Published in final edited form as:
Addiction. 2008 June ; 103(6): 990–997. doi:10.1111/j.1360-0443.2008.02210.x.

The association between cannabis abuse and dependence and childhood physical and sexual abuse: Evidence from an offspring of twins design:

Cannabis use disorder and child abuse

Alexis E. Duncan, Ph.D.[1,*], **Carolyn E. Sartor, Ph.D.**[1,3], **Jeffrey F. Scherrer, Ph.D.**[1,2], **Julia D. Grant, Ph.D.**[1], **Andrew C. Heath, D.Phil.**[1], **Elliot C. Nelson, M.D.**[1], **Theodore Jacob, Ph.D.**[3], and **Kathleen Keenan Bucholz, Ph.D.**[1]

1 *Midwest Alcoholism Research Center, Department of Psychiatry, Washington University School of Medicine, St. Louis, MO*

2 *St. Louis Veterans Administration Medical Center, Research Service, St. Louis, MO*

3 *Palo Alto Veterans Affairs Health Care System, Menlo Park, CA*

Abstract

Aims—*T*his study examines the association between childhood physical abuse (CPA) and sexual abuse (CSA) and the development of cannabis abuse and dependence among adolescents and young adults while controlling for genetic and environmental risk factors.

Design—To control for familial risk differences related to paternal drug dependence that might confound the relationship between CSA and CPA and cannabis abuse/dependence, we created four groups based on father's and uncle's substance use dependence (SUD) status reflecting different degrees of genetic and environmental risks to offspring: 1) high genetic, high environmental risk; 2) high genetic, low environmental risk, 3) medium genetic, low environmental risk; and 4) low genetic, low environmental risk.

Participants—Adolescent and young adult offspring of monozygotic and dizygotic US military veteran twin fathers (n= 819).

Measurements—Data on CPA and CSA, DSM-IV offspring cannabis abuse/dependence, other SUD and psychopathology, and maternal and paternal SUD and psychopathology were collected via semi-structured telephone interview.

Findings—Twenty-three percent of the offspring sample met lifetime criteria for cannabis abuse/dependence, 8.55% and 12.82% reported CSA and CPA, respectively. Offspring exposed to CSA, but not CPA, were at significantly greater risk of developing cannabis abuse/dependence compared to those who had not experienced CSA (HR=2.16; 95% CI=1.48–3.16) after controlling for genetic and familial environmental risk and offspring gender, alcohol abuse and dependence and conduct disorder.

Conclusions—These results indicate that there are effects of CSA on development of cannabis abuse/dependence in addition to the genetic and familial environmental risk imparted by having a drug dependent father.

*Correspondence to: Alexis E. Duncan, Ph.D., Department of Psychiatry, Washington University School of Medicine, 660 S. Euclid, Box 8134, St. Louis, MO 63110, 314-286-2210 (phone), 314-286-2213 (fax), duncana@psychiatry.wustl.edu.

Keywords

physical abuse; sexual abuse; cannabis abuse and dependence; offspring of twins

Introduction

Childhood sexual abuse (CSA) and childhood physical abuse (CPA) have been identified as risk factors for the development of substance-related problems during adolescence and adulthood (1–4). Both CSA and CPA have been associated with illicit drug use in adolescents and young adults (5–12) as well as higher prevalence of multi-substance use (5) and substance use disorders (SUDs) (10–14). Parental SUD has been identified as a risk factor for CSA and CPA as well as for SUD in offspring (1;15–17).

CPA and CSA frequently occur in families with elevated rates of other risk factors for the development of SUDs, such as marital discord, parental substance use problems, and low parent-child attachment (16) that reflect an overall dysfunctional family environment (10). The relationship between CSA and CPA and SUDs may be a direct one in which CPA and/or CSA leads to problem substance use, potentially as a means of attempting to regulate negative affect associated with the abuse. Alternatively, there may be an indirect relationship in which both abuse and SUDs result from a shared risk factor, such as parental SUD itself or with risk factors associated with parental SUD (e.g., poor parental supervision (17) or parental psychopathology (16–18)). SUDs may also be secondary to psychiatric disorders that result from exposure to abuse (e.g., depression) (4).

A number of investigations seeking to clarify the nature of the relationship between childhood abuse and SUDs have measured and adjusted for the influences of other relevant familial risk factors, including alcohol and drug problems in parents, which are associated with increased risk of exposure to CPA and CSA (17;18). In combination with the literature demonstrating family history of drug and alcohol problems as a risk factor for SUDs, these findings suggest the potential role of parental SUDs as mediators of the association between offspring substance use problems and abuse history. Whether offspring SUDs are the result of a purely indirect relationship is unknown, although existing evidence is not strong. After adjusting for family history reports of parental SUDs and psychopathology, many studies have demonstrated a significant association between SUDs and CSA (1;10;11;19) or CPA (2).

The current study seeks to extend the existing literature by using an offspring of twins (OOT) study design to determine whether CSA and CPA are associated with elevated risk for cannabis abuse and dependence (CA/D) after adjusting for genetic and environmental risk and relevant confounders. The OOT design, also called “pseudo-adoption study,” includes offspring hypothesized to be at varying levels of genetic and environmental risks for SUDs based on their father’s affected (in this case, drug dependence) status as well as the status of their father’s co-twin (e.g., (20). This design enabled us to control for potential mediating effects of parental SUDs and to distinguish the role of family environment associated with paternal drug dependence from that of genetic liability to SUDs.

Methods

Participants were offspring of male twins who were members of the Vietnam Era Twin Registry (VETR), a national registry of male like-sex twin pairs both of whom served in the military during the Vietnam Era (1965– 1975). Construction of the registry (21;22) and method of determining zygosity have been previously reported (23). The VETR is maintained by custodians at the VA Puget Sound Health Care System. Selection of families was based on

information collected from the twin-fathers in a 1987 survey of general health, in which birth dates of their children (among other items) were obtained, and in a 1992 structured diagnostic psychiatric telephone interview that assessed DSM-III-R drug dependence (DD) disorder history and other psychiatric diagnoses in the twins. In 2002, we began an offspring of twins (OOT) study examining genetic and environmental influences on the inter-generational transmission of illicit DD. Criteria for selection into the present study included membership in a twin pair in which: (i) both completed the 1987 questionnaire and the 1992 interview; (ii) at least one member of the pair had a child born between 1973 and 1987, and (iii) the twin pair was identified as concordant or discordant for DSM-III-R lifetime DD, or as a member of a control pair without DD.

The twin sample was selected using a 4-group OOT design reflecting differing degrees of genetic and environmental risks for DD to offspring. Group 1 (n=511 offspring) consists of fathers with DD, regardless of zygosity, whose offspring are at both high genetic and high environmental risk ("HG-HE") because their fathers have a history of DD. The majority were reared in a household with a DD father (80% lived with their biological father from birth to age 18, or age at interview if <18 years old, and < 1% never lived with their father). Also included in this group are fathers with alcohol dependence (AD) whose cotwins have DD. Groups 2 (n=68 offspring) and 3 (n=72 offspring) are comprised of fathers without DD or AD but whose monozygotic (MZ) cotwin (Group 2) or dizygotic (DZ) cotwin (Group 3) has DD. These offspring are therefore at high (Group 2) or moderate (Group 3) genetic risk by virtue of having a father whose identical or fraternal twin had DD, but at low environmental risk, because they were not reared by a father with DD ("HG-LE"/"MG-LE"). Finally, Group 4 (n=168 offspring) is a random sample of men without DD with non-DD co-twins. Their offspring are at low genetic and low environmental risk ("LG-LE"). This novel study design offers the possibility of differentiating genetic and familial environmental risk to offspring, based on their father's and uncle's DD status. The four group design can also be included in multivariable modeling to control for the sampling design.

An experienced staff of lay interviewers from the Institute for Survey Research (ISR) at Temple University conducted data collection in 2002–03. All participants gave verbal informed consent prior to being interviewed, as approved by the Institutional Review Board at the participating universities. In addition, twin parents of minor offspring provided written consent for those offspring to be recruited, although mothers retained the right to refuse participation for their minor offspring. Offspring also retained the right to refuse.

The 2002–03 telephone interview with the father covered sociodemographic information, relationships with his children, and smoking, lifetime drinking, and updated drug use histories. During the interview, permission was obtained to contact the biological mother of his offspring as well as the offspring themselves. The maternal telephone interview, conducted in 2003, covered her own DSM-IV history of alcohol abuse (AA) and AD, major depression, drug abuse (DA) and DD, and included screens for nicotine dependence, mania, antisocial personality, and drinking, smoking and drug use during each of her pregnancies with the offspring. In addition, mothers reported on offspring attention deficit-hyperactivity disorder, oppositional defiant disorder, and conduct disorder (CD), and family background. The offspring interview was a modification of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), which has been shown to be a reliable and valid instrument (24;25). The interview covered items that operationalized DSM-IV lifetime criteria for AA/AD, DA/DD, nicotine dependence, major depression, CD, and several other diagnostic and non-diagnostic sections. One such section assessed nine traumatic events, including rape, molestation and physical abuse, using an adaptation of the trauma assessment from the National Comorbidity Study (26). In addition, parental discipline and forced sexual intercourse were assessed in the home environment and sexual maturation sections of the interview, respectively.

Of 910 fathers targeted for data collection, 15 were incarcerated, too ill to participate or deceased. Eighty-one percent (n=725) of the remaining 895 twins were interviewed. Among 601 mothers identified by fathers, 444 completed the eligibility screen and 427 (72.8%) met eligibility criteria and were interviewed. Fathers gave consent to contact 950 offspring, of whom 839 (88.3%; mean age (SD)=22.64(4.44) years) took part in the 2003–2004 interview. There were no significant differences in age at interview across risk groups.

We were able to study non-response bias in the present study using data from the 1992 the twin-father diagnostic interview. Fathers with less than a high school education (56.4% vs. 77.1%; p<.01) and those without a history of any illicit DD (73.6% vs. 79.1%; p<.04) were less likely to respond, and mothers were less likely to be interviewed if not currently married to the twin father (53.8% vs. 78.4%; p<.01), or if the father was of a racial minority (49.0% vs. 76.0%; p<.01). Offspring of DZ twins (85.9% vs. 90.9%; p<.05) and of fathers who were not married to their biological mothers were also less likely to have been interviewed (79.1% vs. 90.5%; p<0.01), reflecting greater difficulty in locating those without maternal information (adult age offspring only).

The primary outcome variable in these analyses was offspring self-reported CA/D. An individual was considered to have a cannabis abuse diagnosis if he or she endorsed any of the four DSM-IV cannibis abuse criteria and was considered to have cannabis dependence if they endorsed three or more of seven cannabis dependence symptoms, including withdrawal. The clustering criterion was ignored because of the relative youth of the sample. One hundred twenty individuals (14.7%) had a diagnosis of cannabis abuse only, 7 (0.9%) had a diagnosis of cannabis dependence only and 61 (7.4%) met criteria for both cannabis abuse and dependence. Onset of CA/D was defined as the age at onset of the first symptom of CA/D among those with a diagnosis.

Separate variables were constructed to reflect CPA and CSA. An individual was considered to have experienced CPA if he or she a) reported having been physically abused before the age of 16 in the traumatic events section of the interview, or b) answered “yes” to “When you were 6 to 12, did any adult ever physically injure or hurt you on purpose?” from the early home environment section or c) reported “often” being “punched or hit with a belt or stick or something like that by your mother or father?” between ages 6 to 12. “Often” was chosen as the only response to indicate CPA because other response choices were endorsed by an inordinately large proportion of the sample (had individuals responding “sometimes” and “rarely” been considered affected, 51% of the sample would have considered to have experienced CPA). All instances of physical abuse began before age 16. CSA was considered to have occurred if an individual reported having been a) raped or b) sexually molested before age 16 (in the trauma section of the interview) or c) forced to have sex before age 16 (in the sexual maturation section of the interview). Age 16 is a commonly used cutoff for CSA (e.g., (27;28)). Preliminary analyses confirmed that CSA & CPA each could be collapsed into 2-level variables (present/absent).”

Data analysis was conducted using SAS (29) and Stata, version 8 (30). Given the non-independence of observations inherent in the OOT design, p-values for bivariate analyses were adjusted for clustering using the method of Rao and Scott (1984), which corrects for the family clustering in the data and converts the chi-square into an F statistic (31). Cox proportional hazards models with time dependent covariates were used for multivariate regression for time-to-event data (32). Data were transformed into a “person years” format with each individual having a row of data for each year of his or her life. For a given time dependent variable (CSA, CD, major depression, AD, nicotine dependence), an individual is coded zero for each line of data until he or she reaches the age of onset, after which the variable is coded one. Fixed covariates (e.g., race) or covariates for which age of onset were not available (e.g., physical

abuse, for which individuals were asked if the experience occurred between the ages of 6 and 12 in the early home environment section) were coded as time-invariant, i.e., one on all rows of data for a given participant.

In the present study the outcome was onset of CA/D, which was defined as onset of first CA/D symptom. Separate variables for CPA and CSA, as well as dummy variables representing the 4-group risk design (with Group 4 [LG-LE] serving as the referent) comprised the base model. Demographic variables and offspring, maternal, and paternal diagnostic variables were assessed as potential confounders and effect modifiers of the relationship between CPA and CSA and CA/D by adding the variables into the base model one at a time. If the hazard ratio (HR) for either CPA or CSA changed by more than 10%, the variable was judged to be a confounder and was retained in the model (33). If the HRs changed less than 10%, the variable was dropped from the model. Effect modification was assessed by entering two way interactions between the variable in question and CPA or CSA into the model. If a variable interacted significantly with CSA or CPA, it was considered an effect modifier. Offspring characteristics assessed in this manner were gender, living separately from the father for ≥12 months before age 18 (or age at interview for respondents younger than 18) and DSM-IV major depression, nicotine dependence, AA/AD and CD, with the psychiatric diagnoses included as time dependent covariates. Other illicit DA/DD was not included in the model because onset of CA/D preceded onset of other DA/DD in all but five cases. Based on the literature, paternal covariates considered were past-year income (from the 2002–03 interview) and DSM-III-R antisocial personality disorder (ASPD), AA/AD, nicotine dependence and major depression. Maternal regular smoking (100+ cigarettes lifetime) and DSM-IV AA/AD, DA/DD, major depression, and CD were also examined. There were no data on the mothers of 164 (20.2%) offspring. The prevalence of missing maternal data did not differ significantly among risk groups. Maternal variables were entered into the model as a set of 2 dummy variables representing missing maternal data and mother affected, with the reference category being mother unaffected. Once the final model was obtained, the proportional hazards assumption that risk remains constant over time was assessed using the Grambsch and Therneau test of the Schoenfeld residuals (34). Confidence intervals were adjusted for family clustering using Huber-White robust standard errors.

Results

Due to missing data, 20 (2.38%) offspring in the sample were not included in the present analyses, including three people (0.36%) who were excluded because they had their first CA/D symptom before CSA/CPA onset. Of the remaining 819, 458 (55.92%) had ever used cannabis, 327 (39.93%) had used cannabis ≥6 times and 188 (22.95%) met criteria for CA/D (68 [8.30%] with dependence and 120 [14.65%] with abuse only). The average age of onset of first symptom of CA/D in those with a diagnosis was 15.99 years (range 12–25 years, SD=2.01), and did not differ by CSA or CPA status. The most frequently endorsed CA/D symptom among those with a diagnosis was the hazardous use symptom of abuse (93.09%) and the least frequently endorsed was the legal problems abuse symptom (5.32%). Seventy offspring (8.55%; 13.96% of women and 3.53% of men) had experienced CSA, 105 (12.82%; 10.41% of women and 15.06% of men) had experienced CPA. Of the 175 offspring who had experienced either CSA or CPA, 10.29% (n=18) had experienced both forms of abuse (25.45% of women and 26.67% of men). CPA was more common in HG-HE group members than in members of the other risk groups (16.24% vs. 4.76 – 6.55%; p=.011); however, there were no significant differences in CSA rates between risk groups. Rates of demographic variables, childhood abuse, and offspring, paternal and maternal psychopathology and SUDs by presence or absence of CA/D are presented in Table 1. Compared to offspring without CA/D, offspring with CA/D were significantly more likely to have experienced CSA, but not CPA, before the age of 16. They were also significantly older than those without CA/D and were more likely

to be male, to have lived separately from their fathers for 12 months or longer during childhood, to be in the HG-HE group, and to have AA/AD, CD, major depression, nicotine dependence and any other illicit DA/DD than offspring without CA/D. Offspring with CA/D were also more likely to have mothers with a history of CD, and fathers with lifetime ASPD and nicotine dependence than those without CA/D.

In separate Cox proportional hazards models with CSA or CPA as the sole predictor of onset of CA/D, CSA (HR=2.11; 95% CI: 1.46–3.05), but not CPA (HR=1.32; 95% CI: 0.89–1.97), was associated with increased risk for CA/D. Results from the multivariable Cox proportional hazards models are presented in Table 2. In the base model, which consisted of CSA, CPA, and dummy variables for the 4 group design, only CSA (HR=2.01; 95% CI: 1.37–2.95) and membership in the HG-HE risk group (HR=1.92; 95% CI: 1.21–3.04) were significant predictors of CA/D. The interaction between CSA and CPA was not significant (HR: 0.48; 95% CI: 0.19–1.23; not shown). Offspring male gender, AA/AD and CD confounded the relationship between CPA and/or CSA and CA/D and were therefore retained in the final model, although none of the interactions between these covariates and the CSA and CPA variables were statistically significant. Because there was a violation of the proportional hazards assumption for CD, separate hazard ratios were estimated for CD for the age periods before 16 and age 16+. In the final model, CSA, adjusted for CPA, genetic and environmental risk groups, male gender, and offspring AA/AD and CD, was a significant predictor of CA/D (HR=2.27; 95% CI: 1.48–3.17); however, the effect of CPA was reduced and not statistically significant. The effect of being in the HG-HE paternal risk group was also reduced (HR=1.40 vs. 1.92) and no longer statistically significant in the final model. Offspring AA/AD was, however, strongly associated with developing CA/D: those with an AA/AD diagnosis were over three times as likely to develop CA/D as those without AA/AD. Offspring CD imparted a substantially elevated risk of CA/D onset before age 16 (HR=7.36; 95% CI: 4.60 – 11.79) and was associated with a much lower, but still significant, risk of CA/D onset at age 16 or older (HR=1.84; 95% CI: 1.17 – 2.90). None of the parental variables were retained in the model, as they did not impact the strength of the relationship between CA/D and CSA or CPA.

Discussion

These results demonstrate that CSA is a significant predictor of CA/D, even after adjusting for CPA, genetic and environmental risk, gender, alcohol abuse and dependence, and CD. The association between CPA and CA/D in adjusted or unadjusted analyses was, however, not statistically significant. Additional offspring psychopathology and paternal and maternal psychopathology and SUD were not found to affect the relationships between CPA and CSA and CA/D.

These results are consistent with those of previous studies that found that individuals who had experienced CSA were significantly more likely to develop SUDs (10;12;14;19;28). The lack of association between CPA and CA/D in both adjusted and unadjusted models, however, is somewhat unexpected given previous findings. Several studies have reported CPA to be associated with marijuana and/or other illicit drug use in high school students (5;7;35;36). MacMillan et al (2001) found that women who had been physically abused had higher risk of SUDs, although the model was not adjusted for CSA or parental psychopathology (14). The discrepancy in our results could be a function of the more specific outcome (CA/D rather than cannabis use or any drug abuse or dependence).

This study is not without limitations. The assessments of CPA and CSA were brief and did not include questions regarding frequency, severity or the perpetrator of the abuse, all of which have been found to be associated with higher rates of SUDs (19;28). However, the prevalence of CSA in our sample (13.96% of women and 3.53% of men) is very similar to that reported

in other epidemiologic studies that have used more detailed assessments of CSA (e.g., 11;14;16;17). While the prevalence of CPA is somewhat low in comparison to that reported in the aforementioned studies, this was largely due to the decision to only consider as physical abuse a response of "often" to the question of whether respondents had been "punched or hit with a belt or stick or something like that by your mother or father?" between ages 6 to 12. Individuals who answered "sometimes," "rarely", or "never" were coded as unaffected. Including individuals answered "sometimes" as having experienced CPA, however, did not alter the results. Another potential limitation is that our interview did not include an assessment of posttraumatic stress disorder (PTSD), which has been shown to mediate or moderate the relationship between experience of traumatic events and substance use, abuse, and dependence (37;38). Inclusion of a PTSD module in our diagnostic interview could have given insight into the mechanism by which CSA leads to DA/D. This omission has been corrected in our current assessment, which is now in the field. Finally, the low prevalence of CSA among male respondents resulted in low power to detect an interaction between gender and CSA; therefore, it is possible that the relationship between CA/D and CSA differs by gender, despite the fact that the gender × CSA interaction was not statistically significant in our analyses.

It is of note that the majority of individuals with CA/D in our sample (93.09%) endorsed the hazardous use criterion of cannabis abuse, and 44.68% of those with CA/D met only the hazardous use criterion. To ensure that our findings were not an artifact of the hazardous use component of the abuse diagnosis, we investigated whether abusers who met the diagnosis by virtue of hazardous use only differed from those who met criteria for abuse without hazardous use or endorsed criteria in addition to hazardous use and did not find any significant associations with parental SES as indicated by household income, education levels, (either paternal or maternal) or with physical abuse (all p values $\geq$.483; data available from first author by request). Thus it is unlikely that our findings for the abuse/dependence diagnosis may be explained by the nosological vagaries of one criterion item sufficing for the abuse diagnosis.

This study is unique in that the OOT design allows for control of both genetic and familial environmental factors associated with paternal drug abuse and dependence, as well as unmeasured aspects of the environment imparted by paternal traits that may share a common genetic liability with drug abuse and dependence. Adjusting for familiality using a variable for paternal SUDs, as has been done in some previous studies (13;18;28), does not capture this additional component of risk associated with paternal substance dependence. Furthermore, our thorough diagnostic assessments of both maternal and paternal self-reported SUDs offer an advantage over some other studies, which have used the family history method to assess parental psychopathology and SUD (2;19). Finally, the fact that CSA, CPA, and all other covariates were only coded positive if the subjects reported that they occurred before onset of CA/D allows for a more accurate representation of the risk imparted by CSA and CPA than in some previous studies that did not assess the order of these events (e.g., (14)). Thus, it may be possible to draw causal inferences from the results presented here.

These results add to the literature indicating that CSA is an independent risk factor for any drug abuse and dependence. We did not find CPA to be associated with CA/D in bivariate or multivariate analyses. Future research is needed to investigate gender as a possible moderator of the relationship between CSA and CA/D as well as to explore the role of posttraumatic stress disorder in the causal pathway between CSA and CA/D.

Acknowledgements

This study was supported by grant DA14363 from the National Institute on Drug Abuse and grants AA11667, AA11822, AA07728, T32 AA07580-06 and Center Grant AA11998 from the National Institute on Alcohol Abuse and Alcoholism. The United States Department of Veterans Affairs has provided financial support for the development and maintenance of the VET Registry. Numerous organizations have provided invaluable assistance in the conduct of

this study, including: Department of Defense, National Personnel Records Center, National Archives and Records Administration, the Internal Revenue Service, National Opinion Research Center, National Research Council, National Academy of Sciences, and the Institute for Survey Research at Temple University. Most importantly, the authors gratefully acknowledge the continued cooperation and participation of the members of the VET Registry and their families. Without their contribution this research would not have been possible.

Reference List

1. Dinwiddie SH, Heath AC, Dunne MP, Bucholz KK, Madden PAF, Slutske WS, et al. Early sexual abuse and lifetime psychopathology: A co-twin-control study. Psych Med 2000;30:41–52.
2. Kilpatrick DG, Acierno R, Saunders B, Resnick HS, Best CL, Schnurr PP. Risk factors for adolescent substance abuse and depedence: Data from a national sample. Journal of Consulting & Clinical Psychology 2000;68(1):19–30. [PubMed: 10710837]
3. Simpson TL, Miller WR. Concomitance between childhood sexual and physical abuse and substance use problems: A review. Clin Psychol Rev 2002;22(1):27–77. [PubMed: 11793578]
4. Moncrieff J, Farmer R. Sexual abuse and the subsequent development of alcohol problems. Alcohol & Alcoholism 1998;33(6):592–601. [PubMed: 9872346]
5. Harrison PA, Fulkerson JA, Beebe TJ. Multiple substance use among adolescent physical and sexual abuse victims. Child Abuse & Neglect 1997;21(6):529–39. [PubMed: 9192142]
6. Edgardh K, Ormstad K. Prevalence and characteristics of sexual abuse in a national sample of Swedish seventeen-year-old boys and girls. Acta Paediatr 2000;88:310–9. [PubMed: 10772279]
7. Bensley LS, Spieker SJ, Van Eenwyk J, Schoder J. Self-reported abuse history and adolescent problem behaviors. II Alcohol and drug use. J Adolesc Health 1999;24:173–80. [PubMed: 10195800]
8. Dube SR, Felitti V, Dong M, Chapman DP, Giles WH, Anda RF. Childhood abuse, neglect, and household dysfunction and the risk of ilicit drug use: The Adverse Childhood Experiences Study. Pediatrics 2003;111(3):564–72. [PubMed: 12612237]
9. Hussey JM, Chang JJ, Kotch JB. Child maltreatment in the United States: Prevalence, risk factors, and adolescent health consequences. Pediatrics 2006;118:933–42. [PubMed: 16950983]
10. Kendler KS, Bulik CM, Silberg JL, Hettema JM, Myers J, Prescott CA. Childhood sexual abuse and adult psychiatric and substance use disorders in women: An epidemiological and cotwin control analysis. Arch Gen Psychiatry 2000;57:953–9. [PubMed: 11015813]
11. Nelson EC, Heath AC, Madden PAF, Cooper ML, Dinwiddie SH, Bucholz KK, et al. Association between self-reported childhood sexual abuse and adverse psychosocial outcomes: Results from a twin study. Arch Gen Psychiatry 2002;59:139–45. [PubMed: 11825135]
12. Nelson EC, Heath AC, Lynskey MT, Bucholz KK, Madden PAF, Statham DB, et al. Childhood sexual abuse and risks for licit and illicit drug-related outcomes: A twin study. Psych Med 2006;36(10): 1473–83.
13. Boden JM, Fergusson DM, Horwood LJ. Illicit drug use and dependence in a New Zealand birth cohort. Aust N Z J Psychiatry 2006;40:156–63. [PubMed: 16476134]
14. MacMillan HL, Fleming JE, Streiner DL, Lin E, Boyle MH, Jamieson E, et al. Childhood abuse and lifetime psychopathology in a community sample. Am J Psychiatry 2001;158(11):1878–83. [PubMed: 11691695]
15. Anda RF, Whitfield CL, Felitti VJ, Chapman D, Edwards VJ, Dube SR, et al. Adverse childhood experiences, alcoholic parents, and later risk of alcoholism and depression. Psychiatr Serv 2002;53:1001–9. [PubMed: 12161676]
16. Fergusson DM, Lynskey MT, Horwood LJ. Childhood sexual abuse and psychiatric disorder in young adulthood: I. Prevalence of sexual abuse and factors associated with sexual abuse. J Am Acad Child Adolesc Psychiatry 1996;35(10):1355–64. [PubMed: 8885590]
17. Walsh C, MacMillan HL, Jamieson E. The relationship between parental substance abuse and child maltreatment: Findings from the Ontario Health Supplement. Child Abuse & Neglect 2003;27(12): 1409–25. [PubMed: 14644058]
18. Vogeltanz ND, Wilsnack SC, Harris TR, Wilsnack RW, Wonderlich SA, Kristjanson AF. Prevalence and risk factors for childhood sexual abuse in women: National survey findings. Child Abuse & Neglect 1999;23(6):579–92. [PubMed: 10391515]

19. Molnar BE, Buka SL, Kessler RC. Child sexual abuse and subsequent psychopathology: Results from the National Comorbidity Survey. Am J Public Health 2001;91(5):753–60. [PubMed: 11344883]
20. Jacob T, Waterman B, Heath AC, True WR, Bucholz KK, Haber JR, et al. Genetic and environmental effects on offspring alcoholism: New insights using an offspring-of-twins design. Arch Gen Psychiatry 2003;60:1265–72. [PubMed: 14662559]
21. Eisen SA, True WR, Goldberg J, Henderson WG, Robinette CD. The Vietnam Era Twin (VET) Registry: Method of construction. Acta Geneticae Medicae et Gemellologiae (Roma) 1987;36:61–6.
22. Henderson WG, Eisen SA, Goldberg J, True WR, Barnes JE, Vitek ME. The Vietnam Era Twin Registry: A resource for medical research. Public Health Rep 1990;105(4):368–73. [PubMed: 2116638]
23. Eisen SA, Neuman RJ, Goldberg J, Rice J, True WR. Determining zygosity in the Vietnam Era Twin Registry: An approach using questionnaires. Clin Genet 1989;35:423–32. [PubMed: 2736790]
24. Bucholz KK, Cadoret R, Cloninger C, Dinwiddie SH, Hesselbrock VM, Nurnberger JI, et al. A new, semi-structured psychiatric interview for use in genetic linkage studies: A report of the reliability of the SSAGA. J Stud Alcohol 1994;55:149–58. [PubMed: 8189735]
25. Heath AC, Madden PAF, Grant JD, McLaughlin TL, Todorov AA, Bucholz KK. Resiliency factors protecting against teenage alcohol use and smoking: influences of religion, religious involvement and values, and ethnicity in the Missouri Adolescent Female Twin Study. Twin Res 1999;2:145–55. [PubMed: 10480749]
26. Kessler RC, Sonnega A, Evelyn B, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995;52:1048–60. [PubMed: 7492257]
27. al Mamun A, Alati R, O'Callaghan M, Hayatbakhsh MR, O'Callaghan FV, Najman JM, et al. Does childhood sexual abuse have an effect on young adults' nicotine disorder (dependence or withdrawal)? Evidence from a birth cohort study. Addiction. 2007eprint before publication
28. Fergusson DM, Horwood LJ, Lynskey MT. Childhood sexual abuse and psychiatric disorder in young adulthood: II. Psychiatric outcomes of childhood sexual abuse. J Am Acad Child Adolesc Psychiatry 1996;35(10):1365–74. [PubMed: 8885591]
29. SAS Institute. AS/STAT Users Guide, Version 8.00. Cary, NC: SAS Institute, Inc; 2000.
30. Stata Corporation. Stata Statistical Software: Release 8.2. College Station, TX: Stata Corporation; 2003.
31. Rao JNK, Scott AJ. On chi-squared tests for multiway contingency tables with cell proportions estimated from survey data. The Annals of Statistics 1984;12(1):46–60.
32. Cox DR. Regression models and life tables. Journal of the Royal Statistical Society 1972;34:187–220.
33. Greenland S. Modeling and variable selection in epidemiologic analysis. Am J Public Health 1989;79:340–9. [PubMed: 2916724]
34. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika 1994;81:515–26.
35. Diaz A, Simantov E, Rickert VI. Effect of abuse on health: Results of a national survey. Archives of Pediatrics & Adolescent Medicine 2002;156:811–7. [PubMed: 12144373]
36. Moran PB, Vuchinich S, Hall NK. Associations between types of maltreatment and substance use during adolescence. Child Abuse & Neglect 2004;28:565–74. [PubMed: 15159070]
37. Breslau N, Davis GC, Schultz LR. Posttraumatic stress disorder and the incidence of nicotine, alcohol, and other drug disorders in persons who have experienced trauma. Arch Gen Psychiatry 2004;60:289–94. [PubMed: 12622662]
38. Epstein JN, Saunders BE, Kilpatrick DG, Resnick HS. PTSD as a mediator between childhood rape and alcohol use in adult women. Child Abuse & Neglect 1998;22(3):223–34. [PubMed: 9589176]

Table 1

Characteristics of 819 offspring of twins. NOTE: All values are percentages unless otherwise indicated.

	Cannabis abuse or dependence								
	All			Men			Women		
Offspring variables	**Yes (n=188)**	**No (n=631)**	***p*-value**	**Yes (n=118)**	**No (n=307)**	***p*-value**	**Yes (n=70)**	**No (n=324)**	***p*-value**
Physical abuse	15.96	11.89	.164	17.80	14.01	.324	12.86	9.88	.460
Sexual abuse	15.96	6.34	<.001	10.17	0.98	<.001	25.71	11.42	.003
Mean age at interview (SD)	23.35 (3.59)	22.43 (4.67)	.013	23.69 (3.43)	22.31 (4.70)	.001	22.79 (3.81)	22.54 (4.60)	.655
Family income <40 K/year	37.77	35.78	.654	37.29	36.18	.842	38.57	35.40	.631
Four group paternal drug dependence design[1]									
Group 1: HGHE	72.34	59.43	.019	69.49	60.59	.083	77.14	58.33	.017
Group 2: HGLE	7.98	8.40		11.02	8.14		2.86	8.64	
Group 3: MGLE	6.38	9.51		4.24	10.42		10.00	8.64	
Group 4: LGLE	13.30	22.66		15.25	20.85		10.00	24.38	
Alcohol abuse or dependence	69.15	24.09	<.001	73.73	29.32	<.001	61.43	19.14	<.001
Nicotine dependence	30.81	7.51	<.001	30.77	8.22	<.001	30.88	6.83	<.001
Other illicit drug abuse or dependence	43.62	1.74	<.001	44.92	1.63	<.001	41.43	1.85	<.001
Conduct disorder[2]	45.74	8.40	<.001	56.78	14.98	<.001	27.14	2.16	<.001
Major depression	18.09	10.46	.006	15.25	7.82	.022	22.86	12.96	.034
Paternal lifetime psychiatric diagnostic variables									
Alcohol abuse or dependence	71.28	65.98	.216	67.80	67.10	.896	77.14	64.91	.068
Nicotine dependence	67.02	56.10	.013	66.95	54.07	.021	67.14	58.02	.164
Antisocial personality disorder	11.17	5.10	.009	8.47	3.92	.105	15.71	6.21	.010
Major depression	17.02	15.92	.740	19.93	19.49	.924	12.86	12.11	.865
Maternal lifetime psychiatric diagnostic variables									
Maternal data missing[3]	19.68	20.13	.902	20.34	18.57	.690	18.57	21.60	.589
Alcohol abuse or dependence	16.04	16.32	.873	11.86	17.43	.163	23.19	15.26	.078
Regular smoking[4]	43.62	41.52	.641	40.68	42.67	.723	48.57	40.43	.224
Drug abuse or dependence	12.23	9.98	.381	12.71	11.07	.620	11.43	8.95	.509
Conduct disorder	11.17	6.02	.021	10.17	6.51	.211	12.86	5.56	.014
Major depression	22.28	17.45	.190	16.52	17.67	.801	31.88	17.24	.003

	Cannabis abuse or dependence								
	All			Men			Women		
Offspring variables	**Yes (n=188)**	**No (n=631)**	***p*-value**	**Yes (n=118)**	**No (n=307)**	***p*-value**	**Yes (n=70)**	**No (n=324)**	***p*-value**

[1] HGHE: High genetic and low environmental risk; HGLE: High genetic and low environmental risk; MGLE: Medium genetic and low environmental risk; LGLE: Low genetic and low environmental risk

[2] Three or more conduct disorder symptoms

[3] Maternal data were only available for 655 offspring: 151 with and 504 without CAD.

[4] 100 or more cigarettes

Table 2

Results from the base and final Cox proportional hazards models of time to onset of cannabis abuse or dependence.

		95% Confidence Interval	
	Hazard Ratio	**Lower**	**Upper**
Base model			
Sexual Abuse	2.01	1.37	2.95
Physical Abuse	1.10	0.73	1.66
Paternal risk group:[1]			
Group 1 - HGHE	1.92	1.21	3.04
Group 2 - HGLE	1.52	0.75	3.05
Group 3 - MGLE	1.19	0.59	2.39
Group 4 – LGLE	1.00	--	--
Final model			
Sexual Abuse	2.16	1.48	3.16
Physical Abuse	0.74	0.50	1.10
Paternal risk group:[1]			
Group 1 - HGHE	1.40	0.88	2.12
Group 2 - HGLE	1.10	0.57	2.13
Group 3 - MGLE	1.01	0.49	2.11
Group 4 – LGLE	1.00	--	--
Male gender	1.23	0.90	1.69
Alcohol abuse or dependence	3.85	2.77	5.35
Conduct disorder[2] at ages <16 years	7.36	4.60	11.79
Conduct disorder[2] at ages ≥16 years	1.84	1.17	2.90

[1] HGHE: High genetic and low environmental risk; HGLE: High genetic and low environmental risk; MGLE: Medium genetic and low environmental risk; LGLE: Low genetic and low environmental risk

[2] Three or more conduct disorder symptoms