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Associations Between Substance Use Disorders and Major Depression in Parents and Late Adolescent-Emerging Adult Offspring: An Adoption Study

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Abstract

Aims—To examine whether major depressive disorder (MDD) and substance use disorders (SUDs: specifically, nicotine dependence (ND), alcohol use disorders (AUDs), and cannabis use disorders (CUDs)) in parents predicted increased risk for these disorders in late adolescent-emerging adult offspring and, specifically, the extent to which the pattern of risk differed for adopted and non-adopted youth.

Participants—Late adolescent and emerging adult participants from the Sibling Interaction and Behavior Study (mean age=18.8), a community-based investigation of adopted and non-adopted adolescents, and their parents (adoptive parents of adopted youth, biological parents of non-adopted adolescents) were included.

Measurements—Structured interviews were used to assess these disorders.

Findings—(1) when the same disorder in parents and adolescents was examined, parental MDD was associated with increased risk for MDD among both adopted ($p<.001$) and non-adopted ($p<.01$) adolescents; in contrast, SUDs were associated with increased risk for the same SUD in non-adopted offspring (all $p<.01$). (2) When cross-SUD effects were examined, for the most part, each SUD was associated with increased risk for other SUDs among non-adopted but not adopted offspring (most $p<.05$). (3) When MDD-SUD associations were examined, parental ND and CUDs predicted increased risk for MDD in non-adopted ($p<.001$), but not adopted, adolescents. These effects tended to remain significant when adjusting for within-person comorbidity ($p<.05$).

Conclusions—Major depressive disorder in parents appears to be a risk factor for late adolescent-emerging adult major depressive disorder but not substance use disorder in offspring, with this risk being environmentally mediated. Substance use disorder in parents appears, via genetic mediation, to increase risk of substance use disorder in adolescent offspring, and cannabis and nicotine use disorders in parents similarly contribute to major depressive disorder in those offspring.

Substance use disorders (SUDs) are highly comorbid and also frequently occur with major depressive disorder (MDD; 1,2). This study examined how SUDs—nicotine dependence

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(ND), alcohol use disorders (AUDs), and cannabis use disorders (CUDs)—and MDD in parents were associated in a sample of late adolescent-emerging adult offspring and whether these associations differed according to whether the offspring were adopted or non-adopted. Significant associations between parents and adopted youth would imply that environmental influences are accounting for the similarity. A pattern of stronger associations among non-adopted, compared to adopted, offspring would imply that genetic influences were contributing to these associations. Because adoptive parents are environmentally but not genetically related to their adopted children, this adoption design allows for direct estimation of shared environmental influences on these disorders.

SUDs run in families (8), and comorbidity among SUDs can be partially explained by their occurrence on a broad, heritable externalizing spectrum (3,4). The majority of genetic variance among SUDs is shared (9). Genetic risk factors for substance dependence fall into two highly intercorrelated factors—one for vulnerability to illicit drug dependence and a second for licit drug dependence—and a portion of the genetic influences on ND may be substance-specific (5).

Findings regarding genetic and environmental influences on the comorbidity of MDD with SUDs have been less consistent. Support for a shared, heritable factor increasing risk for smoking and MDD is strong (10–15). For alcohol, evidence for shared familial risk is mixed (6,16). For cannabis, the nature and pattern of aggregation of CUDs and MDD within families remains unclear (17, 18).

The goal of this study was to examine SUDs and MDD in parents and adopted and non-adopted late adolescent-emerging adult offspring. We addressed three issues: (1) within-disorder transmission (whether associations between disorders in parents and the same disorders in their offspring differed for adopted and non-adopted youth); (2) transmission across types of SUDs (the degree to which each SUD in parents was associated with different SUDs among their adopted and non-adopted offspring); and (3) associations across “disorder classes” (the extent to which SUDs in parents predicted MDD in offspring, and the extent to which MDD in parents predicted SUDs among offspring).

Three studies of this same sample during early adolescence examined related issues. Tully et al. (19) found that parental MDD was associated with increased risk for MDD among both adopted and non-adopted adolescents (indicating that it was an environmental risk factor), though parental MDD was not associated with increased risk for offspring SUDs. King et al. (20) found that parental alcohol dependence was associated with increased risk for a broad “disinhibition” construct among non-adopted offspring, but a specific risk for alcohol use among adoptees. Keyes et al. (21) found that parental smoking represented an environmental risk factor for tobacco and marijuana use and a genetic risk factor for substance use among adolescents. The present investigation extended these studies in several ways: (1) by examining the youth during late adolescence and emerging adulthood (with the average age of the sample five years older than in these initial investigations), during a stage when substance use escalates and they are more likely to have experienced the onset of MDD and SUDs; (2) by examining both within-disorder and cross-disorder effects for different SUDs (ND, AUDs, and CUDs) among both parents and offspring; (3) by focusing on SUDs, as opposed to substance use, among offspring; and (4) by examining associations between MDD and each SUD in parents and offspring.

When within-disorder associations were examined, we expected to find an environmental effect for parental MDD on MDD in youth (19), though we considered the possibility that effects for non-adopted offspring would be relatively stronger than those for adoptees. We expected to find significant associations between each parental SUD and that same SUD in

nonadopted youth, but reduced associations for adopted youth (consistent with a genetic influence on SUDs; 3,4). Turning to cross-disorder associations, we expected that each SUD would have genetic effects on other SUDs (9). Considering associations between SUDs and MDD, we expected to find genetically-based (i.e., stronger for non-adopted than for adopted adolescents) associations between ND and MDD and between CUDs and MDD (7). Based on the mixed evidence indicating shared familial risk for MDD and AUDs (6,16), we did not predict differential risk for the other disorder among adopted versus non-adopted offspring. Finally, we conducted analyses adjusting for the effects of within-person comorbidity (e.g., when examining parental CUDs and offspring MDD, adjusting for parental MDD and offspring CUDs) in order to statistically isolate the effects of each disorder (e.g., if CUDs and MDD occur together among parents at rates greater than chance, a finding of a parental CUD-offspring MDD association could simply be due to the fact that many parents with CUDs have MDD and MDD in parents and offspring is correlated). We expected that these associations would diminish but remain significant when we adjusted for within-person comorbidity

Methods

Participants

Participants were drawn from the Sibling Interaction and Behavior Study (SIBS), a community-based longitudinal study of adopted and non-adopted adolescents and their families ($n=409$ adoptive families, 208 non-adoptive families; biological parents of adopted adolescents were not included in this study). A comprehensive characterization of the design of this study is available in McGue et al. (22). At the time of the intake assessment, all families had two adolescents (both included in this study) between the ages of 11 and 20 who were no more than 5 years apart in age (22). Of eligible families, 63% and 57% of adoptive and non-adoptive families (youth, mothers, and fathers), respectively, participated; these families were broadly representative of the populations from which they were drawn (22). Three years later, adolescents and one parent (typically the mother) were invited to return to the study; 94.3% did so. For this study, data from the first and second assessments were used for youth and for maternal MDD; other maternal diagnoses and all paternal diagnoses were derived from the intake assessment. Youth who were at least age 16 at this second assessment and who were not being reared by step-parents (i.e., non-biological rearing parents of non-adopted adolescents) were included in this study ($n=998$ [566 adopted, 432 non-adopted; 590 families total; 87 families included both an adopted and a non-adopted youth; maternal $n=587$; paternal $n=529$; mean age=18.8, $SD=1.7$, range=16 to 25; mean adopted age=18.9, $SD=1.8$; mean non-adopted age=18.7, $SD=1.7$). We did not include youth being reared by step-parents in order to preserve the biological relationship in non-adoptive families and keep the adoptive families comparable to this requirement. Participating families may have had two adopted adolescents who were not genetically related to either parent or each other, one adopted adolescent and one adolescent who was genetically related to one or both parents, or two adolescents who were full biological siblings and biological offspring of one or both parents. Adoptive adolescents were identified through infant placements conducted by three private adoption agencies that are representative of these types of agencies in the state of Minnesota and recruited from these placement lists (mean age at placement in rearing home=4.7 months, $SD=3.4$ months). A majority (74%) of the adopted sample was born outside the United States (23). Non-adopted adolescents were identified and recruited from state birth records and are broadly representative of the population of the state of Minnesota.

Adopted and non-adopted adolescents did not significantly differ in mean age or gender (56.7% of the sample was female). Among non-adopted adolescents, 95.4% were Caucasian and the rest were another non-Asian ethnicity. Adopted adolescents were 20.7% Caucasian,

67.3% Asian, and 12.0% other (representative of adoptions in Minnesota when these youth were adopted).

In this sample, adoptive and non-adoptive parents are broadly similar in their rates of psychiatric disorder. Variance in disinhibitory psychopathology and SES was smaller in the adoptive as compared to non-adoptive families, but analyses examining the effects of these factors on adoptive-sibling correlations for important outcomes indicated that this difference in variance had little effect (22). Lifetime rates of disorder among parents (at least one parent affected) were similar (not significantly different) for MDD, ND, and AUDs in adoptive and non-adoptive families. Although there were more CUDs among non-adoptive, compared to adoptive, parents ($\chi^2=18.8$, $df=1$, $p<.0001$), nearly a quarter of adoptive families had at least one parent with a history of a CUD (see Table 1 for all prevalence rates).

Written informed consent from parents and adult children and assent from minors were obtained. This study was approved by the University of Minnesota IRB.

Measures

Diagnoses were based on DSM-IV criteria and assessed via structured interviews administered by trained interviewers.

MDD—The Structured Clinical Interview for DSM-III-R (24), with additional probes to assess DSM-IV symptoms, was used to assess MDD in parents and adolescents. MDD was considered present if it was endorsed at a definite (meeting all DSM-IV criteria) or probable (having 4 rather than the required 5 “Criterion A” symptoms) level. The use of “probable” diagnoses is common in community-based studies such as this (25,26). Mothers and adolescents were asked about MDD symptoms in the adolescent; symptoms were combined to create diagnoses, counting a symptom reported by either informant as present (the best-estimate method; 27–29). Among fathers, MDD was assessed at intake. Among mothers and adolescents, MDD was assessed at both intake and follow-up. Lifetime MDD was considered present if endorsed at either assessment; it was coded as missing if a participant did not have MDD by the intake assessment but did not return for follow-up.

SUD—DSM-IV diagnoses of ND, AUDs, and CUDs among parents and adolescents were determined using an expanded version of the Substance Abuse Module of the Composite International Diagnostic Interview (30). If a participant endorsed definite abuse or definite (meeting all DSM-IV criteria) or probable (meeting all DSM-IV criteria except one symptom) dependence on the relevant substance (alcohol or cannabis), he or she was considered to have a SUD (for nicotine, only dependence was considered because there is no nicotine abuse syndrome). Among parents, lifetime SUDs were assessed at intake. Among adolescents, SUDs were assessed at both intake and follow-up; participants who fulfilled criteria for a disorder at either assessment were considered to have a lifetime SUD.

Statistical Analyses

Generalized estimating equations (GEEs) were used to conduct logistic regression models while appropriately accounting for nested data (siblings within families; i.e., these analyses adjusted the standard errors and resulting significance tests for the fact that data within families—i.e., sibling observations—were correlated; 31). Analyses adjusted for the effects of adolescent age, gender, and ethnicity.

Parental MDD (considered present if either parent had a history of MDD; if one parent had missing data but the other did not have MDD, it was coded as missing) was used to predict

adolescent MDD, ND, AUD, and CUD, first examining adopted adolescents, then non-adopted adolescents, then all adolescents along with an interaction term representing the interaction between parental MDD and adoption status (to examine whether the effect of parental MDD differed based on the adoption status of the adolescent). These analyses were repeated three times, using parental ND, AUD, and CUD instead of parental MDD. Finally, all analyses were repeated examining maternal and paternal disorders separately.

We considered offspring ethnicity and gender as possible moderators of these associations. In preliminary analyses, offspring ethnicity did not significantly moderate any of the within-disorder associations being examined. Offspring gender was similar—it did not significantly moderate the main associations—with one exception. Specifically, the effect of parental MDD on non-adopted offspring MDD depended on the gender of the adolescent, with the effect being stronger on male adolescents.

Mothers are valid reporters of their child's psychopathology even when they experience psychopathology themselves (e.g., 19). However, to ensure that specific maternal effects were not related to the mothers reporting on the adolescents' MDD, when an effect of a maternal, but not the same paternal, disorder on MDD was found, we repeated the analysis using only adolescent self-reports of their own MDD.

When significant cross-disorder effects were found (e.g., parental CUDs predicting adolescent MDD), these analyses were repeated adjusting for the other disorder in the parent and the adolescent (e.g., in the example above, entering parental MDD and adolescent CUD into the model as covariates) to examine whether the association was related to within-person comorbidity.

Results

Descriptive statistics are presented in Tables 1 and 2, showing overall prevalences of each disorder among youth and parents (by adoption status) (Table 1) and the prevalence of each disorder among adopted and non-adopted offspring of parents (either parent, mothers, and fathers) with and without each disorder (Table 2). Table 3 presents odds ratios describing risk for disorders among adopted and non-adopted adolescents by parental diagnosis. A significant chi-square value for the interaction term indicates that the association between the parental disorder and risk for the outcome disorder differs according to adoption status. Table 4 presents analogous information for maternal and paternal diagnoses separately.

Following the diagonal extending from the upper right to the lower left in Table 3, it is evident that within-disorder parent-offspring effects show a significant effect for non-adopted offspring for all four disorders (with the interaction effect by adoption status being significant for all except MDD). Only for MDD is the effect for adoptive families also significant. This pattern supports genetic mediation for the SUDs, but environmental mediation for MDD.

Turning to cross-disorder effects within ND, AUDs, and CUDs, with one exception, if parents were affected by any of the three SUDs, the odds of offspring developing a different SUD were elevated only for non-adoptive families (though the interaction effect by adoption status was not significant in two cases). The exception was for parental AUDs, which did not lead to elevated odds of offspring ND in either family type. This indicates that the genetic mediation for these SUDs is similar across SUDs and not specific to a single SUD subtype.

Turning to MDD-SUD associations, there was no evidence that parental MDD increased the odds of offspring SUDs in either adoptive or non-adoptive families. In contrast, parental ND

and CUDs were associated with MDD in non-adoptive offspring. When within-person comorbidity was adjusted for, the effects were quite similar to the unadjusted results. Specifically, parental ND continued to predict non-adopted adolescents' risk for MDD (OR=1.74, CI=1.02–2.98), and parental CUDs were associated at a trend level with non-adopted adolescents' risk for MDD (OR=1.64, CI=.93–2.88, $p<.09$; the interaction effect by adoption status was also evident at a trend level: $\chi^2=3.26$, $p=.07$). These associations are consistent with a genetic effect of parental ND and CUDs on risk for offspring MDD. These effects are not fully accounted for by within-person comorbidity.

To facilitate the comparison of our results to those of other studies that focus on the effects of individual parents (typically mothers), results are presented separately for each parent in Table 4. Broadly speaking, the results for mothers and fathers mirrored the overall results (with some differences in the patterns of significance, often due to decreased sample sizes). The genetic effects of paternal ND and CUDs on offspring MDD appeared to be somewhat stronger than those of maternal ND and CUDs; when these analyses were followed-up with analyses adjusting for within-person comorbidity, the paternal effects were more robust. Specifically, paternal ND continued to predict risk for MDD among non-adopted adolescents (OR=2.44, CI=1.43–4.19; interaction effect by adoption status: $\chi^2=6.92$, $p<.01$), while maternal ND was not significantly associated with risk for MDD among non-adopted adolescents (OR=1.45, CI=.82–2.56). Paternal CUDs continued to be associated with increased risk for MDD among non-adopted adolescents (OR=1.99, CI=1.16–3.42; interaction effect by adoption status: $\chi^2=3.25$, $p=.07$). Although the association between maternal AUDs and non-adopted offspring MDD was initially significant, once within-person comorbidity was adjusted for, this association was no longer significant (OR=1.74, CI=.88–3.44).

Discussion

The results indicate that MDD in parents was associated with risk for MDD in late adolescent-emerging adult offspring whether they were adopted or non-adopted, indicating that this risk was primarily environmental. In contrast, SUDs in parents tended to be associated with risk for the same disorder as well as other SUDs among non-adopted, but not adopted, offspring, indicating that SUD risk transmission had a significant genetic component and was similar across substances. Turning to associations between SUDs and MDD, parental, and particularly paternal, ND and CUDs were associated with risk for MDD among non-adopted, but not adopted, offspring. These effects tended to remain significant after adjusting for within-person comorbidity. This supports the notion that the genetically-based risk associated with parental ND and CUDs extends to increased risk for MDD among offspring.

The MDD findings are consistent with Tully et al. (19) and extend these results to this sample at a later age (32). These findings contrast somewhat with twin studies, which have found generally minimal evidence for shared environment in the transmission of MDD (e.g., 33), though a recent study of children of twins found an environmental effect of parental depression on child depression (34). Genetic and environmental contributions to depressive symptoms vary with age (35); therefore, our findings may be unique to this age group and reflect these developmental differences.

The finding that the genetically-based risk for SUDs tends to apply across SUDs is consistent with twin studies that have shown that disorders on the externalizing spectrum are moderately heritable (3). However, these results, which are based on diagnostic rates, differ from those obtained from SIBS investigations of early adolescence that have reported that parental smoking conferred environmental as well as genetic risk on offspring substance use

(21) and that parental alcohol dependence conferred a specific environmental risk for alcohol use (20). Together, these adoption study results suggest that there is an environmental component to the risk conferred by parental smoking and alcohol dependence on early adolescent substance use but only a genetically-mediated contribution to risk for the later development of a SUD. This is consistent with the findings of several twin studies, which indicate stronger roles for shared environment for substance initiation than for substance dependence (36–38).

The results of this study indicate that a portion of the comorbidity between MDD and ND and between MDD and CUDs can be explained by shared genetic vulnerabilities. These findings extend the results of Lynskey et al. (7) and are consistent with the notion of shared genetic vulnerabilities to ND and MDD (10–13). It is unclear why parental MDD was mostly not significantly associated with offspring SUDs. However, the significant association between maternal MDD and ND among non-adopted offspring may point to a weak or inconsistent link between parental MDD and offspring SUDs, and is consistent with the notion that maternal MDD relates to child psychopathology more strongly than does paternal MDD (39). Perhaps ND and CUDs occurring in late adolescence-emerging adulthood represent a heterogeneous group, comprised of people who will continue to evidence SUDs into adulthood and those who are experimenting with heavy use but whose disorders are likely to remit.

This study had limitations. We did not examine potential interaction effects with offspring gender. Within-disorder analyses indicated that in almost all cases there were no differences by offspring gender or ethnicity, though the effect of parental MDD on non-adopted offspring MDD was stronger for male offspring. Although some Asian people may be protected from AUDs by genetic effects, the influence of such an effect is not evident in the rates of AUDs among adoptees (who were mostly Asian) and non-adoptees in this sample (21.1% and 22.5%, respectively). These youth were in the middle of risk periods for the onset of MDD and SUDs; we would expect some to develop these disorders after this assessment. We do not have information about the prenatal environment (and, in the case of those adopted after birth, the early life experiences) of the adopted youth. Because biological mothers who place their children for adoption may experience stressful circumstances and/or psychopathology, these factors could increase risk for psychopathology among the adoptive youth. Although overall family functioning is similar in families of adopted and non-adopted youth (22), it is possible that parents use different parenting styles with adoptive and non-adoptive youth. When parent-offspring effects were significant for non-adoptive families but not for adoptive families, interaction effects by adoption status were usually but not always significant; this may be because the true effect did not vary with adoption status or there was a small difference in the magnitude of the effect we did not have power to detect. Although the pattern of results was broadly consistent with our hypotheses, some of our results only approached or were marginally significant and therefore warrant replication and extension with a larger sample.

These results lead to several broad conclusions. First, MDD in parents confers environmentally-based risk for MDD among late adolescent-emerging adult offspring. Second, parental SUDs confer broad, genetically-based risk for SUDs among offspring in this age group. Third, parental, and particularly paternal, ND and CUDs confer genetically-based risk for MDD among late adolescent-emerging adult offspring. Future research examining the mechanisms behind these associations will be helpful in further clarifying the nature of these risks and potentially developing interventions for vulnerable youth.

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References

1. Grant BF, Stinson FS, Dawson DA, Chou P, Dufour MD, Compton W, Pickering RP, Kaplan K. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004; 61:807–816. [PubMed: 15289279]
2. Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. Comorbidity of mental disorders with alcohol and other drug abuse: Results From the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990; 264:2511–2518. [PubMed: 2232018]
3. Hicks BM, Krueger RF, Iacono WG, McGue M, Patrick CJ. Family transmission and heritability of externalizing disorders: A twin-family study. *Arch Gen Psychiatry*. 2004; 61:922–928. [PubMed: 15351771]
4. Krueger RF, Hicks BM, Patrick CJ, Carlson SR, Iacono WG, McGue M. Etiologic connections among substance dependence, antisocial behavior, and personality: Modeling the externalizing spectrum. *J Abnorm Psychol*. 2002; 111:411–424. [PubMed: 12150417]
5. Kendler KS, Myers J, Prescott CA. Specificity of genetic and environmental risk factors for symptoms of cannabis, cocaine, alcohol, caffeine, and nicotine dependence. *Arch Gen Psychiatry*. 2007; 64:1313–1320. [PubMed: 17984400]
6. Prescott CA, Aggen SH, Kendler KS. Sex-specific genetic influences on the comorbidity of alcoholism and major depression in a population-based sample of US twins. *Arch Gen Psychiatry*. 2000; 57(5):803–811. [PubMed: 10920470]
7. Lynskey MT, Glowinski AL, Todorov AA, Bucholz KK, Madden PAF, Nelson EC, Statham DJ, Martin N, Heath AC. Major depressive disorders, suicidal ideation, and suicide attempt in twins discordant for cannabis dependence and early onset cannabis use. *Arch Gen Psychiatry*. 2004; 61:1026–1031. [PubMed: 15466676]
8. Merikangas KR, Dierker LC, Szatmari P. Psychopathology among offspring of parents with substance abuse and/or anxiety disorders: A high-risk study. *J Child Psychol Psychiatry*. 1998; 39:711–720. [PubMed: 9690934]
9. Tsuang MT, Lyons MJ, Meyer JM, Doyle T, Eisen SA, Goldberg J, et al. Co-occurrence of abuse of different drugs in men: The role of drug-specific and shared vulnerabilities. *Arch Gen Psychiatry*. 1998; 55:967–972. [PubMed: 9819064]
10. Johnson EO, Rhee SH, Chase GA, Breslau N. Comorbidity of depression with levels of smoking: An exploration of the shared familial risk hypothesis. *Nicotine Tobacco Res*. 2004; 6:1029–1038.
11. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression: A causal analysis. *Arch Gen Psychiatry*. 1993; 50:36–43. [PubMed: 8422220]
12. Lyons M, Hitsman B, Xian H, Panizzon MS, Jerskey BA, Santangelo S, Grant MD, Rende R, Eisen S, Eaves L, Tsuang MT. A twin study of smoking, nicotine dependence, and major depression in men. *Nicotine Tobacco Res*. 2008; 10:97–108.
13. McCaffery JM, Papandonatos GD, Stanton C, Lloyd-Richardson EE, Niaura R. Depressive symptoms and cigarette smoking in twins from the National Longitudinal Study of Adolescent Health. *Health Psychol*. 2008; 27:S207–S215. [PubMed: 18979973]
14. Dierker LC, Avenevoli S, Stolar M, Merikangas KR. Smoking and depression: An examination of mechanisms of comorbidity. *Am J Psychiatry*. 2002; 159:947–953. [PubMed: 12042182]
15. Korhonen T, Broms U, Varjonen J, Romanov K, Koskenvuo M, Kinnunen T, Kaprio J. Smoking behavior as a predictor of depression among Finnish men and women: A prospective cohort study of adult twins. *Psychol Med*. 2007; 37:705–715. [PubMed: 17181913]
16. Kuo PH, Gardner CO, Kendler KS, Prescott CA. The temporal relationship of the onsets of alcohol dependence and major depression: Using a genetically informative study design. *Psychol Med*. 2006; 36:1153–1162. [PubMed: 16734951]

17. Lynskey MT, Heath AC, Nelson EC, Bucholz KK, Madden PAF, Slutske WS, Statham DJ, Martin NG. Genetic and environmental contributions to cannabis dependence in a national young adult twin sample. *Psychol Med*. 2002; 32:195–207. [PubMed: 11871371]
18. Merikangas KR, Li JJ, Stipelman B, Yu K, Fucito L, Swendsen J, Zhang H. The familial aggregation of cannabis use disorders. *Addiction*. 2009; 104:622–629. [PubMed: 19335660]
19. Tully EC, Iacono WG, McGue M. An adoptive study of parental depression as an environmental liability for adolescent depression and childhood disruptive disorders. *Am J Psychiatry*. 2008; 165:1148–1153. [PubMed: 18558644]
20. King SM, Keyes M, Malone SM, Elkins I, Legrand LN, Iacono WG, McGue M. Parental alcohol dependence and the transmission of adolescent behavioral disinhibition: A study of adoptive and non-adoptive families. *Addiction*. 2009; 104:578–586. [PubMed: 19215604]
21. Keyes M, Legrand LN, Iacono WG, McGue M. Parental smoking and adolescent problem behavior: An adoption study of general and specific effects. *Am J Psychiatry*. 2008; 165:1338–1344. [PubMed: 18676589]
22. McGue M, Keyes M, Sharma A, Elkins I, Legrand L, Johnson W, Iacono WG. The Environments of adopted and non-adopted youth: Evidence on range restriction from the Sibling Interaction and Behavior Study (SIBS). *Beh Genetics*. 2007; 37:449–462.
23. Keyes MA, Sharma A, Elkins IJ, Iacono WG, McGue M. The mental health of US adolescents adopted in infancy. *Arch Pediatr Adolesc Med*. 2008; 162:419–425. [PubMed: 18458187]
24. Spitzer, RL.; Williams, JBW.; Gibbon, M. Structured Clinical Interview for DSM-III-R (SCID). New York: New York State Psychiatric Institute, Biometrics Research; 1987.
25. Spitzer RL, Endicott J, Robins E. Research diagnostic criteria: Rationale and reliability. *Arch Gen Psychiatry*. 1978; 35:772–782.
26. Iacono WG, Carlson SR, Taylor J, Elkins IJ, McGue M. Behavioral disinhibition and the development of substance-use disorders: Findings from the Minnesota Twin Family Study. *Psychol Med*. 31:411–423. [PubMed: 11305849]
27. Baillargeon RH, Boulerice B, Tremblay RE, Zoccolillo M, Vitaro F, Kohen DE. Modeling interinformant agreement in the absence of a “gold standard”. *J Child Psychol Psychiatry*. 2001; 42:463–473. [PubMed: 11383962]
28. Burt SA, Krueger RF, McGue M, Iacono WG. Sources of covariation among attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder: The importance of shared environment. *J Abnorm Psychol*. 2001; 101:516–525. [PubMed: 11727941]
29. Cantwell DP, Lewinsohn PM, Rohde P, Seeley JR. Correspondence between adolescent report and parent report of psychiatric diagnostic data. *J Am Acad Child Adolesc Psychiatry*. 1997; 36:610–619. [PubMed: 9136495]
30. Robins LN, Wing J, Wittchen HU, et al. The Composite International Diagnostic Interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Arch Gen Psychiatry*. 1988; 45:1069–77. [PubMed: 2848472]
31. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 79:13–22.
32. Schulenberg JE, Sameroff AJ, Cicchetti D. The transition to adulthood as a critical juncture in the course of psychopathology and mental health. *Dev Psychopath*. 2004; 16:799–806.
33. Kendler KS, Gatz M, Gadner CO, Pedersen NL. A Swedish national twin study of lifetime major depression. *Am J Psychiatry*. 2006; 163:109–114. [PubMed: 16390897]
34. Silberg JL, Maes H, Eaves LJ. Genetic and environmental influences on the transmission of parental depression to children’s depression and conduct disturbance: An extended Children of Twins study. *J Child Psychol Psychiatry*. 2010; 51:734–744. [PubMed: 20163497]
35. Thapar A, McGuffin P. A twin study of depressive symptoms in childhood. *Br J Psychiatry*. 1994; 165:259–265. [PubMed: 7953041]
36. Maes HH, Sullivan PF, Bulik CM, Neale MC, Prescott CA, Eaves LJ, Kendler KK. A twin study of genetic and environmental influences on tobacco initiation, regular tobacco use and nicotine dependence. *Psychol Med*. 2004; 34:1–11.

37. True WR, Heath AC, Scherrer JF, Waterman B, Goldberg J, Lin N, Eisen SA, Lyons MJ, Tsuang MT. Genetic and environmental contributions to smoking. *Addiction*. 1997; 92:1277–1288. [PubMed: 9489045]
38. Vink JM, Willemsen G, Boomsma DI. Heritability of smoking initiation and nicotine dependence. *Beh Genetics*. 2005; 35:397–406.
39. Marmorstein NR, Malone SM, Iacono WG. Psychiatric disorders among offspring of depressed mothers: Associations with paternal psychopathology. *Am J Psychiatry*. 2004; 161:1588–1594. [PubMed: 15337648]

Table 1

Rates of disorders among adopted and non-adopted youth and parents

	Adopted Youth (N=566)	Non-Adopted Youth (N=432)	Parents of Adopted Youth			Parents of Non-Adopted Youth		
			Either parent	Mother (N=392)	Father (N=361)	Either parent	Mother (N=195)	Father (N=168)
MDD	31.9%	24.6%	41.0%	28.9%	16.6%	40.6%	28.7%	17.9%
ND	21.4%	15.8%	42.1%	19.1%	32.8%	48.9%	20.1%	37.5%
AUD	21.1%	22.5%	38.0%	7.7%	34.0%	43.1%	14.4%	38.1%
CUD	18.2%	19.2%	24.3%	8.7%	19.4%	41.2%	12.4%	33.9%

MDD=major depressive disorder; ND=nicotine dependence; AUD=alcohol use disorder; CUD=cannabis use disorder. Sample sizes under "Parents" columns refer to the number of parents of the indicated type of youth (adopted or non-adopted) who provided data on their own psychopathology for this study. Parents with both one adopted and one non-adopted child are included under "Parents of Adopted Youth."

Table 2Prevalence (%) of disorders among adolescents, by parental disorder and adoption status¹

	MDD			ND			AUD			CUD		
	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted
Parental MDD:												
Either parent MDD:												
Yes	39.8	34.0	22.8	21.0	21.6	23.7	22.4	19.9				
No	24.1	19.5	18.5	12.5	20.5	21.9	15.2	18.8				
Maternal MDD:												
Yes	41.5	40.7	23.4	23.3	22.4	25.8	23.5	20.2				
No	27.0	18.0	20.0	12.5	20.3	20.8	15.7	18.6				
Paternal MDD:												
Yes	39.3	25.0	23.3	18.3	21.2	20.3	19.8	18.6				
No	29.1	25.8	19.8	13.4	21.0	21.5	17.2	18.5				
Parental ND:												
Either parent ND:												
Yes	32.8	32.8	24.4	23.9	21.4	28.3	17.2	26.3				
No	30.1	19.8	17.6	8.8	20.7	17.6	17.7	11.9				
Maternal ND:												
Yes	34.9	35.2	30.1	27.1	27.5	29.4	23.3	31.8				
No	30.9	21.9	19.1	12.8	19.4	20.5	16.9	15.9				
Paternal ND:												
Yes	31.3	35.8	23.6	23.4	21.4	27.3	14.9	26.0				
No	30.5	19.0	18.8	9.2	20.9	18.0	19.2	14.4				
Parental AUD:												
Either parent AUD:												
Yes	28.8	28.9	21.2	17.2	20.8	31.2	13.0	25.6				
No	31.6	23.8	19.6	13.8	21.1	16.3	20.3	14.8				
Maternal AUD:												
Yes	42.5	39.3	25.0	21.8	25.6	34.6	17.5	34.6				
No	30.9	22.3	20.9	14.7	20.6	20.3	18.2	16.7				
Paternal AUD:												

	MDD		ND		AUD		CUD	
	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted	Adopted	Non-adopted
Yes	28.7	23.9	21.3	14.9	22.0	27.6	14.0	23.3
No	31.9	26.1	20.1	14.0	20.7	17.7	19.5	15.8
Parental CUD:								
Either parent CUD:								
Yes	30.1	34.5	22.2	20.5	21.6	29.6	18.8	30.5
No	30.8	20.4	19.5	12.2	21.1	17.0	17.8	11.7
Maternal CUD:								
Yes	33.3	36.7	26.1	29.2	28.9	27.1	26.1	37.5
No	31.5	23.2	20.7	14.1	20.2	21.6	17.4	16.6
Paternal CUD:								
Yes	29.9	36.0	23.9	19.1	22.0	30.5	15.2	32.7
No	31.0	20.5	19.7	12.3	20.9	17.5	18.3	12.7

MDD=major depressive disorder; ND=nicotine dependence; AUD=alcohol use disorder; CUD=cannabis use disorder.

¹ Because some families had two affected parents and families where data on one parent was missing could not be included in the “either parent affected” analyses if the participating parent was unaffected, the rates for the “either parent” rows cannot be estimated from the rates for each parent considered separately.

Table 3

Associations between parental disorders and offspring disorders, by adoption status.

	Adolescent MDD			Adolescent ND			Adolescent AUD			Adolescent CUD		
	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption
Parental MDD:	2.13 *** (1.46–3.11)	1.95 ** (1.20–3.17)	.07	1.30 (.82–2.07)	1.80 (.98–3.30)	.76	1.08 (.69–1.69)	1.04 (.61–1.76)	.00	1.62 (.99–2.68)	1.09 (.61–1.94)	1.01
Parental ND:	1.12 (.76–1.65)	1.99 ** (1.21–3.27)	3.57	1.38 (.86–2.22)	3.43 *** (1.78–6.59)	4.60 *	.94 (.59–1.50)	1.79 * (1.06–3.01)	3.80 *	.90 (.53–1.53)	2.71 ** (1.45–5.08)	7.48 **
Parental AUDs:	.94 (.63–1.41)	1.22 (.75–2.00)	.68	1.21 (.76–1.95)	1.31 (.69–2.48)	.01	.99 (.61–1.59)	2.40 ** (1.39–4.13)	6.09 *	.58 * (.34–1.00)	2.10 * (1.15–3.84)	10.04 **
Parental CUDs:	1.02 (.65–1.62)	2.17 ** (1.34–3.52)	4.51 *	1.47 (.87–2.49)	1.95 * (1.05–3.61)	.47	1.20 (.73–1.97)	2.21 ** (1.27–3.85)	2.45	1.21 (.67–2.20)	3.53 *** (1.90–6.56)	6.05 *

* *p* .05;
** *p* .01;
*** *p* .001.

MDD=major depressive disorder; ND=nicotine dependence; AUD=alcohol use disorder; CUD=cannabis use disorder. All effects are adjusted for adolescent gender, age, and ethnicity. Interaction effects by adoption status are represented by chi-square values. All chi-square analyses are on 1 degree of freedom. All odds ratios are accompanied by 95% confidence intervals.

Table 4

Associations between maternal and paternal disorders and offspring disorders, by adoption status.

	Adolescent MDD			Adolescent ND			Adolescent AUD			Adolescent CUD		
	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption	Adopted OR	Non- adopted OR	Parental disorder × adoption
Maternal Diagnoses:												
MDD:	1.99*** (1.35–2.93)	2.93*** (1.81–4.77)	1.58	1.20 (.76–1.91)	1.97* (1.05–3.70)	1.49	1.12 (.71–1.76)	1.17 (.68–2.02)	.08	1.63 (.98–2.71)	1.07 (.58–1.96)	1.06
ND:	1.26 (.78–2.03)	1.82* (1.02–3.22)	1.09	1.75* (.99–3.10)	2.39** (1.26–4.55)	.46	1.45 (.86–2.47)	1.45 (.78–2.70)	.01	1.39 (.77–2.53)	2.49** (1.37–4.54)	1.95
AUDs:	1.82 (.91–3.67)	2.39** (1.27–4.48)	.29	1.31 (.55–3.08)	1.76 (.70–4.39)	.21	1.32 (.59–2.96)	2.41* (1.15–5.06)	1.03	.92 (.39–2.16)	2.92** (1.49–5.72)	4.40*
CUDs:	1.24 (.68–2.28)	1.96 (.98–3.91)	.98	1.69 (.77–3.71)	2.78** (1.37–5.64)	.92	1.83* (1.02–3.29)	1.42 (.65–3.11)	.32	1.85 (.82–4.15)	3.38*** (1.70–6.74)	1.30
Paternal Diagnoses:												
MDD:	1.67* (1.02–2.71)	.92 (.48–1.77)	1.96	1.34 (.72–2.49)	1.38 (.63–3.03)	.02	1.07 (.57–2.01)	.90 (.49–1.66)	.13	1.18 (.63–2.24)	1.04 (.52–2.08)	.09
ND:	1.02 (.69–1.51)	2.47*** (1.49–4.11)	7.65**	1.29 (.79–2.12)	3.15*** (1.64–6.07)	4.27*	.99 (.60–1.63)	1.69 (.98–2.92)	2.29	.71 (.40–1.27)	2.09* (1.13–3.86)	6.47**
AUDs:	.91 (.60–1.38)	.82 (.49–1.38)	.10	1.21 (.74–1.96)	1.05 (.54–2.06)	.18	1.12 (.69–1.82)	1.73 (.98–3.03)	1.35	.68 (.39–1.16)	1.66 (.89–3.10)	4.70*
CUDs:	1.00 (.60–1.65)	2.29*** (1.41–3.71)	5.17*	1.52 (.88–2.61)	1.71 (.89–3.30)	.09	1.20 (.70–2.05)	2.24** (1.27–3.97)	2.24	.86 (.46–1.62)	3.53*** (1.90–6.56)	9.66**

*
p .05;
**
p .01;

p .001.

MDD=major depressive disorder; ND=nicotine dependence; AUD=alcohol use disorder; CUD=cannabis use disorder. All effects are adjusted for adolescent gender, age, and ethnicity. Interaction effects by adoption status are represented by chi-square values. All chi-square analyses are on 1 degree of freedom. All odds ratios are accompanied by 95% confidence intervals.