co-occurrence.

Keywords: adolescence, alcohol, suicidal thoughts and behaviors, polygenic score, neurocognition.

Introduction

Suicidal thoughts and behaviors (STB) are public health concerns of extreme importance. STB often co-occur with substance use disorders(1, 2), with a growing number of studies showing associations between alcohol use/problems and STB(3-7). Prior findings also indicate an association between low levels of alcohol use and STB in adolescents as young as nine years old(8), suggesting a shared liability between these phenotypes. Studies conducted in adults support both a causal association between alcohol use disorder and STB (5, 6) and a shared genetic liability(9, 10). Genetic studies have also revealed genetic correlations between alcohol problems, STB, and potentially shared endophenotypes such as risk-taking, impulsivity, behavioral disinhibition, and cognitive performance(11-13). Those processes relate to cognitive and affective mechanisms broadly involved in decision-making and could contribute to the co-occurrence between alcohol use/problems and STB. However, few if any studies have explored the roles of these mechanisms using well-validated behavioral tasks.

Whether stemming from a shared genetic vulnerability (9) or due to neurotoxic effects of chronic alcohol use on the brain(14), alcohol use may promote STB by way of altered decision-making propensities. Decision-making is a complex process in which individuals weigh the costs and benefits of alternative decisions according to the subjective value of their related consequences. Research asserts that decision-making cannot be defined as a unitary concept but rather results from the interaction between different brain systems involved in rule-based (executive functions) and affective-based (reward processing, delay discounting) processes(15-17). Both alcohol use disorder and heavy drinking are characterized by disadvantageous decision-making, impaired executive performance, and risk-taking(18-23).

Literature on STB mostly consider unitary measures of decision-making rather than a combination of cognitive and affective behavioral mechanisms. Findings show that, compared to controls, individuals with STB exhibited poor decision-making skills(24, 25). Research also demonstrates altered brain activity during decision-making processes in individuals with a history of STB(26, 27). With regards to specific processes, evidence indicates that individuals with STB exhibit high levels of risk-taking(28, 29), elevated sensation seeking(30), disinhibition(31-33), aversion to expending cognitive effort(34), and poor flexibility(35).

Although STB often emerges in adolescence(36, 37), most previous work focused on adult populations. Investigating the mechanisms explaining the co-occurrence of alcohol use and STB in young adolescents who have limited exposure to alcohol offers a unique opportunity to detect the role of neurodevelopmentally-governed decision-making in STB, while limiting the confound of alcohol toxic effects(38), therefore allowing the exploration of their shared liability. This exploration in early adolescence is facilitated by findings showing that early alcohol sipping may serve as a reasonable proxy for propensity to subsequent regular/excessive alcohol use(39-41).

To improve our understanding of the co-occurrence between alcohol use and STB during adolescence, we designed two conceptual models (Figure 1). Models evaluate the roles of neurocognitive measures related to decision-making and the influence of neurocognitive function alongside genetic influences. In line with prior studies(42, 43), all models test a mediational process via decision-making related mechanisms. In particular, we aimed to study (i) the specific pathway by which those mechanisms are involved in alcohol use-STB co-occurrence (Figure 1.A), and (ii) how much of the genetic liability to STB operates through behavioral predictors (Figure 1.B)(13, 44). We used longitudinal data from the Adolescent Brain Cognitive Development (ABCD ®; abcdstudy.org) study to test these models. First, we selected specific cognitive and

affective behavioral mechanisms related to decision-making (16) and conducted a factor analysis to evaluate the latent structure of these mechanisms in young adolescents. Previous studies using ABCD assessed the structure of cognitive tasks related to general abilities, learning, and memory(45, 46), but, to our knowledge, none have included neurocognitive measures related to decision-making. To consider the influence of genetic liability, we computed measures of aggregate genetic liability (polygenic scores, PGS) for suicidal behavior, alcohol use/problems, and decision-making-related processes based on available genome-wide association studies (GWAS). Second, we evaluated the association between alcohol experimentation (> 1 sip) and STB in adolescents in three genetically-defined ancestry groups (i.e., European, African, and the Americas). Third, we combined logistic regression and structural equation modeling to investigate the mechanisms underlying the co-occurrence of alcohol use and STB. To leverage the longitudinal nature of the data, alcohol experimentation was selected from the baseline assessment and STB from the follow-up 2 assessment. All neurocognitive measures were assessed from baseline to follow-up 2.

Methods

Study Cohort

Data were from the ABCD Study, a longitudinal multisite study of 11,868 adolescents in the United States (US). At baseline, participants were between ages 9-10 and they were assessed annually on a variety of social, emotional, cognitive, behavioral, and psychopathological outcomes(47, 48). In addition, ABCD participants provided a DNA sample(for more details, see 49, 50). After quality control, genotyped data were available for 11,666 individuals at ~500,000 variants. We used ABCD Release 5.0 (https://nda.nih.gov/study.html?id=2147), which includes

data through the 3-year follow-up visit. The present analyses included two databases: (1) the full ABCD sample, which we utilized to perform a factor analysis using decision-making-related mechanisms; and (2) subgroups of individuals from European (EUR, N=6,080), African (AFR, N=2,085), and American (AMR, N=2,712) genetically-defined ancestries (see Supplement). The term American here was used to be consistent with the Genome Aggregation Database (51) and encompasses participants of admixed American ancestry. We followed current recommendations and conducted ancestry-specific analyses to evaluate the association between alcohol experimentation and STB and its possible explanatory mechanisms, as (i) a single analysis including all groups will likely be influenced by the majority group, and (ii) population-specific results of understudied groups might provide more actionable findings(52, 53). ABCD includes 21 data collection sites across the US, relying on a central Institutional Review Board at the University of California San Diego with additional local IRB approvals obtained at each participating site. Parents or guardians provided written informed consent, and adolescents assented before participation in the study.

Measures

Neurocognitive assessments

For all the tasks/questionnaires, the section below provides a brief description of the mechanism evaluated by each task and the dependent variables. More details are available in the Supplement.

Emotional face Stroop task (follow-up 1 assessment)**.** This task measures executive control in the context of processing the semantic meaning of an emotional word, while simultaneously being presented with potentially distracting emotional information via facial

expressions(54). Two scores represented executive control abilities: the accuracy score (percentage of correct responses) and reaction time (RT) based on interference score (incongruent trials – congruent trials). For the factor analysis, the two scores were standardized, and the reaction time score was reversed such that, for both variables, higher scores represent better performance.

Flanker task (follow-up 2 assessment). This task assesses the ability to control interference coming from surrounding visual stimuli(54, 55). As with the Stroop task, we used both the accuracy and RT based on interference score (incongruent - congruent). For the factor analysis, the two scores were standardized, and the reaction time score was reversed such as higher scores represent better performance.

Dimensional Change Card Sorting task (baseline assessment)**.** This task measures cognitive flexibility and evaluates the ability to switch between two rule sets for correct responses(54, 56). The total flexibility score was based on both accuracy and RT. The RT score was rescaled before being added to the accuracy score, so that for the total flexibility score, higher values represent better flexibility.

Game of dice task (follow-up 2 assessment)**.** This task evaluates the propensity to take risks while betting on the outcome of a rolled die(57). Risk taking is evaluated by a net score reflecting the proportion between safe and risky bets, with larger scores reflecting more risk-aversion (i.e., a larger tendency to avoid risks). A standardized score was used for the factor analysis.

Delay discounting task (follow-up 1 assessment)**.** The adjusting delay discounting task evaluates the severity with which the respondent devalues a hypothetical monetary reward the longer they would have to wait to receive it. We calculated the area under the empirical discounting function, which ranges from 0 (steepest possible discounting) to 1 (less/no delay discounting)

(Myerson et al., 2001). For the factor analysis, we converted this score to a standardized score so that higher scores reflect more self-disciplined choice behavior (i.e., minimal discounting of delayed rewards).

Impulsive personality traits (baseline assessment)**.** Impulsivity was assessed by the youth version of the UPPS-P Impulsive Behavior Scale(58), which evaluates five dimensions of impulsivity: negative urgency (the tendency to act rashly in negative emotional contexts), positive urgency (the tendency to act rashly in positive emotional contexts), lack of premeditation (the tendency to act without taking into account the consequences of an action), lack of perseverance (the tendency to give up in complex tasks), and sensation seeking (the tendency to seek out excitement). Prior studies using ABCD data confirmed the factor structure, reliability, and validity of the UPPS-P in this sample(59). In the full ABCD sample (used for the factor analysis), the internal consistency was $\alpha = 0.49$ for sensation seeking, $\alpha = 0.63$ for negative urgency, $\alpha = 0.70$ for lack of perseverance, $\alpha = 0.73$ for lack of premeditation, and $\alpha = 0.77$ for positive urgency. Each dimension score was standardized and reversed so that a higher score reflects better performance (i.e., lower impulsivity).

Genetic liability

To evaluate aggregate genetic liability, we computed PGS for alcohol outcomes(60), suicidal behavior(12), and decision-making-related constructs according to available GWAS: educational attainment(61), executive functions(62), externalizing behaviors(63), delay discounting(64), and UPPS-P impulsivity traits(65).

We used PRS-CS (66) and PLINK 2.0 (67) to compute PGS in the EUR, AFR, and AMR groups. All GWAS summary statistics were from participants of European ancestry. We utilized PRS-CS to apply a continuous shrinkage prior to the effect sizes of SNPs using the appropriate

linkage disequilibrium reference panel, and PLINK 2.0 to derive a PGS for each individual in the ABCD sample. Within each ancestral group, we regressed the PGS on the first 10 ancestral principal components to correct for population stratification and used the standardized residuals for subsequent analyses.

Covariates

Sex and parental education (as a proxy for socioeconomic status) were included as covariates. Sex was coded as 1 for females and 0 for males. Parents' highest level of education was coded from 1 to 4, with 1 representing 11th grade or less and 4 a college degree(68).

Alcohol experimentation

Alcohol use was evaluated at baseline by the Timeline Follow Back Interview (69) using the following item "Have you ever tried a sip of alcohol such as beer, wine or liquor (rum, vodka, gin, whiskey) at any time in your life?" Alcohol sipping at early age was used as a proxy for later alcohol use: Prior studies show that early drinking onset is related to higher alcohol consumption in adolescence (39) and higher risk of later alcohol use disorder(70-72). In the ABCD cohort, early sipping was related to higher positive alcohol expectancies, greater impulsivity, mood disorders, and externalizing behaviors(40).

Suicidal thoughts and behaviors

STB were evaluated using the Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime Version based on DSM-5 criteria(73). For suicide ideation, participants were asked "Was there ever a time in the past when you often wished you were dead or thought you would be better off dead?" For suicide attempt, they were asked "Was there ever a time when you did something to try to kill yourself and actually made a suicide attempt?" To increase statistical power in our analyses, we combined those data into an ordinal outcome ranging from 0

to 2, where 0 indicates no suicide ideation/attempt, 1 indicates suicide ideation, and 2 indicates suicide attempt. This approach is consistent with studies showing that the severity of ideation/attempt best predicted subsequent suicide attempt(74, 75). However, suicide attempt was not conditioned on ideation, i.e., some participants reported suicide attempt with no suicide ideation[1].

Statistical Analysis

To explore the latent structure of cognitive and affective mechanisms related to decision-making in adolescence, we first conducted a random split-half exploratory and confirmatory factor analysis (EFA and CFA). In the first split-half of the sample, we performed an EFA with maximum likelihood as the estimator and an oblique rotation to allow for correlations between factors (promax) using the psych R package. Missing data were imputed using pairwise associations. In the EFA, we aimed to select latent factors including at least 3 manifest variables and retained variables that had a factor loading greater or equal to 0.20. This cutoff is consistent with previous studies using neurocognitive tasks(45, 46). Variables with factor loadings below 0.2 were dropped from the analyses due to weak associations with the latent processes of decision-making. If one of the latent factors was best represented by only 2 manifest variables, the parameter estimates were fixed to be equal and correlations between latent factors were allowed(76). The Tucker-Lewis Index (TLI), Comparative Fit Index (CFI), and Root Mean Square Error of Approximation (RMSEA) were used to assess model fit (CFI should be > 0.90, TLI > 0.90, RMSEA < 0.08). Eigenvalues were also used to measure the amount of variance in latent factors (eigenvalues should be >1). In the second split-half of the sample, we performed a CFA using the best-fitting model

[1] N = 8, 3, and 7 in EUR, AFR, and AMR, respectively.

identified by the EFA. As the ABCD sample included participants from the same family, we accounted for family relatedness using the cluster function in lavaan. Assuming a good fit, we computed a final CFA model in the full ABCD sample to extract factor scores using the lavPredict function.

Second, we evaluated the roles of decision-making latent factors and genetic liability in the co-occurrence of alcohol experimentation and STB during adolescence. Analyses were stratified by ancestry group (EUR, AFR, AMR) and controlled for sex and parental education. In a preliminary step, we used univariate logistic regressions to observe the association between alcohol experimentation and STB in each ancestry group. We also evaluated the univariate association between decision-making latent factors, PGS, and STB to design mediation models using specific behavioral and genetic predictors (i.e., those significantly related to STB according to 95% Confidence Intervals [CI]). We conducted a sensitivity analysis using the lmtest package to adjust the regression results for familial clustering (Supplement). This package allows the calculation of robust standard errors that account for the non-independence within clusters.

Once we replicated a relationship between alcohol experimentation and STB and the roles of genetic and neurocognitive factors, we pursued mediation analyses to further clarify the relationship. Importantly, the mediation model used in this is not a causal inference method and does not assume causal associations between variables(77, 78). The first mediation model tested whether the association between alcohol experimentation and STB was mediated by decision-making latent factors (Figure 1.A). The second mediation model examined whether the association between genetic risk and STB acted through decision-making and/or alcohol experimentation (Figure 1.B). Analyses were conducted using the lavaan R package. We used the ordered function to specify the ordinal outcome (STB) and the diagonally weighted least squares (DWLS) estimator.

Missing data were handled with pairwise associations. Results are presented as standardized beta values and significance was set at $p < 0.05$. As lavaan does not directly support random effects or clustering when the outcome is a factor, sensitivity analyses have been conducted on the mediation models by excluding related participants (Supplement).

The analyses reported in this paper have not been pre-registered and should be considered exploratory.

Results

Description of the sample

Table 1 reports descriptive characteristics of the samples. The prevalence of alcohol experimentation was between 12.21-27.89%. The prevalence of suicide ideation was between 3.52-4.17% and suicide attempt between 0.86-1.37%.

Factor structure of neurobehavioral measures

First, we conducted an EFA in the first split-half of the sample (N=5,934). Findings from the EFA suggested a 3-factor solution as the best-fitting model (CFI=0.96, TFI=0.92, RMSEA=0.03). This was confirmed by looking at the eigenvalues for the 3-factor model (Table S2). Though the 4-factor solution also indicated an appropriate fit and an eigenvalue value slightly higher than 1, it did not allow us to select the appropriate number of variables for each factor and, therefore, failed to converge. The 3-factor solution (Table S3) showed that the emotional Stroop accuracy score, the game of dice net score, and the dimensional change card sorting task net score significantly loaded onto one factor (hereafter the "cognitive factor") with no significant cross-loading on other factors. Three subcomponents of impulsivity loaded significantly on the second factor: negative urgency, positive urgency, and sensation seeking (the "emotional impulsivity

factor"). Finally, two subcomponents of impulsivity, lack of premeditation and lack of perseverance, loaded onto the third factor (the "premeditation-perseverance factor"). The other variables (Stroop reaction time, delay discounting, and flanker task scores) were dropped from the analysis due to factor loadings <0.20.

We used the 3-factor solution from the EFA to conduct a CFA in the second split-half of the sample (N=5,934). As one of the latent factors (premeditation-perseverance) only included two items, we fixed the parameter estimates to be the same. Results confirmed an appropriate model fit (CFI=0.96, TFI=0.93, RMSEA=0.04); therefore, a final CFA was fitted in the full sample (Table S4) and factor scores were extracted. Sensitivity analyses confirmed that the 3-factor solution identified in the full sample fit well in the EUR, AFR, and AMR ancestry groups (Supplement).

Association between alcohol use and STB

Results indicated that alcohol experimentation was related to a 44% increase in odds of STB in EUR participants. These associations did not reach statistical significance in the AFR and AMR subgroups (Table 2). Accounting for family relatedness did not change these associations (Table S5).

Model I: mediators of the association between alcohol use and STB

EUR subgroup. Table 2 reports results from the logistic regression and indicates that alcohol experimentation and the emotional impulsivity and premeditation-perseverance latent factors were related to STB in EUR. Mediation models, presented in Figure 2, indicated that the association between alcohol experimentation and STB was partially and independently mediated via both the emotional impulsivity latent factor (proportion mediated 15.33%, p=0.04) and the premeditation-perseverance factor (proportion mediated 22.60%, p=0.03).

Model II: mediators of the association between genetic liability and STB

EUR subgroup. As shown in Table 2, PGS for suicidal behavior, positive urgency, externalizing behaviors, and delay discounting were associated with STB in EUR. Separate mediation models were designed to test the associations between those PGS, decision-making latent factors, alcohol experimentation, and STB (Figure 3).

Mediation via the emotional impulsivity latent factor. The first model included PGS for suicidal behavior, and the second model included PGS for positive urgency. In those models, we did not observe significant mediation via the latent factors nor alcohol use (Figure 3.A).

The third model included PGS for externalizing behaviors and results showed that PGS was related to STB, alcohol use, and the emotional impulsivity latent factor (Figure 3.A). The emotional impulsivity factor partially mediated the association between genetic liability for externalizing disorders and STB (proportion mediated=6.98%, p=0.02), but we found no mediation via alcohol experimentation.

The fourth model included PGS for delay discounting, and results indicated associations between PGS, STB, alcohol experimentation, and the emotional impulsivity latent factor. The emotional impulsivity factor also mediated the association between genetic liability for delay discounting and STB (proportion mediated=10.30%, p=0.05).

Mediation via the premeditation-perseverance latent factor. In the first two models, including PGS for suicidal behavior and PGS for positive urgency, respectively, we did not find evidence of mediation via the latent neurobehavioral factors or alcohol experimentation.

Results from the third model indicated that the PGS for externalizing behaviors was related to STB, alcohol experimentation, and the premeditation-perseverance latent factor (Figure 3.B). The premeditation-perseverance factor mediated the association between genetic liability for

externalizing disorders and STB (proportion mediated=8.41%, p=0.02), but we found no mediation via alcohol experimentation.

Finally, using PGS for delay discounting, results showed that PGS was associated with STB, alcohol experimentation, and the premeditation-perseverance factor. However, the proportion mediated by the premeditation-perseverance factor was not significant (p=0.101).

The results of two additional analyses are presented in the Supplement. In the first, we conducted mediation analyses for AFR and AMR participants. In the second, we conducted mediation analyses within the subsample of unrelated individuals, with no substantial changes observed in terms of direction of effects and significance (Figures S1 and S2).

Discussion

This study investigated the association between alcohol experimentation and STB in adolescence and identified the mechanisms that can contribute to their co-occurrence. We used structural equation modeling to test conceptual models involving genetic and neurocognitive mechanisms. Our models were built upon prior research showing bivariate associations between alcohol experimentation, STB, and cognitive/affective components of decision-making. We integrated these variables into an inclusive model to evaluate their complex relationships. In particular, models were designed to identify the neurobehavioral mediators of (i) the association between alcohol experimentation and STB, and (ii) the association between genetic risk and STB. Analyses were conducted in three empirically-defined ancestry groups but most of the significant results were observed in the EUR subgroup, where statistical power was greatest. Findings suggest that subclinical alcohol use is relevant to understanding STB risk, though behavioral measures play a more important role in this young cohort. Results support the roles of emotional impulsivity

and premeditation-perseverance latent processes, and measures of genetic liability for suicidal behavior, externalizing behaviors, and delay discounting.

The neurocognitive measures included in this study were represented by three latent factors corresponding to cognitive performance (inhibition, flexibility, risk-taking), trait-like emotional action tendencies (positive and negative urgency, sensation seeking), and premeditation-perseverance traits. Findings supported the relevance of the emotional impulsivity and premeditation-perseverance factors in different analyses, but the cognitive latent factor was not related to STB or alcohol use. Given the nature of the ABCD sample, the absence of associations with the cognitive factor is in line with prior observations. Though cognitive difficulties have been associated with alcohol use (38) and STB(35), cognitive functions appear to be preserved in adolescents with low to moderate alcohol use(79-81). In addition, research focusing on STB has mainly included clinical populations with other comorbidities; cognitive difficulties might, therefore, be confounded with a history of psychopathology.

We caution, however, that poor test-retest reliability of neurobehavioral markers constrains its ability to show relationships with other phenotypes. We restricted our analyses to behavioral metrics that centered on decision-making-related processes, which are ostensibly most relevant to suicidal behavior. The lack of associations with neurocognitive tasks may stem from the relatively poor reliability of individual computerized performance tasks (as opposed to multiple-subtask composites such as fluid intelligence(82)). This is confirmed by small but significant differences in brain and cognitive measures across collection sites(83). Conversely, questionnaire metrics of typical daily behavioral propensities (e.g., UPPS-P) tend to be more stable with much higher test-retest reliability, especially for assessments related to self-control(84).

The emotional impulsivity and premeditation-perseverance latent factors isolated herein were derived from trait-like questionnaire assessments of different facets of impulsivity. In line with prior studies, results showed that those traits are associated with both alcohol use (85, 86) and STB(87, 88). The separation of those variables in two latent factors replicate prior studies dividing impulsivity into emotional and cognitive components(87). Our results in EUR added to this literature by underscoring their roles as behavioral mediators: (i) The emotional impulsivity and premeditation-perseverance factors explained part of the association (~15-22%) between alcohol use and STB, suggesting that early alcohol exposure is associated with propensity for emotion-driven impulsive behaviors and with low premeditation and poor perseverance traits, which in turn increase the risk of STB; (ii) In a model controlling for alcohol experimentation, the emotional impulsivity and premeditation-perseverance factors also explained a small part of the association (~7-10%) between genetic risk and STB, suggesting that genetic liability may predispose to impulsive behaviors driven by emotions or may predispose to low premeditation-perseverance abilities, thereby increasing the risk of STB.

Genetic liability was characterized by different measures. In EUR, we found that four PGS were related to STB risk. The most noticeable results were found with PGS for externalizing behaviors and delay discounting, which can be considered as two complementary measures of impulsive decision-making(89). Genetic liability for externalizing behaviors plays an important role in adolescence and may constitute an indicator of propensity for behaviors characterized by poor self-control(90-92). To our knowledge, this is one of the first studies (93) to show associations between genetic liability for externalizing behaviors, delay discounting, and STB. Findings revealed that those indicators of genetic liability were related to low emotional control (impulsive behaviors driven by mood) and to poor premeditation-perseverance abilities, which in turn

increased the risk of STB. As the current effect sizes are small, further explorations are needed before drawing any conclusions. However, the fact that one's genetic liability could translate into behavioral processes to impact STB risk might lead to promising treatment avenues, as those processes can be modified using (neuro)psychological interventions. Interestingly, in models including both genetic and neurocognitive measures, the significant association between alcohol experimentation and STB disappeared, suggesting that this association may only be indirect in nature. A potential explanation could be that the association between early alcohol exposure and poor decision-making is related to genetic and familial factors(44, 94). In this young cohort, we observed that: 1) genetic liability for externalizing behaviors was related to early drinking and poorer abilities on the latent behavioral factors, 2) drinking was also directly related to poor behavioral abilities, and 3) trait-based behavioral features directly related to STB.

Though we mainly discussed findings from the EUR group, it is important to comment on the roles of decision-making-related mechanisms in the other groups. The emotional impulsivity (AFR, AMR) and the premeditation-perseverance (AFR only) latent factors were related to lower STB. In addition, higher genetic liability for alcohol problems was related to STB in AMR, strengthening support for prior evidence of shared genetic liability between those phenotypes(9). Though these analyses were statistically underpowered, limiting the conclusions that can be drawn, conducting ancestry-stratified analyses is an important effort to pursue.

These results should be considered in light of different perspectives and limitations. First, we selected a sample of adolescents with limited alcohol exposure to reduce the impact that alcohol may have on neurocognitive functions and explore the mechanisms related to their shared liability. Although we were able to support the relevance of alcohol experimentation, genetic, and

neurocognitive mechanisms on STB risk, the nature of the sample may explain some of the small effect sizes and a possible lack of power in the AFR and AMR groups. Relatedly, our model assumed and supported a direct path from alcohol experimentation at baseline to decision-making-related mechanisms at follow-ups. Future studies should also investigate how those mechanisms are related to later alcohol use and further increase the risk of STB.

Second, our ordinal scale of STB relied on self-report from the KSADS, where the vast majority of youth endorsed "rarely" feeling suicidal. It is possible that with advancing adolescent development, greater suicidality will become evident. However, due to the low number of STB in this study, we had to consider the lifetime KSADS assessment, which prevented us from drawing any firm conclusion regarding the longitudinal nature of those associations. Adolescence is a dynamic period for all the neurocognitive phenotypes/processes evaluated in the current study. While these results provide us with a first snapshot, future studies should consider neurocognitive maturation, continuity of alcohol use and STB, and genetic influences across development.

Third, although the ABCD cohort was recruited to match the racial and economic representation in the United States(95), due to the typically higher attrition and difficulty in maintaining contact with families of lower socioeconomic status(96), it is possible that ABCD youth from sociodemographically marginalized groups might be underrepresented. In the factor analysis, we handled missing data using pairwise association, as this method has been shown to give reliable estimates in prior studies(97). All the final measures included in this study had less than 20% of missingness. Though this is consistent with prior ABCD studies (59), the internal consistency of the sensation seeking subcomponent of the UPPS was low. Because our main results relied on an emotional impulsivity latent factor, we do not believe this may impact our conclusion.

However, future studies should replicate the factor structure of the neurocognitive assessments using later ABCD data release and additional samples.

Finally, we used PGS as an indicator of genetic liability for different phenotypes/processes. Though PGS are informative for basic research, they are not currently clinically informative(98). Moreover, the GWAS used to compute PGS in this study are almost exclusively based on adult samples, precluding consideration of qualitative differences in genetic influences on STB (99) and alcohol use (100) across time. Similarly, GWAS summary statistics were from European samples, while PGS were computed for three distinct ancestry groups. The predictive power of PGS based on European data declines when applied to other ancestry groups(101); this may also explain the absence of results in the AFR and AMR groups. Lastly, because of the correlations between our latent factors and PGS scores, we could not precisely determine how many independent tests were performed, and therefore, did not correct for multiple testing. These results should be considered exploratory to help design future studies.

To conclude, this study evaluates the association between alcohol experimentation and STB in three empirically-defined ancestry groups (EUR, AFR, AMR). Results supported the relevance of subclinical alcohol use in STB risk in the EUR group. Conceptual models were tested to identify explanatory mechanisms for the association between alcohol experimentation and STB and the association between genetic risk and STB. Measures of genetic liability relevant to STB risk were related to suicidal behaviors and the affective components of decision-making. Findings also indicate the importance of behavioral processes such as decision-making driven by emotional impulsivity and premeditation-perseverance factors. These mechanisms explained part of the association between early alcohol use and STB and were involved in the association between

genetic risk and STB. Though one's genetic liability is immutable, it is possible to work on the cognitive and affective processes involved in the ability to make decisions(102, 103). This may lead to explorations of how neurocognitive mechanisms could mitigate the risk of STB, either directly or indirectly. These results should provide guidance and context future studies to continue the investigation of genetics and decision-making-related mechanisms in the co-occurrence of alcohol use and STB.

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Author Contributions

SL, AE, JB, and MS contributed to the conception and design of the study. All authors have data access, KP prepared the genetic data and performed the ancestry assignment, and SSR and SL conducted the polygenic scores analysis. SL led the analysis while all authors contributed to the interpretation of the data. SL drafted the manuscript; all authors critically reviewed and edited the manuscript. SL and AE obtained the funding. All authors approved the final version of the manuscript. SL and AE are the guarantors of this work and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data Availability

Data can be accessed following approval from the Adolescent Brain Cognitive Development (ABCD) Study (https://abcdstudy.org). The analytic code can be shared upon request (severine.lannoy@vcuhealth.org).

References

1. Barak-Corren Y, Castro VM, Javitt S, Hoffnagle AG, Dai Y, Perlis RH, et al. Predicting Suicidal Behavior From Longitudinal Electronic Health Records. American Journal of Psychiatry. 2017;174(2):154-62.

2. Isaacs JY, Smith MM, Sherry SB, Seno M, Moore ML, Stewart SH. Alcohol use and death by suicide: A meta-analysis of 33 studies. Suicide Life Threat Behav. 2022;52(4):600-14.

3. Yuodelis-Flores C, Ries RK. Addiction and suicide: A review. Am J Addict. 2015;24(2):98-104.

4. Pompili M, Serafini G, Innamorati M, Dominici G, Ferracuti S, Kotzalidis GD, et al. Suicidal behavior and alcohol abuse. Int J Environ Res Public Health. 2010;7(4):1392-431.

5. Edwards AC, Ohlsson H, Sundquist J, Sundquist K, Kendler KS. Alcohol Use Disorder and Risk of Suicide in a Swedish Population-Based Cohort. American Journal of Psychiatry. 2020;177(7):627-34.

6. Edwards AC, Ohlsson H, Moscicki E, Crump C, Sundquist J, Kendler KS, et al. Alcohol use disorder and non-fatal suicide attempt: findings from a Swedish National Cohort Study. Addiction. 2022;117(1):96-105.

7. Coryell W, Horwitz A, Albucher R, Zheng K, Pistorello J, Eisenberg D, et al. Suicidality and Alcohol Use as Predictors of Future Suicidal Behavior in College Students. Alcohol Alcohol. 2022;57(6):643-7.

8. Aguinaldo LD, Goldstone A, Hasler BP, Brent DA, Coronado C, Jacobus J. Preliminary analysis of low-level alcohol use and suicidality with children in the adolescent brain and cognitive development (ABCD) baseline cohort. Psychiatry Res. 2021;299:113825.

9. Edwards AC, Ohlsson H, Lannoy S, Stephenson M, Crump C, Sundquist J, et al. Shared genetic and environmental etiology between substance use disorders and suicidal behavior. Psychological Medicine. 2023;53(6):2380-8.

10. Mullins N, Kang J, Campos AI, Coleman JRI, Edwards AC, Galfalvy H, et al. Dissecting the shared genetic architecture of suicide attempt, psychiatric disorders and known risk factors. Biological Psychiatry. 2022;91(3):313-27.

11. Colbert SMC, Hatoum AS, Shabalin A, Coon H, Nelson EC, Agrawal A, et al. Exploring the genetic overlap of suicide-related behaviors and substance use disorders. 2021.

12. Docherty AR, Mullins N, Ashley-Koch AE, Qin X, Coleman JRI, Shabalin A, et al. GWAS Meta-Analysis of Suicide Attempt: Identification of 12 Genome-Wide Significant Loci and Implication of Genetic Risks for Specific Health Factors. Am J Psychiatry. 2023;180(10):723-38.

13. Stephenson M, Lannoy S, Edwards AC. Shared genetic liability for alcohol consumption, alcohol problems, and suicide attempt: Evaluating the role of impulsivity. Transl Psychiatry. 2023;13(1):87.

14. Crews FT, Boettiger CA. Impulsivity, frontal lobes and risk for addiction. Pharmacol Biochem Behav. 2009;93(3):237-47.

15. Mukherjee K. A dual system model of preferences under risk. Psychol Rev. 2010;117(1):243-55.

16. Shulman EP, Smith AR, Silva K, Icenogle G, Duell N, Chein J, et al. The dual systems model: Review, reappraisal, and reaffirmation. Dev Cogn Neurosci. 2016;17:103-17.

17. Steinberg L. A Social Neuroscience Perspective on Adolescent Risk-Taking. Dev Rev. 2008;28(1):78-106.

18. Carbia C, Cadaveira F, Caamano-Isorna F, Rodriguez Holguin S, Corral M. Binge Drinking Trajectory and Decision-Making during Late Adolescence: Gender and Developmental Differences. Front Psychol. 2017;8:783.

19. Korner N, Schmidt P, Soyka M. Decision making and impulsiveness in abstinent alcohol-dependent people and healthy individuals: a neuropsychological examination. Subst Abuse Treat Prev Policy. 2015;10:24.

20. Arias AJ, Ma L, Bjork JM, Hammond CJ, Zhou Y, Snyder A, et al. Altered effective connectivity of the reward network during an incentive-processing task in adults with alcohol use disorder. Alcohol Clin Exp Res. 2021;45(8):1563-77.

21. Bjork JM, Hommer DW, Grant SJ, Danube C. Impulsivity in abstinent alcohol-dependent patients: relation to control subjects and type 1-/type 2-like traits. Alcohol. 2004;34(2-3):133-50.

22. Ariesen AD, Neubert JH, Gaastra GF, Tucha O, Koerts J. Risky Decision-Making in Adults with Alcohol Use Disorder-A Systematic and Meta-Analytic Review. J Clin Med. 2023;12(8).

23. Camchong J, Endres M, Fein G. Decision making, risky behavior, and alcoholism. Handb Clin Neurol. 2014;125:227-36.

24. Sastre-Buades A, Alacreu-Crespo A, Courtet P, Baca-Garcia E, Barrigon ML. Decision-making in suicidal behavior: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2021;131:642-62.

25. Jollant F, Bellivier F, Leboyer M, Astruc B, Torres S, Verdier R, et al. Impaired Decision Making in Suicide Attempters. American Journal of Psychiatry. 2005;162:304-10.

26. Alacreu-Crespo A, Olie E, Le Bars E, Cyprien F, Deverdun J, Courtet P. Prefrontal activation in suicide attempters during decision making with emotional feedback. Transl Psychiatry. 2020;10(1):313.

27. Liu S, Duan M, Sun Y, Wang L, An L, Ming D. Neural responses to social decision-making in suicide attempters with mental disorders. BMC Psychiatry. 2023;23(1):19.

28. Athey A, Overholser J, Bagge C, Dieter L, Vallender E, Stockmeier CA. Risk-taking behaviors and stressors differentially predict suicidal preparation, non-fatal suicide attempts, and suicide deaths. Psychiatry Res. 2018;270:160-7.

29. May AM, Czyz EK, West BT. Differentiating Adolescent Suicide Attempters and Ideators: A Classification Tree Analysis of Risk Behaviors. J Adolesc Health. 2020;67(6):837-50.

30. Abdoli N, Salari N, Farnia V, Khodamoradi M, Jahangiri S, Mohammadi M, et al. Risk-Taking Behavior among Suicide Attempters. J Clin Med. 2022;11(14).

31. Wojnar M, Ilgen MA, Czyz E, Strobbe S, Klimkiewicz A, Jakubczyk A, et al. Impulsive and non-impulsive suicide attempts in patients treated for alcohol dependence. J Affect Disord. 2009;115(1-2):131-9.

32. Wang YG, Chen S, Xu ZM, Shen ZH, Wang YQ, He XY, et al. Family history of suicide and high motor impulsivity distinguish suicide attempters from suicide ideators among college students. J Psychiatr Res. 2017;90:21-5.

33. Gifuni AJ, Perret LC, Lacourse E, Geoffroy MC, Mbekou V, Jollant F, et al. Decision-making and cognitive control in adolescent suicidal behaviors: a qualitative systematic review of the literature. Eur Child Adolesc Psychiatry. 2021;30(12):1839-55.

34. Bjork JM, Sawyers CK, Straub LK, Garavito DMN, Westbrook A. Cognitive effort avoidance in veterans with suicide attempt histories. Acta Psychol (Amst). 2022;231:103788.

35. MacPherson HA, Kim KL, Seymour KE, Wolff J, Esposito-Smythers C, Spirito A, et al. Cognitive Flexibility and Impulsivity Deficits in Suicidal Adolescents. Res Child Adolesc Psychopathol. 2022.

36. Ivey-Stephenson AZ, Demissie Z, Crosby AE, Stone DM, Gaylor E, Wilkins NJ, et al. Suicidal Ideation and Behaviors Among High School Students — Youth Risk Behavior Survey, United States, 2019. 2020. Contract No.: 69 (Suppl-1).

37. Geoffroy MC, Bouchard S, Per M, Khoury B, Chartrand E, Renaud J, et al. Prevalence of suicidal ideation and self-harm behaviours in children aged 12 years and younger: a systematic review and meta-analysis. Lancet Psychiatry. 2022;9(9):703-14.

38. Sullivan EV, Lannoy S, Le Berre AP, Fama R, Pfefferbaum A. Alcohol drinking and alcohol use disorder across the ages: Dynamic effects on the brain and function. In: Association AP, editor. Handbook of Neuropsychology2022.

39. Sjodin L, Raninen J, Larm P. Early Drinking Onset and Subsequent Alcohol Use in Late Adolescence: a Longitudinal Study of Drinking Patterns. J Adolesc Health. 2024;74(6):1225-30.

40. Watts AL, Wood PK, Jackson KM, Lisdahl KM, Heitzeg MM. Incipient alcohol use in childhood: Early alcohol sipping and its

relations with psychopathology and personality. Development and Psychopathology. 2020:1-13.

41. Murphy MA, Dufour SC, Gray JC. The association between child alcohol sipping and alcohol expectancies in the ABCD study. Drug Alcohol Depend. 2021;221:108624.

42. Carballo JJ, Llorente C, Kehrmann L, Flamarique I, Zuddas A, Purper-Ouakil D, et al. Psychosocial risk factors for suicidality in children and adolescents. Eur Child Adolesc Psychiatry. 2020;29(6):759-76.

43. Rizk MM, Herzog S, Dugad S, Stanley B. Suicide Risk and Addiction: The Impact of Alcohol and Opioid Use Disorders. Curr Addict Rep. 2021;8(2):194-207.

44. Loughnan RJ, Palmer CE, Makowski C, Thompson WK, Barch DM, Jernigan TL, et al. Unique prediction of developmental psychopathology from genetic and familial risk. J Child Psychol Psychiatry. 2022;63(12):1631-43.

45. Moore DM, Conway ARA. The Structure of Cognitive Abilities and Associations with Problem Behaviors in Early Adolescence: An Analysis of Baseline Data from the Adolescent Brain Cognitive Development Study. J Intell. 2023;11(5).

46. Thompson WK, Barch DM, Bjork JM, Gonzalez R, Nagel BJ, Nixon SJ, et al. The structure of cognition in 9 and 10 year-old children and associations with problem behaviors: Findings from the ABCD study's baseline neurocognitive battery. Dev Cogn Neurosci. 2019;36:100606.

47. Bjork JM, Straub LK, Provost RG, Neale MC. The ABCD study of neurodevelopment: Identifying neurocircuit targets for prevention and treatment of adolescent substance abuse. Curr Treat Options Psychiatry. 2017;4(2):196-209.

48. Volkow ND, Koob GF, Croyle RT, Bianchi DW, Gordon JA, Koroshetz WJ, et al. The conception of the ABCD study: From substance use to a broad NIH collaboration. Dev Cogn Neurosci. 2018;32:4-7.

49. Fan CC, Loughnan R, Wilson S, Hewitt JK, Group AGW. Genotype Data and Derived Genetic Instruments of Adolescent Brain Cognitive Development Study((R)) for Better Understanding of Human Brain Development. Behav Genet. 2023;53(3):159-68.

50. Uban KA, Horton MK, Jacobus J, Heyser C, Thompson WK, Tapert SF, et al. Biospecimens and the ABCD study: Rationale, methods of collection, measurement and early data. Dev Cogn Neurosci. 2018;32:97-106.

51. Karczewski KJ, Francioli LC, Tiao G, Cummings BB, Alfoldi J, Wang Q, et al. The mutational constraint spectrum quantified from variation in 141,456 humans. Nature. 2020;581(7809):434-43.

52. Khan AT, Gogarten SM, McHugh CP, Stilp AM, Sofer T, Bowers ML, et al. Recommendations on the use and reporting of race, ethnicity, and ancestry in genetic research: Experiences from the NHLBI TOPMed program. Cell Genom. 2022;2(8).

53. Saragosa-Harris NM, Chaku N, MacSweeney N, Guazzelli Williamson V, Scheuplein M, Feola B, et al. A practical guide for researchers and reviewers using the ABCD Study and other large longitudinal datasets. Dev Cogn Neurosci. 2022;55:101115.

54. Luciana M, Bjork JM, Nagel BJ, Barch DM, Gonzalez R, Nixon SJ, et al. Adolescent neurocognitive development and impacts of substance use: Overview of the adolescent brain cognitive development (ABCD) baseline neurocognition battery. Dev Cogn Neurosci. 2018;32:67-79.

55. Zelazo PD, Anderson JE, Richler J, Wallner-Allen K, Beaumont JL, Weintraub S. II. NIH Toolbox Cognition Battery (CB): measuring executive function and attention. Monogr Soc Res Child Dev. 2013;78(4):16-33.

56. Zelazo PD. The Dimensional Change Card Sort (DCCS): a method of assessing executive function in children. Nat Protoc. 2006;1(1):297-301.

57. Brand M, Fujiwara E, Borsutzky S, Kalbe E, Kessler J, Markowitsch HJ. Decision-making deficits of korsakoff patients in a new gambling task with explicit rules: associations with executive functions. Neuropsychology. 2005;19(3):267-77.

58. Cyders MA, Littlefield AK, Coffey S, Karyadi KA. Examination of a short English version of the UPPS-P Impulsive Behavior Scale. Addict Behav. 2014;39(9):1372-6.

59. Watts AL, Smith GT, Barch DM, Sher KJ. Factor structure, measurement and structural invariance, and external validity of an abbreviated youth version of the UPPS-P Impulsive Behavior Scale. Psychol Assess. 2020;32(4):336-47.

60. Mallard TT, Savage JE, Johnson EC, Huang Y, Edwards AC, Hottenga JJ, et al. Item-Level Genome-Wide Association Study of the Alcohol Use Disorders Identification Test in Three Population-Based Cohorts. Am J Psychiatry. 2022;179(1):58-70.

61. Okbay A, Wu Y, Wang N, Jayashankar H, Bennett M, Nehzati SM, et al. Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. Nat Genet. 2022;54(4):437-49.

62. Hatoum AS, Morrison CL, Mitchell EC, Lam M, Benca-Bachman CE, Reineberg AE, et al. Genome-wide Association Study Shows That Executive Functioning Is Influenced by GABAergic Processes and Is a Neurocognitive Genetic Correlate of Psychiatric Disorders. Biol Psychiatry. 2023;93(1):59-70.

63. Karlsson Linner R, Mallard TT, Barr PB, Sanchez-Roige S, Madole JW, Driver MN, et al. Multivariate analysis of 1.5 million people identifies genetic associations with traits related to self-regulation and addiction. Nat Neurosci. 2021;24(10):1367-76.

64. Thorpe HHA, Cupertino RB, Pakala SR, Fontanillas P, Jennings MV, Yang J, et al. 2024.

65. Sanchez-Roige S, Fontanillas P, Elson SL, Gray JC, de Wit H, MacKillop J, et al. Genome-Wide Association Studies of Impulsive Personality Traits (BIS-11 and UPPS-P) and Drug Experimentation in up to 22,861 Adult Research Participants Identify Loci in the CACNA1I and CADM2 genes. J Neurosci. 2019;39(13):2562-72.

66. Ge T, Chen CY, Ni Y, Feng YA, Smoller JW. Polygenic prediction via Bayesian regression and continuous shrinkage priors. Nature Communications. 2019;10(1):1776.

67. Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: rising to the challenge of larger and richer datasets. Gigascience. 2015;4:7.

68. Jaeger DA. Reconciling the old and new Census Bureau education questions: Recommendations for researchers. Journal of Business & Economic Statistics. 1997;15(3):300-9.

69. Sobell LC, Sobell MB. Alcohol Timeline Followback Users' Manual. Toronto, Canada: Addiction Research Foundation; 1995.

70. Gruber E, DiClemente RJ, Anderson MM, Lodico M. Early Drinking Onset and Its Association with Alcohol Use and Problem

Behavior in LateAdolescence. Preventive Medicine. 1996;25:293-300.

71. Raninen J, Callinan S, Gmel G, Brunborg GS, Karlsson P. Age of Onset and DSM-5 Alcohol Use Disorder in Late Adolescence - A Cohort Study From Sweden. J Adolesc Health. 2024;75(4):620-5.

72. Kim SY, Jeong SH, Park EC. Age at onset of alcohol consumption and its association with alcohol misuse in adulthood. Neuropsychopharmacol Rep. 2023;43(1):40-9.

73. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36(7):980-8.

74. Posner K, Brown GK, Stanley B, Brent DA, Yershova KV, Oquendo MA, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry. 2011;168(12):1266-77.

75. Franklin JC, Ribeiro JD, Fox KR, Bentley KH, Kleiman EM, Huang X, et al. Risk factors for suicidal thoughts and behaviors: A meta-analysis of 50 years of research. Psychological Bulletin. 2017;143(2):187-232.

76. Yong AG, Pearce S. A Beginners Guide to Factor Analysis: Focusing on Exploratory Factor Analysis. Tutorials in Quantitatve Methods for Psychology. 2013;9(2):79-94.

77. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the Mediation, Confounding and Suppression Effect. Prev Sci. 2000;1:173.

78. Ohlsson H, Kendler KS. Applying Causal Inference Methods in Psychiatric Epidemiology: A Review. JAMA Psychiatry. 2020;77(6):637-44.

79. Lannoy S, Pfefferbaum A, Le Berre AP, Thompson WK, Brumback T, Schulte T, et al. Growth trajectories of cognitive and motor control in adolescence: How much is development and how much is practice? Neuropsychology. 2022;36(1):44-54.

80. Infante MA, Nguyen-Louie TT, Worley M, Courtney KE, Coronado C, Jacobus J. Neuropsychological Trajectories Associated with Adolescent Alcohol and Cannabis Use: A Prospective 14-Year Study. J Int Neuropsychol Soc. 2020;26(5):480-91.

81. Morin JG, Afzali MH, Bourque J, Stewart SH, Seguin JR, O'Leary-Barrett M, et al. A Population-Based Analysis of the Relationship Between Substance Use and Adolescent Cognitive Development. Am J Psychiatry. 2019;176(2):98-106.

82. Anokhin AP, Luciana M, Banich M, Barch D, Bjork JM, Gonzalez MR, et al. Age-related changes and longitudinal stability of individual differences in ABCD Neurocognition measures. Dev Cogn Neurosci. 2022;54:101078.

83. Marek S, Tervo-Clemmens B, Nielsen AN, Wheelock MD, Miller RL, Laumann TO, et al. Identifying reproducible individual differences in childhood functional brain networks: An ABCD study. Dev Cogn Neurosci. 2019;40:100706.

84. Enkavi ZA, Eisenberg IW, Bissett PG, Mazza GL, MacKinnon DP, Marsch LA, et al. Large-scale analysis of test–retest reliabilities of self-regulation measures. PNAS. 2019;116(2):5472-7.

85. Maurage P, Lannoy S, Naassila M, Rolland B, Billieux J. Impulsivity and Binge Drinking: A Neurocognitive Perspective. Neuroscience of Alcohol2019. p. 335-43.

86. Coskunpinar A, Dir AL, Cyders MA. Multidimensionality in impulsivity and alcohol use: a meta-analysis using the UPPS model of impulsivity. Alcohol Clin Exp Res. 2013;37(9):1441-50.

87. Bruno S, Anconetani G, Rogier G, Del Casale A, Pompili M, Velotti P. Impulsivity traits and suicide related outcomes: A systematic review and meta-analysis using the UPPS model. J Affect Disord. 2023;339:571-83.

88. Beach VL, Gissandaner TD, Schmidt AT. The UPPS Model of Impulsivity and Suicide: A Systematic Literature Review. Arch Suicide Res. 2022;26(3):985-1006.

89. Gustavson DE, Morrison CL, Mallard TT, Jennings MV, Fontanillas P, Elson SL, et al. Executive Function and Impulsivity Predict Distinct Genetic Variance in Internalizing Problems, Externalizing Problems, Thought Disorders, and Compulsive Disorders: A Genomic Structural Equation Modeling Study. Clin Psychol Sci. 2024;12(5):865-81.

90. Kendler KS, Gardner C, Dick DM. Predicting alcohol consumption in adolescence from alcohol-specific and general externalizing genetic risk factors, key environmental exposures and their interaction. Psychol Med. 2011;41(7):1507-16.

91. Young SE, Friedman NP, Miyake A, Willcutt EG, Corley RP, Haberstick BC, et al. Behavioral disinhibition: liability for externalizing spectrum disorders and its genetic and environmental relation to response inhibition across adolescence. J Abnorm Psychol. 2009;118(1):117-30.

92. Brislin SJ, Salvatore JE, Meyers JM, Kamarajan C, Plawecki MH, Edenberg HJ, et al. Examining associations between genetic and neural risk for externalizing behaviors in adolescence and early adulthood. Psychol Med. 2024;54(2):267-77.

93. Barr PB, Stephenson M, Poore HE, Chatzinakos C, Qin X, Ashley-Koch AE, et al. 2025.

94. Khemiri L, Franck J, Jayaram-Lindstrom N. Effect of alcohol use disorder family history on cognitive function. Psychol Med. 2022;52(4):757-69.

95. Garavan H, Bartsch H, Conway K, Decastro A, Goldstein RZ, Heeringa S, et al. Recruiting the ABCD sample: Design considerations and procedures. Dev Cogn Neurosci. 2018;32:16-22.

96. Green SM, Navratil JL, Loeber R, Lahey BB. Potential Dropouts in a Longitudinal Study: Prevalence, Stability, and Associated Characteristics. Journal of Child and Family Studies. 1994;3(1):69-87.

97. Shi D, Lee T, Fairchild AJ, Maydeu-Olivares A. Fitting Ordinal Factor Analysis Models With Missing Data: A Comparison Between Pairwise Deletion and Multiple Imputation. Educ Psychol Meas. 2020;80(1):41-66.

98. Docherty A, Kious B, Brown T, Francis L, Stark L, Keeshin B, et al. Ethical concerns relating to genetic risk scores for suicide. Am J Med Genet B Neuropsychiatr Genet. 2021;186(8):433-44.

99. Edwards AC, Ohlsson H, Moscicki E, Crump C, Sundquist J, Lichtenstein P, et al. On the Genetic and Environmental Relationship Between Suicide Attempt and Death by Suicide. American Journal of Psychiatry. 2021;178(11):1060-9.

100. Edwards AC, Kendler KS. Alcohol consumption in men is influenced by qualitatively different genetic factors in adolescence and adulthood. Psychol Med. 2013;43(9):1857-68.

101. Duncan L, Shen H, Gelaye B, Meijsen J, Ressler K, Feldman M, et al. Analysis of polygenic risk score usage and performance in diverse human populations. Nat Commun. 2019;10(1):3328.

102. Myslowski J, McClure SM, Lisinski J, Tomlinson DC, Kablinger AS, MacKillop J, et al. Connectivity Changes Following Episodic Future Thinking in Alcohol Use Disorder. Brain Connect. 2024;14(10):550-9.

103. Bickel WK, Moody L, Quisenberry A. Computerized Working-Memory Training as a Candidate Adjunctive Treatment for Addiction. Alcohol Research: Current Reviews. 2014;36(1):123-6.

Figure legends

Figure 1. Conceptual models used to investigate the potential explanatory mechanisms for the co-occurrence of alcohol experimentation and suicidal thoughts and behaviors (STB). Model A aims to identify behavioral mediators (indexed by cognitive and affective processes related to decision-making) of the association between alcohol experimentation and STB. Model B aims to identify behavioral mediators and test the role of alcohol experimentation in the association between genetic liability (for suicidal behavior, alcohol use/problems, and decision-making-related mechanisms depending on the model) and STB. A separate model was specified for every possible combination of genetic and behavioral indicators of decision-making. Sex and parental education were included as covariates.

Figure 2. Figure 2 illustrates the first mediation models designed to test if the association between alcohol experimentation and STB was mediated by the behavioral latent factors. All models are controlled for parental education and sex. Figure 1.A depicts mediation via the emotional impulsivity latent factor and Figure 1.B the mediation via the premeditation-perseverance factor. Path estimates are standardized beta and significance is set at $p < 0.05$. parent_ed = parental education (range 1-4), Sex was coded as 1 for females and 0 for males, Alcohol = alcohol experimentation at baseline, Imp = emotional impulsivity latent factor, PersPrem = premeditation-perseverance latent factor, STB2 = suicidal thoughts and behaviors at follow-up 2. Results indicated that the association between alcohol experimentation and STB was mediated by both the emotional impulsivity latent factor (mediation proportion = 15.33%) and the premeditation-perseverance factor (mediation proportion = 22.60%).

Figure 3. Figure 3 illustrates the second mediation models designed to test if the association between genetic liability and STB was mediated by alcohol experimentation and/or latent factors related to decision-making. All models are controlled for parental education and sex. Figure 3.A evaluates mediation models via the emotional impulsivity latent factor and Figure 3.B mediation models via the premeditation-perseverance factor. Path estimates are standardized beta and significance is set at $p < 0.05$. PGS_SA = polygenic score for suicidal behavior, PGS_PosUrg = polygenic score for positive urgency, PGS_Ext = polygenic score for externalizing behaviors, PGS_DD = polygenic score for delay discounting, Sex was coded as 1 for females and 0 for males, parent_ed = parental education (range 1-4), Alcohol = alcohol experimentation at baseline, Imp = emotional impulsivity latent factor, PersPrem = premeditation-perseverance latent factor, STB2 = suicidal thoughts and behaviors at follow-up 2. Results indicated that the association between PGS for externalizing behaviors and STB was mediated by both the emotional impulsivity and premeditation-perseverance latent factors (mediation proportion = 6.98% and 8.41%, respectively). In addition, the association between PGS for delay discounting and STB was mediated by the emotional impulsivity latent factor (mediation proportion = 10.30%).

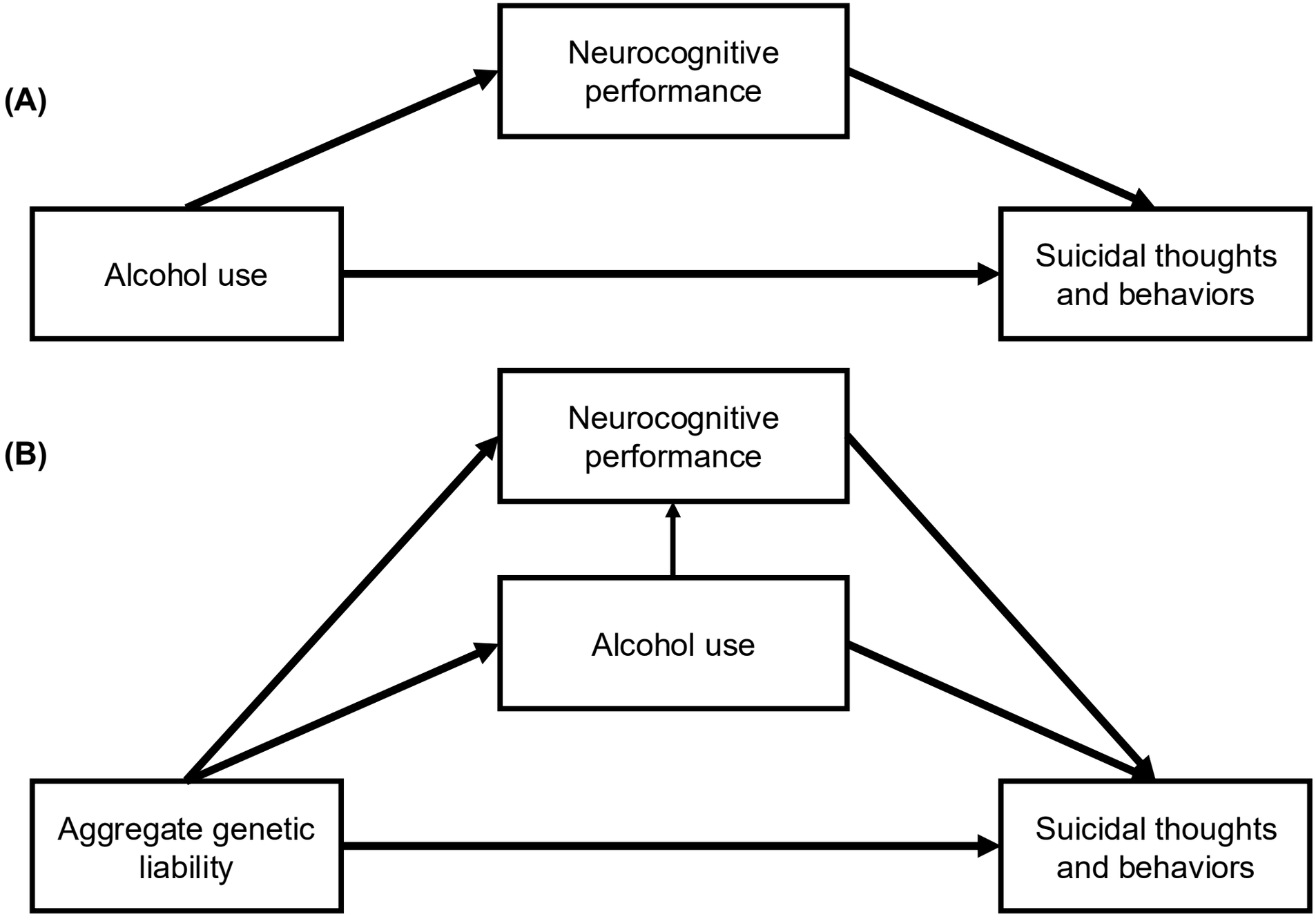
Table 1. Description of the sample

	Participants of **European Ancestry** N = 6,080	Participants of **African Ancestry** N = 2,085	Participants of **American Ancestry** N = 2,712
Biological sex (% females)	47.38	49.90	47.25
Parental education (%)			
11th grade or less	0.41	5.95	9.96
12th grade	3.41	24.65	19.17
some college	18.95	41.54	33.00
college graduate	77.22	27.67	37.61
Alcohol experimentation (%)	27.89	12.21	21.05
Suicide ideation (%)	3.52	4.17	3.63
Suicide attempt (%)	0.86	1.00	1.38

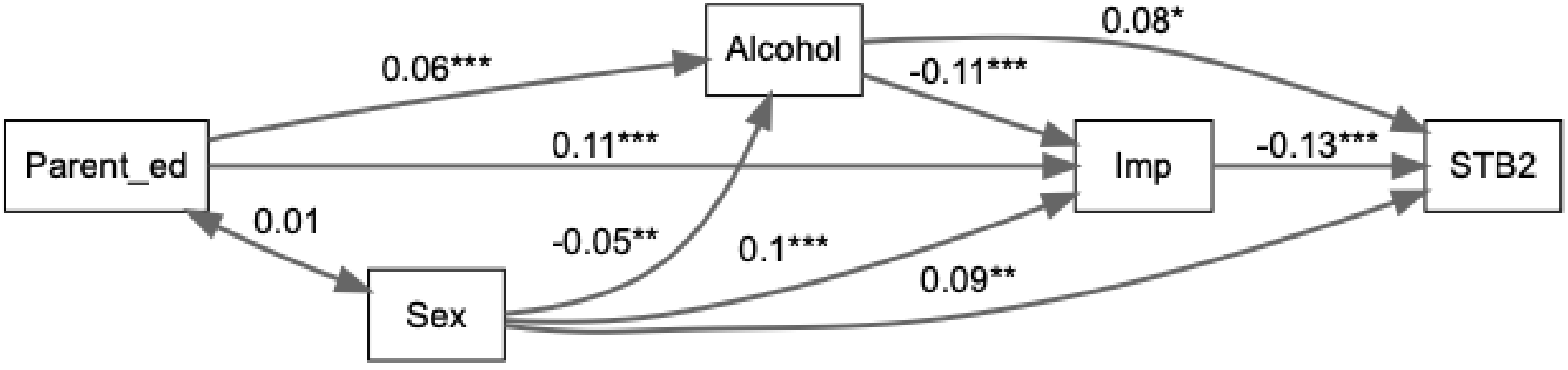
Table 2. Univariate Logistic regressions with Suicidal Thoughts and Behaviors as outcome

	European	African	American
Alcohol experimentation	**1.44 [1.10; 1.89]**	0.85 [0.40; 1.59]	1.14 [0.72;1.74]
Behavioral predictors			
Cognitive factor	0.80 [0.63; 1.01]	0.84 [0.60; 1.19]	1.03 [0.72; 1.51]
Premeditation-Perseverance	**0.57 [0.49; 0.67]**	**0.72 [0.56; 0.94]**	0.96 [0.75; 1.25]
Emotional impulsivity	**0.69 [0.60; 0.81]**	**0.77 [0.60; 0.98]**	**0.73 [0.59; 0.91]**
Genetic predictors			
Suicidal behavior	**1.35 [1.16; 1.58]**	1.13 [0.81; 1.58]	1.10 [0.87; 1.39]
Alcohol use	0.90 [0.79; 1.02]	1.06 [0.82; 1.39]	1.16 [0.96; 1.41]
Alcohol problems	1.01 [0.90; 1.14]	1.08 [0.83; 1.40]	**1.23 [1.02; 1.50]**
Educational attainment	1.01 [0.88; 1.15]	1.02 [0.73; 1.41]	1.17 [0.94; 1.45]
Executive functions	0.94 [0.83; 1.05]	0.95 [0.73; 1.23]	1.06 [0.88; 1.28]
Externalizing behaviors	**1.33 [1.15; 1.54]**	1.27 [0.91; 1.80]	1.00 [0.80; 1.25]
Delay discounting	**1.27 [1.05; 1.53]**	0.94 [0.65; 1.38]	1.02 [0.76; 1.35]
Negative urgency	1.16 [0.84; 1.58]	1.38 [0.90; 2.12]	1.24 [0.83; 1.86]
Positive urgency	**1.32 [1.06; 1.65]**	0.96 [0.70; 1.33]	0.94 [0.70; 1.27]
Lack of premeditation	0.88 [0.72; 1.07]	0.92 [0.70; 1.21]	1.12 [0.85; 1.46]
Lack of perseverance	1.03 [0.90; 1.18]	1.07 [0.88; 1.31]	0.92 [0.76; 1.11]
Sensation seeking	1.13 [0.98; 1.31]	0.99 [0.80; 1.23]	1.04 [0.86; 1.26]

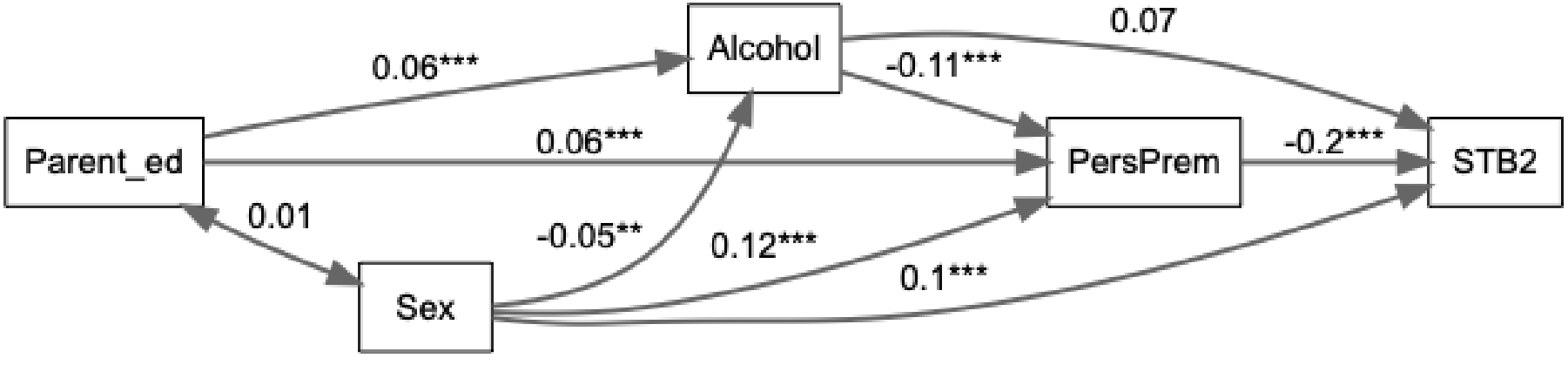
Note: all regressions are controlled for sex and parental education.


(A)
Neurocognitive performance
Alcohol use
Suicidal thoughts and behaviors
(B)
Neurocognitive performance
Alcohol use
Aggregate genetic liability
Suicidal thoughts and behaviors

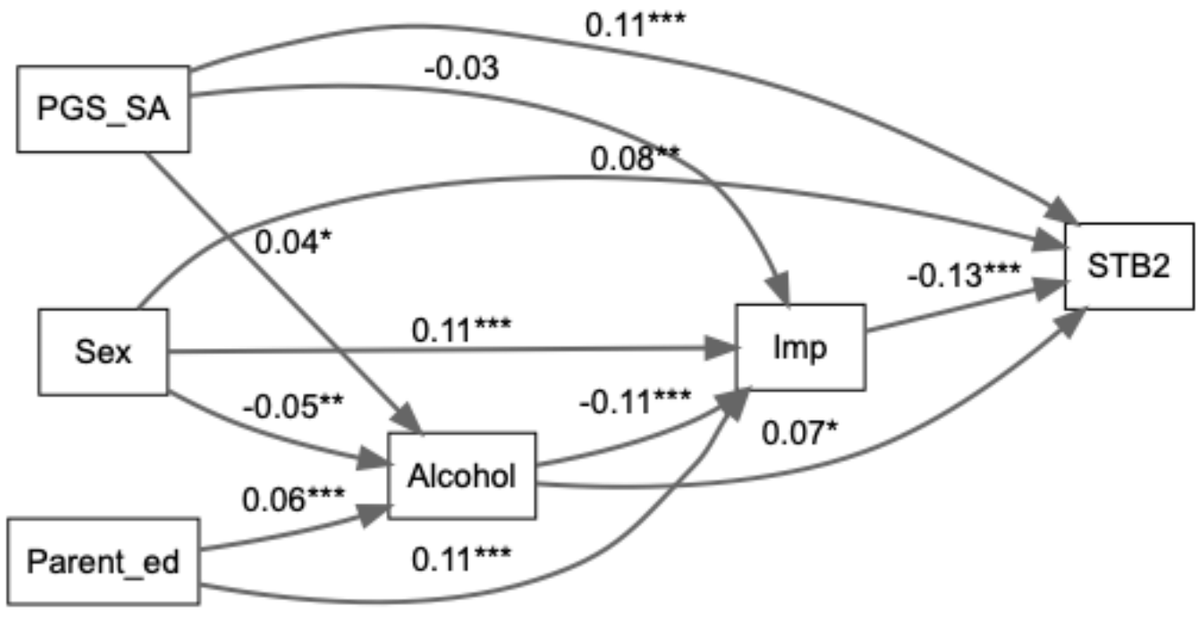
A. Mediation via the emotional impulsivity latent factor

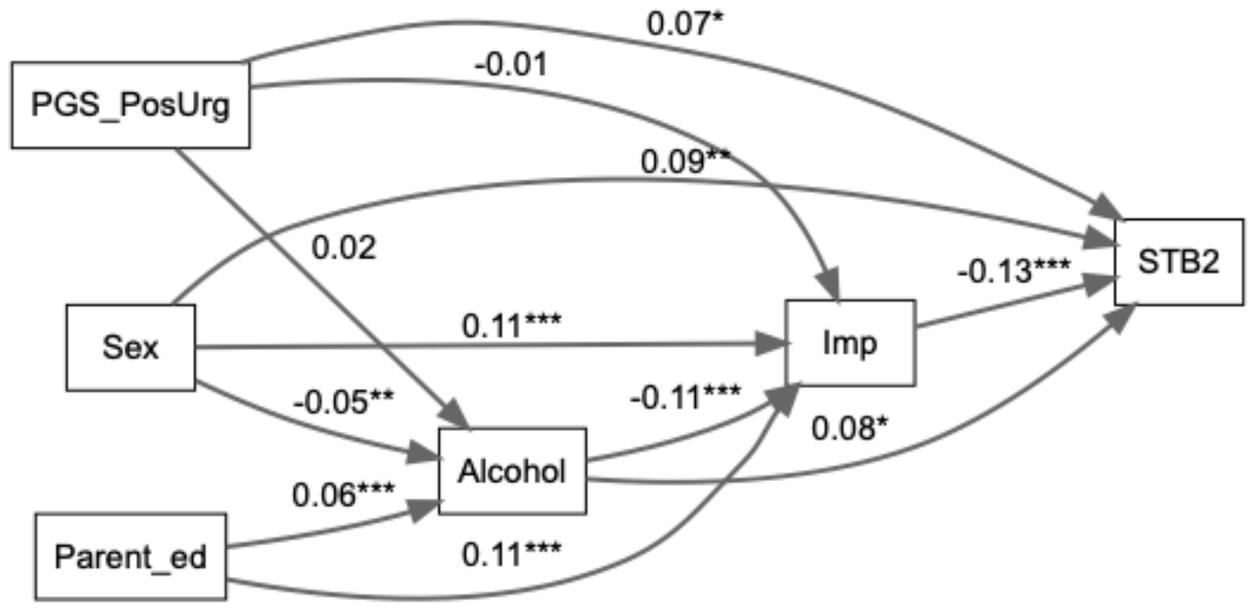


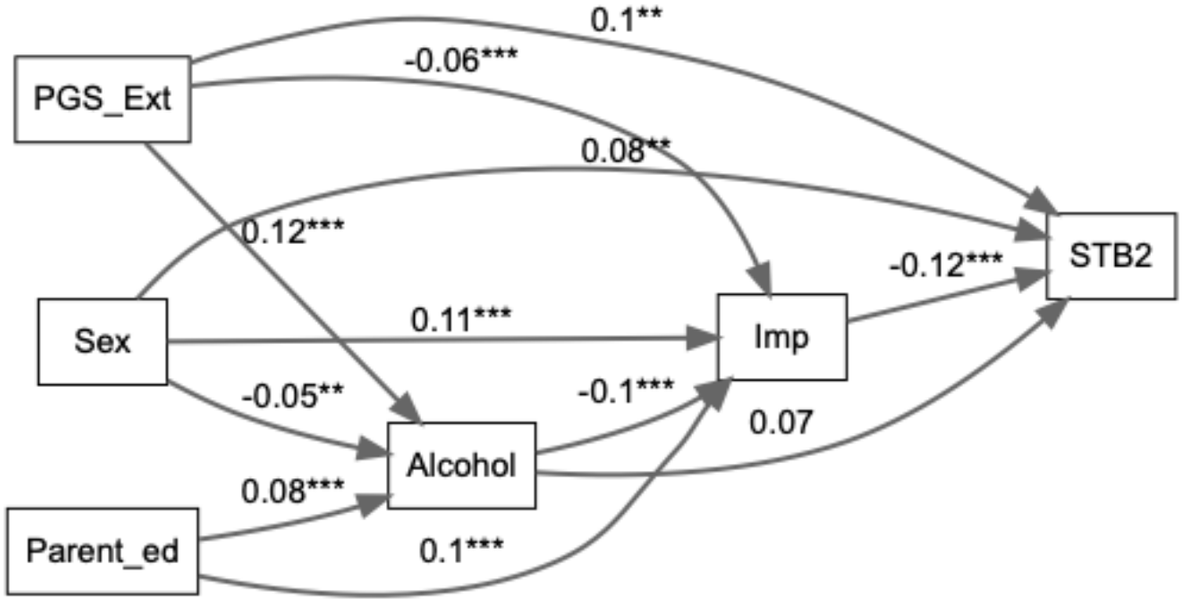
B. Mediation via the premeditation-perseverance latent factor

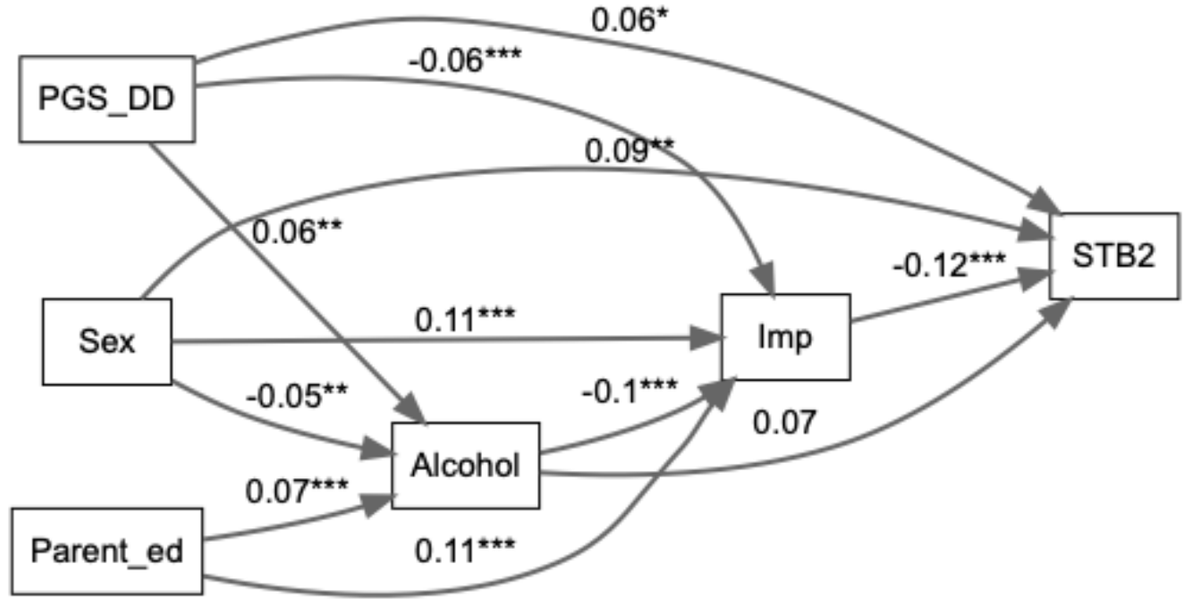


A. Mediation via the emotional impulsivity latent factor









B. Mediation via the premeditation-perseverance latent factor