Published in final edited form as:
J Am Acad Child Adolesc Psychiatry. 2010 April ; 49(4): 321–431.

The Effects of Child Maltreatment and Inherited Liability on Antisocial Development: An Official Records Study

Melissa Jonson-Reid, Ph.D., **Ned Presnall, M.S.W.**, **Brett Drake, Ph.D.**, **Louis Fox, Ph.D.**, **Laura Bierut, M.D.**, **Wendy Reich, Ph.D.**, **Phyllis Kane, M.S.W.**, **Richard D. Todd, Ph.D., M.D.**, and **John N. Constantino, M.D.**
Dr. Jonson-Reid, Mr. Presnall, and Dr. Drake are with the George Warren Brown School of Social Work, Washington University, St. Louis Missouri; Dr. Fox, Dr. Bierut, Dr. Reich, and Mrs. Kane are with the Department of Psychiatry, Dr. Todd (posthumously) was with the Departments of Psychiatry and Genetics, and Dr. Constantino is with the Departments of Psychiatry and Pediatrics, Washington University School of Medicine, St. Louis, Missouri.

Abstract

Objective—Evidence is steadily accumulating that a preventable environmental hazard, child maltreatment, exerts causal influences on the development of long-standing patterns of antisocial behavior in humans. The relationship between child maltreatment and antisocial outcome, however, has never previously been tested in a large-scale study in which official-reports (rather than family-member reports) of child abuse and neglect were incorporated, and genetic influences comprehensively controlled for.

Method—We cross-referenced official-report data on child maltreatment from the Missouri Division of Social Services (DSS) with behavioral data from 4,432 epidemiologically-ascertained Missouri twins from the Missouri Twin Registry (MOTWIN). We performed a similar procedure for a clinically-ascertained sample of singleton children ascertained from families affected by alcohol dependence participating in the Collaborative Study on the Genetics of Alcoholism (COGA, n=428) in order to determine whether associations observed in the general population held true in an "enriched" sample at combined inherited and environmental risk for antisocial development.

Results—For both the twin and clinical samples, *additive* effects (not interactive effects) of maltreatment and inherited liability on antisocial development were confirmed, and were highly statistically significant.

Conclusions—Child maltreatment exhibited causal influence on antisocial outcome when controlling for inherited liability in both the general population and in a clinically-ascertained sample. Official-report maltreatment data represents a critical resource for resolving competing hypotheses on genetic and environmental causation of child psychopathology, and for assessing intervention outcomes in efforts to prevent antisocial development

Keywords

Conduct Disorder; genetics; child abuse; administrative data; externalizing behavior

Correspondence to: John N. Constantino, M.D., Washington University School of Medicine. 660 S. Euclid Avenue, Campus Box 8134, Saint Louis, Missouri 63110; Phone: 314-747-6772, FAX: 314-747-6777, constantino@wustl.edu.
We continue to be inspired by our memories of Henri Begleiter and Theodore Reich, founding PI and Co-PI of COGA, and also owe a debt of gratitude to other past organizers of COGA, including Ting-Kai Li, P. Michael Conneally, Raymond Crowe, and Wendy Reich, for their critical contributions.
This article is discussed in an editorial by Dr. Kaufman on page xxx.

Disclosure: Drs. Jonson-Reid, Drake, Fox, Beirut, Reich, Todd, and Constantino, and Mr. Presnall and Mrs. Kane report no biomedical financial interests or potential conflicts of interest.

INTRODUCTION

Decades of research have indicated that chronic patterns of serious antisocial behavior originate in childhood. [1] Child maltreatment is a known risk factor for the development of antisocial behavior[2], but studies to elucidate the nature of that association—specifically to establish causality—have historically been compromised by modest sample size, inadequate control for inherited influence on antisocial outcome, over reliance on self- or family-report of maltreatment, and/or ascertainment bias. Given that child maltreatment is preventable, [3] it is crucial to firmly establish its association with antisocial development in order to inform public policy on prevention. In this study we attempted to mitigate shortcomings of prior research by conducting a large-scale analysis of the effect of maltreatment on antisocial outcome in an epidemiologic sampling frame; one in which inherited factors were fully controlled (via the twin design) and the ascertainment of maltreatment was standardized by the use of official-report data acquired from a state administrative database.

Attempts to disentangle the relative contributions of the array of genetic and environmental factors that influence antisocial behavior have consistently supported a role for both nature and nurture. [3–6] Questions persist, however, about *which* aspects of the environment most critically influence antisocial development in the population. Following Widom's classic "Cycle of Violence" study [7], squarely implicating the salient role of child maltreatment, subsequent research has shown that inherited factors render some children particularly vulnerable to the effects of child abuse and neglect.[8] A landmark study by Caspi and colleagues [9] provided the first evidence of the interaction between a specific candidate gene (Monoamine Oxidase A) and the occurrence of child maltreatment predicting enduring patterns of antisocial behavior. A meta-analysis of subsequent studies examining that interaction [10] supported the original finding, but recent studies have also suggested that the magnitude-of-effect of inherited vulnerability (whether incurred by MAOA or other parameters of genetic risk) varies as a function of the presence or absence of numerous modifying factors such as gender, ethnicity, and the severity of adversity of life events. [11] [12] [13]

Historically, genetically-informative research on maltreatment and antisocial development has generally relied upon retrospective parent-or self-reports of maltreatment. Such reports suffer from a high prevalence of false negatives [14] as well as marginal reliability when multiple self-reports are collected over time, [15] or when compared with reports of other family members. [16] In contrast, due to their scope and demonstrated predictive capacity, official records represent an unparalleled resource for studying the broad-based impact of child maltreatment on public health. Unfortunately, the promise of combining official records of maltreatment with genetically-informative data has thus far remained largely unfulfilled. The prior studies that have done so [11] [13] had the limitation of controlling for allelic variation in a single gene (MAOA) rather than for the totality of genetic influences on outcome, which can be parameterized in a twin design, as employed in this study.

Thus, although an existing body of research has suggested that maltreatment is one of the most potent (and preventable) environmental influences on antisocial development, there remain persistent questions about the relative magnitude and impact of maltreatment in the general population, especially when controlling for inherited risk. We undertook this study to provide the first observation of the effects of maltreatment on the development of conduct problems in children using official-report maltreatment data in a large-scale epidemiologic twin sample.

Our research questions were: 1) Are children with official-reports of maltreatment in the general population at significantly higher risk of conduct problems, controlling for inherited liability? 2) Do the effects of official-report maltreatment observed in an epidemiologic sample

replicate in a clinically-ascertained contrast sample? 3) Are indices of inherited risk that might be feasibly ascertained in public health settings (e.g. by family history methods) robustly predictive of antisocial outcome? Demonstration of the relative contributions of officially-reported maltreatment and familial liability to antisocial development would lend further support to the allocation of specific and sustained targeted efforts to prevent maltreatment and maltreatment recidivism among vulnerable children in the United States.

METHOD

Sample

This study integrated pre-existing data from three sources: Official records of the Missouri Department of Social Services (DSS) covering the years from 1981 to 2008 (source 1) were cross-referenced with a) behavioral data from the Missouri Twin Registry (MOTWIN, source 2; birth years 1981–1996; study years 1989–2008), an epidemiologic twin sample ascertained from birth records; and b) behavioral and family history data on 7–21 year old family members of adults enrolled in the Collaborative Study on the Genetics of Alcoholism (COGA, source 3; birth years 1981–1996; study years 1989–2008), these adults were ascertained on the basis of alcohol dependence.

From the available data for each subject in COGA and MOTWIN, we derived and utilized personal identifiers, demographic data (gender, race, and birth year), zygosity (for MOTWIN), a polychotomous index of *familial liability to antisocial development*; and presence or absence of *antisocial outcome in the children*. All of the research information *except the identifiers* was encrypted. The encrypted information was submitted *with* identifiers to the DSS, where it was cross-referenced with official-report records at an individual level, and the linked data set was subsequently stripped of individual identifiers before returning to the research team.

The study was reviewed and approved by the Washington University Human Research Protection office (IRB), and authorized by the DSS, with a waiver of informed consent, a stipulation of which was that the research data set had to have the following characteristics (in order to avoid *any* possibility that individual subjects could be identified after the data merge procedure): 1) a low total number of variables; 2) each variable with a limited number of values; 3) no variables in which a given value would identify a specific subject or family.

Data preparation

The merged data set included 5,056 MOTWIN subjects and 511 COGA subjects To minimize the likelihood of matching the maltreatment registry as a perpetrator rather than as a victim, cases with reports occurring after age 17 were deleted (MOTWIN=106; COGA=3). Individuals younger than 17 rarely appear as perpetrators. Because of the demographics of the region, analyses were restricted to Caucasian and African-American subjects, those of other ethnicity or with missing race data were deleted (MOTWIN=56; COGA=31). A number of the subjects were removed due to missing familial liability data (MOTWIN=242; COGA=13) or missing socioeconomic status (SES) data (MOTWIN=220; COGA=36). The above resulted in a final analysis sample of 4,432 subjects in MOTWIN, 428 subjects in COGA.

MEASURES

Socioeconomic Status (SES)

In COGA, interview data was coded to determine whether total family income was below or above the federal poverty level. In MOTWIN, SES indices were estimated by the zip code of the family, [17] which is generally reliable in Missouri on the basis of relative income by geographic segregation; the data was then recoded according to poverty-level classifications.

Inherited liability for antisocial development

In this study inherited liability was parameterized using family history methods in two distinct ways, neither of which involved assays of specific genes. Because inherited liability is a lifetime construct, we selected the best available parameterization of lifetime-risk that could be derived from each respective sample.

In MOTWIN, inherited liability was parameterized by presence or absence of clinical-level externalizing behavior problems in the co-twin, according to the parent-report Child Behavior Checklist (CBCL). This yielded four levels of liability that were dummy coded in the following descending order of severity: Monozygotic (MZ) co-twin affected, dizygotic (DZ) co-twin affected, DZ co-twin unaffected, and MZ co-twin unaffected. Note that all twin pairs were reared together, so distinctions between MZ and DZ twin outcomes for a given co-twin status can be interpreted unequivocally as effects of gradations in inherited liability, [8] given the *equal environment assumption* that underlies all classic twin designs.

In COGA, which comprised a family design (rather than a twin design), affectation status of relatives (particularly parents) reflects both inherited and environmental risk. Thus, although it was possible to specify inherited influences in MOTWIN, the best that could be done in COGA was to parameterize familial risk, which represents an amalgam of genetic and environmental risk, against which independent effects of maltreatment can be examined. Not surprisingly, children in COGA with higher levels of familial risk ascertained in this way were, in addition, at higher risk for child maltreatment. We note that an ordinal index of presumptive risk for maltreatment using SES and life event data obtained throughout the multisite COGA network was found NOT to significantly correlate with official-report maltreatment data for children at the Washington University site.

The requirement for a low total number of variables prompted a decision to index inherited liability to antisocial development using all adult diagnoses known to be associated with offspring antisocial outcome: these include not only antisocial personality disorder (ASPD) (a severe form of antisocial behavior in adults) but also alcohol and/or substance dependence, which are more common predictors of offspring antisocial risk. Thus, in COGA, familial liability was parameterized by ascertaining the closest adult relative with either antisocial personality disorder, alcohol dependence, or drug dependence ascertained by a) the Semi-Structured Assessment for Genetics of Alcoholism (for parents, i.e. first degree adult relatives) and b) the Family Interview for Genetic Studies (FIGS) (for second or third degree relatives). Each child was consequently scored as having 1 of 2 levels of genetic liability: 1—closest relative with any of these disorders is a *first* degree relative; 2—closest relative with any of these disorders is a second degree or higher relative (over 96% of the children in the sample had either a 1^{st} or 2^{nd} degree adult relative with an antisocial disorder as operationalized here).

Official-report maltreatment/foster data

Because the state only retains official-report records of maltreatment for a limited number of years (see below), we limited the MOTWIN and COGA data to persons born 1981 or later, as noted above. Even with this limitation, the match could not be inclusive of all reports since birth, because many unsubstantiated reports were already purged according to legislative mandate. Thus, it is likely that the proportion of children with maltreatment reports identified in the match is an undercount. In contrast, the state data on foster care is not purged and is thus fully inclusive.

Official-reports included placement in foster care (FC), substantiated reports of maltreatment (SRM), unsubstantiated reports of maltreatment (URM), and referrals for preventive services (RPS) without allegation of maltreatment. It should be emphasized that according to the harm/

evidence model of substantiation, a substantiated report is not equivalent to verifying the presence of maltreatment but rather a label used when sufficient evidence and/or risk of harm exists to permit family court intervention if needed. [18] In Missouri, both substantiated and unsubstantiated cases have been eligible to receive in-home or foster care intervention for many years. RPS cases are not cases that are "bogus" or refused for investigation but includes serious family problems like homelessness that require referrals but do not rise to the legislative standard for abuse and neglect. In Missouri, attempts are made to provide referrals to these families to offset risk of subsequently turning into cases of abuse or neglect.

Despite substantial research documenting the relative equivalent risk for unsubstantiated or substantiated reports of child maltreatment [18–22], a records purge cycle was enacted by law in 2003, which mandated the purging of any unsubstantiated case without recurrence or service *within 3 years* and any substantiated cases without recurrence or services *within 10 years*. In other words, either the subsequent receipt of formal service or a recurrence before the purge date extends the retention period for the record. The total proportion of all records purged is unknown, but could represent up to one third of all reports ever made on the children in this study. Maltreatment recurrence following first-time reports in Missouri data is on the order of 50%. [23] We note that maltreatment report rates in Missouri have been fairly consistent over the period from 1997–2006. [24]

In the present study about 11.6% of the MOTWIN sample and 20% of the COGA sample had at least one of the four types of reports specified above; The MOTWIN figure is highly in keeping with published data on the prevalence of officially-reported maltreatment in the U.S. population. [25]

Finally, for MOTWIN, it is important to note that it was not possible to specify with confidence whether one twin or both were subjected to maltreatment; nor could we ascertain the age at which maltreatment first occurred, since a) date of first available report is not the same as the time when maltreatment began; and b) some of the reports represented recurrences of unsubstantiated maltreatment that occurred beyond the 3-year purge cycle. We note that neglect overwhelmingly likely affects all children in a family; however the data available to us did not differentiate abuse versus neglect.

Child mental health outcomes

In both samples, child mental health outcomes were characterized by parent-report, in MOTWIN using the Child Behavior Checklist [26] (which generates a quantitative severity score for current externalizing behavior that is highly predictive of DSM-IV Conduct Disorder Diagnosis), and in COGA using the child and adolescent versions of the Semi-Structured Assessment for the Genetics of Alcoholism. [27] The validity of parent-report methods for ascertaining enduring aspects of child and adolescent antisocial behavior is well-established. [28] Outcomes were dichotomized for the confidentiality reasons cited above.

For MOTWIN, a child or co-twin was designated *affected* if his/her total externalizing problem score fell at or above 60*T* on the parent-report CBCL (the published cutoff for clinical-level symptomatology for the overarching total internalizing and total externalizing problem domains; T-scores account for normal variation as a function of gender and age). For COGA, boys were designated affected if, at the time of assessment, they met three DSM-IIIR criteria for Conduct Disorder (CD); girls were designated affected if they met two DSM-IIIR criteria for CD. This gender-specific designation of affectedness ensures an approximately equal prevalence for boys- and girls-affected, and is consistent with prior research indicating that the psychosocial prognosis of girls with two CD symptoms is as poor as that for boys with three CD symptoms. [29]

Table 1a and Table 1b summarize selected sample characteristics and their bivariate relationships with indices of antisocial outcome and child welfare contact.

DATA ANALYSIS

Proportion of children with presence of antisocial outcome was plotted as a function of degree of familial liability and degree of maltreatment (none *versus* reported *versus* substantiated and/or placed in foster care) for each of the research samples (MOTWIN and COGA). Since, in the twin sample, affectation status of twin A was used to predict affectation status of twin B (and vice versa) subsequent analyses of the twin data considered the pair as the unit of observation , randomly selecting one twin from each pair to depict outcome, and the co-twin to parameterize familial risk. Comparisons of MZ *versus* DZ twins were performed to capture variation in outcome exclusively as a function of *inherited* liability; for this, we employed contingency table analysis, adjusting for zip code clustering.

Logistic regression was subsequently employed to establish the statistical significance of the relative contributions of familial liability and maltreatment on antisocial outcome. PROC SURVEY LOGISTIC in SAS was employed to allow control for clustering (by zip code in MOTWIN and by family in COGA). For these analyses, a nested approach to modeling was taken, so that the model fit and accompanying predictive statistics could be compared as variables were added, beginning with demographics only (Model 1) and progressing through models with the addition of the following variables: child welfare contact (Model 2); familial liability (Model 3); both (a full model (Model 4)); and a full model with interaction between familial liability and child welfare contact (Model 5). In addition to calculating odds ratios (OR) and significance levels, the Wald Chi-square for the sandwich estimator was calculated for model fit, along with the max rescaled r-square, and the c statistic corresponding to the receiver operating curve. The c statistics can be thought of similarly to a grading scale, with . 70 considered adequate, .8 considered good, etc. [30] Because there were so few FC cases they were grouped with SRM cases. Separate runs of analysis were conducted with centering the variables (using Proc Standard in SAS) to avoid spurious associations between reported familial liability, maltreatment, and offspring outcome. Centering did not significantly alter the results for either sample.

RESULTS

Prevalence of antisocial child outcome as a function of familial liability and official-report maltreatment history are depicted in Figure 1, panels A and B. In the epidemiologic twin sample (panel A), we observed a steady increase in the proportion of children with clinical-level elevation in CBCL externalizing score at increasing levels of familial liability (ascertained on the basis of co-twin status). In general, across all levels of familial liability, maltreatment was associated with a 10–25% increase in prevalence of child antisocial outcome, consistent with additive effects (not interactive effects) of inherited liability and maltreatment on antisocial outcome. To isolate the effects of inherited influence we examined discrepancies in externalizing outcome between MZ and DZ twins within each category subsumed by maltreatment and co-twin affectation status. Based on the close correspondence of the tracings for URM and SRM/FC in Figure 1A, we optimized statistical power for these analyses by collapsing these report types into a single maltreatment variable. Rao-Scott Chi-square = 2.79, p=.09 for *maltreated* identical versus non-identical co-twin affected; 6.45, p=.01 for *maltreated*, identical versus non-identical co-twin unaffected; 8.30, p=.004 for *non-maltreated*, identical versus non-identical co-twin affected; 12.16, p<.0005 for *non-maltreated*, identical versus non-identical co-twin unaffected.

Similar effects of familial liability and maltreatment were observed in the COGA sample (panel B); however there was much greater separation between SRM and URM than between URM and absence of maltreatment. Clearly, children with higher levels of familial loading for an antisocial disorder were more likely than their lower-risk counterparts to experience maltreatment, and this strongly suggested the presence of *correlated* genetic and environmental risks operating in this clinically-ascertained sample.

Hierarchical logistic regression analyses confirmed independent and statistically significant effects of both maltreatment and familial liability on antisocial development in children, as presented in Table 2A and Table 2B. In the best-fitting model for the twin sample (#4), odds ratios (OR) were 2.5–3.3 for reported maltreatment ($p<.0001$) and 1.9–19.6 for varying degrees of incremental familial risk ($p<.0001$). For the children in COGA, only substantiated or foster care status was significant among the maltreatment variables (OR=3.7 , $p=.003$ in the best-fitting model), and familial liability (as dichotomously characterized) was moderately associated with conduct problem outcome (OR= 1.9 in that model). There was no evidence to substantiate a statistically-significant interaction effect between familial liability and maltreatment in either model.

DISCUSSION

This is the first large-scale epidemiologic study of maltreatment and antisocial development to simultaneously control for inherited risk and employ administrative data (*official-report*) as the method of ascertaining maltreatment. Significant additive (though *not* interactive) effects of inherited liability and maltreatment were observed. The results in our large twin sample were substantially confirmed in an enriched clinical sample of children at combined genetic and environmental risk for antisocial development, with one notable difference. In the epidemiologic twin sample, the largest discrepancy in risk as a function of maltreatment severity occurs at the level of *reporting* of maltreatment, irrespective of whether the reports are substantiated. In the clinical sample, the greatest contrast was observed between children who were reported and those whose reports were actually substantiated, although we note that even among the non-maltreated children in the COGA sample, the prevalence of conduct disorder symptomatology was elevated (21%). It is possible that within the latter group—which comprised more densely affected families—either the high prevalence of child maltreatment reports (much higher than that observed in any of the twin groupings) or the nature of inherited risk within a sample ascertained on the basis of alcohol dependence, minimizes the relevance of non-report in a way that distinguishes substantiated reports as specific predictors of antisocial outcome. The data for *less* densely affected families in the COGA sample is more difficult to interpret because of sample size limitations.

In contrast to a number of previous research studies employing alternate designs [10], we did *not* observe statistically significant *interactive* effects of inherited liability and maltreatment on antisocial development, despite the fact that our observations of the influence of inherited factors were highly in keeping with those of previous studies. There are many possible reasons for this discrepancy in study outcomes. Use of official-report data results in the inclusion of severe forms of maltreatment that may be under-represented in studies relying on self-report. Although the presence of official-report of maltreatment may be a *more specific* indicator of environmental liability than any other known marker, the absence of such a report may underestimate such influence on the basis of a) instances of maltreatment that go unreported or b) in the case of Missouri, the expungement of some of the records after a specified number of years. Finally, our clinical sample of lower-familial-liability subjects may not have been large enough to demonstrate interactive effects. This study capitalized on the ability to consider the totality of inherited influences on antisocial outcome (rather than a single genetic factor) and to use official-report data. The results from both our population-based and clinically-

ascertained samples represent a convergence with the results of studies incorporating other designs affirming the deleterious effects of maltreatment even when controlling for inherited risk. Future studies of the *mechanisms* by which maltreatment results in enduring patterns of antisocial behavior (including the possible modulation of gene expression and/or direct effects of adverse life experience on neurobehavioral development) may lend new insights into intervention strategies for offsetting the long-term sequellae of maltreatment after it occurs..

The distinction between additive and interactive effects of genetic and environmental influence is relevant to preventive intervention strategies. Additive effects represent simple arithmetic accumulations of risk, such that mitigation of any single risk factor can only reduce the likelihood of an associated adverse outcome to the extent of that single factor's contribution. Interactive effects are, in contrast, multiplicative in nature, such that mitigation of a given risk factor simultaneously dismantles risk incurred by any other factor(s) with which it interacts to exert an effect on outcome.

This study had a number of other important limitations. The richness and range of variation in study variables had to be reduced by necessity, in order to preserve confidentiality and avert the possibility of individual identification of subjects (for whom individual informed consent was waived). Furthermore, the question of whether maltreatment occurred before or after the development of externalizing behavior was not resolvable in the current data set because the dates of earliest report of maltreatment werenot consistently available. Our analysis of the effects of birth year, coupled with a recent study of self-report maltreatment and psychopathology from over 3,000 twins and siblings [31] in the ADD Health Study, have suggested that the direction of causation is from maltreatment to abnormal behavior rather than the other way around.

Despite these limitations, this study reflects the potential scientific contributions that can be made when one of the most salient known environmental risk factors for human psychopathology, child maltreatment, is ascertained accurately and coupled with genetically-informative variables in epidemiologically-defined sampling frames. Official-report maltreatment data is available in every state in the U.S. but is rarely, if ever, used to test hypotheses about genetic *and* environmental causation for major mental health outcomes. We have demonstrated here an ethically acceptable method for harnessing large-scale official-report maltreatment data in the study of additive effects of genetic and environmental influence on developmental outcome, and encourage replication of this procedure using more specific indices of biological risk. It is also clear from this study that the loss of data incurred by the policy of expunging records after relatively brief intervals of developmental time compromise their power to elucidate the critical role of life events on human development from infancy through adulthood.

The results of this study support independent influences of inherited and environmental factors on the development of antisocial behavior in children, and that important parameters of risk can be estimated in large-scale studies by use of a) official-report records, and b) the straightforward and time-honored technique of obtaining a family psychiatric history. Efforts to support the environment and prevent maltreatment [3]—especially among children at elevated familial risk—continue to hold great promise for improving long-term social developmental outcome for our nation's youth.

Acknowledgments

This work was supported in part by The Collaborative Study on the Genetics of Alcoholism (COGA), Principal Investigators B. Porjesz, V. Hesselbrock, H. Edenberg, L. Bierut, includes nine different centers: University of Connecticut (V. Hesselbrock); Indiana University (H.J. Edenberg, J. Nurnberger Jr., T. Foroud); University of Iowa (S. Kuperman, J. Kramer); SUNY Downstate (B. Porjesz); Washington University in St. Louis (L. Bierut, A. Goate,

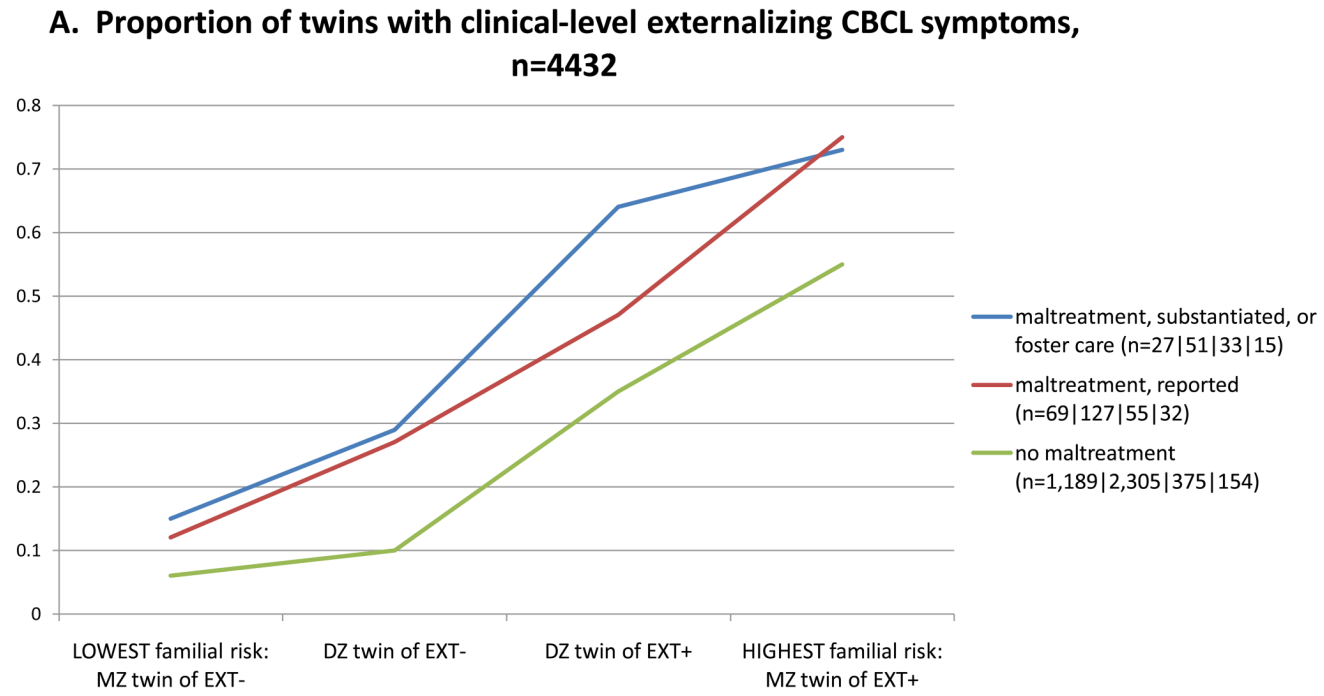
J. Rice, K. Bucholz); University of California at San Diego (M. Schuckit); Rutgers University (J. Tischfield); Southwest Foundation (L. Almasy), and Virginia Commonwealth University (D. Dick). A. Parsian and M. Reilly are the NIAAA Staff Collaborators and Robert Taylor serves as a consultant. This national collaborative study is supported by NIH Grant U10AA008401 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA).

The authors thank the Missouri Department of Social Services for its long-standing collaboration with the George Warren Brown School of Social Work and for facilitating the cross referencing of its administrative data with Washington University family study data as described in this manuscript.

REFERENCES

1. Moffitt TE, Arseneault L, Jaffee SR, et al. Research review: DSM-V conduct disorder: research needs for an evidence base. J Child Psychol Psychiatry 2008;49(1):3–33. [PubMed: 18181878]
2. Cohen P, Brown J, Smaile E. Child abuse and neglect and the development of mental disorders in the general population. Dev Psychopathol 2001;13(4):981–999. [PubMed: 11771917]
3. Olds DL, Sadler L, Kitzman H. Programs for parents of infants and toddlers: recent evidence from randomized trials. J Child Psychol Psychiatry 2007;48(3–4):355–391. [PubMed: 17355402]
4. Blazei RW, Iacono WG, McGue M. Father-child transmission of antisocial behavior: the moderating role of father's presence in the home. J Am Acad Child Adolesc Psychiatry 2008;47(4):406–415. [PubMed: 18388763]
5. Cadoret RJ, Yates WR, Troughton E, Woodworth G, Stewart MA. Genetic-environmental interaction in the genesis of aggressivity and conduct disorders. Arch Gen Psychiatry 1995;52(11):916–924. [PubMed: 7487340]
6. D'Onofrio BM, Slutske WS, Turkheimer E, et al. Intergenerational transmission of childhood conduct problems: a Children of Twins Study. Arch Gen Psychiatry 2007;64(7):820–829. [PubMed: 17606816]
7. Widom CS. The cycle of violence. Science 1989;244(4901):160–166. [PubMed: 2704995]
8. Jaffee SR, Caspi A, Moffitt TE, et al. Nature X nurture: genetic vulnerabilities interact with physical maltreatment to promote conduct problems. Dev Psychopathol 2005;17(1):67–84. [PubMed: 15971760]
9. Caspi A, McClay J, Moffitt TE, et al. Role of genotype in the cycle of violence in maltreated children. Science 2002;297(5582):851–854. [PubMed: 12161658]
10. Taylor A, Kim-Cohen J. Meta-analysis of gene-environment interactions in developmental psychopathology. Dev Psychopathol 2007;19(4):1029–1037. [PubMed: 17931432]
11. Widom CS, Brzustowicz LM. MAOA and the "cycle of violence:" childhood abuse and neglect, MAOA genotype, and risk for violent and antisocial behavior. Biol Psychiatry 2006;60(7):684–689. [PubMed: 16814261]
12. Hicks BM, South SC, Dirago AC, Iacono WG, McGue M. Environmental adversity and increasing genetic risk for externalizing disorders. Arch Gen Psychiatry 2009;66(6):640–648. [PubMed: 19487629]
13. Weder N, Yang BZ, Douglas-Palumberi H, et al. MAOA genotype, maltreatment, and aggressive behavior: the changing impact of genotype at varying levels of trauma. Biol Psychiatry 2009;65(5):417–424. [PubMed: 18996506]
14. Smith CA, Ireland TO, Thornberry TP, Elwyn L. Childhood maltreatment and antisocial behavior: comparison of self-reported and substantiated maltreatment. Am J Orthopsychiatry 2008;78(2):173–186. [PubMed: 18954181]
15. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. J Child Psychol Psychiatry 2004;45(2):260–273. [PubMed: 14982240]
16. Tajima EA, Herrenkohl TI, Huang B, Whitney SD. Measuring child maltreatment: a comparison of prospective parent reports and retrospective adolescent reports. Am J Orthopsychiatry 2004;74(4):424–435. [PubMed: 15554804]
17. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health 1992;82(5):703–710. [PubMed: 1566949]

18. Drake B, Jonson-Reid M, Way I, Chung S. Substantiation and recidivism. Child Maltreat 2003;8(4): 248–260. [PubMed: 14604173]
19. Hussey JM, Marshall JM, English DJ, et al. Defining maltreatment according to substantiation: distinction without a difference? Child Abuse Negl 2005;29(5):479–492. [PubMed: 15970321]
20. Jonson-Reid M, Drake B, Kim J, Porterfield S, Han L. A prospective analysis of the relationship between reported child maltreatment and special education eligibility among poor children. Child Maltreat 2004;9(4):382–394. [PubMed: 15538037]
21. Kohl PL, Jonson-Reid M, Drake B. Time to leave substantiation behind: findings from a national probability study. Child Maltreat 2009;14(1):17–26. [PubMed: 18971346]
22. Leiter J, Myers KA, Zingraff MT. Substantiated and unsubstantiated cases of child maltreatment: Do their consequences differ? Social Work Research 1994;18(2):67–82.
23. Drake B, Jonson-Reid M, Sapokaite L. Re-reporting of child maltreatment: does participation in other public sector services moderate the likelihood of a second maltreatment report? Child Abuse Negl 2006;30(11):1201–1226. [PubMed: 17112587]
24. Missouri Department of Social Services Children's Division. Missoiuri child abuse and neglect, 2006 annual report. 2007
25. Theodore AD, Runyan DK. A medical research agenda for child maltreatment: negotiating the next steps. Pediatrics 1999;104(1 Pt 2):168–177. [PubMed: 10390285]
26. Achenbach, TM. The child behavior checklist. Burlington (VAT): University of Vermont: Department of Psychiatry; 1991.
27. Hesselbrock M, Easton C, Bucholz KK, Schuckit M, Hesselbrock V. A validity study of the SSAGA--a comparison with the SCAN. Addiction 1999;94(9):1361–1370. [PubMed: 10615721]
28. Koot HM, Verhulst FC. Prediction of children's referral to mental health and special education services from earlier adjustment. J Child Psychol Psychiatry 1992;33(4):717–729. [PubMed: 1601945]
29. Zoccolillo M, Tremblay R, Vitaro F. DSM-III-R and DSM-III criteria for conduct disorder in preadolescent girls: specific but insensitive. J Am Acad Child Adolesc Psychiatry 1996;35(4):461–470. [PubMed: 8919708]
30. Drake, B.; Jonson-Reid, M. Social Work Research Methods. From Conceptualization to Dissemination. Allyn & Bacon: 2008.
31. Jay Schulz-Heik R, Rhee SH, Silvern L, et al. Investigation of genetically mediated child effects on maltreatment. Behav Genet 2009;39(3):265–276. [PubMed: 19283463]



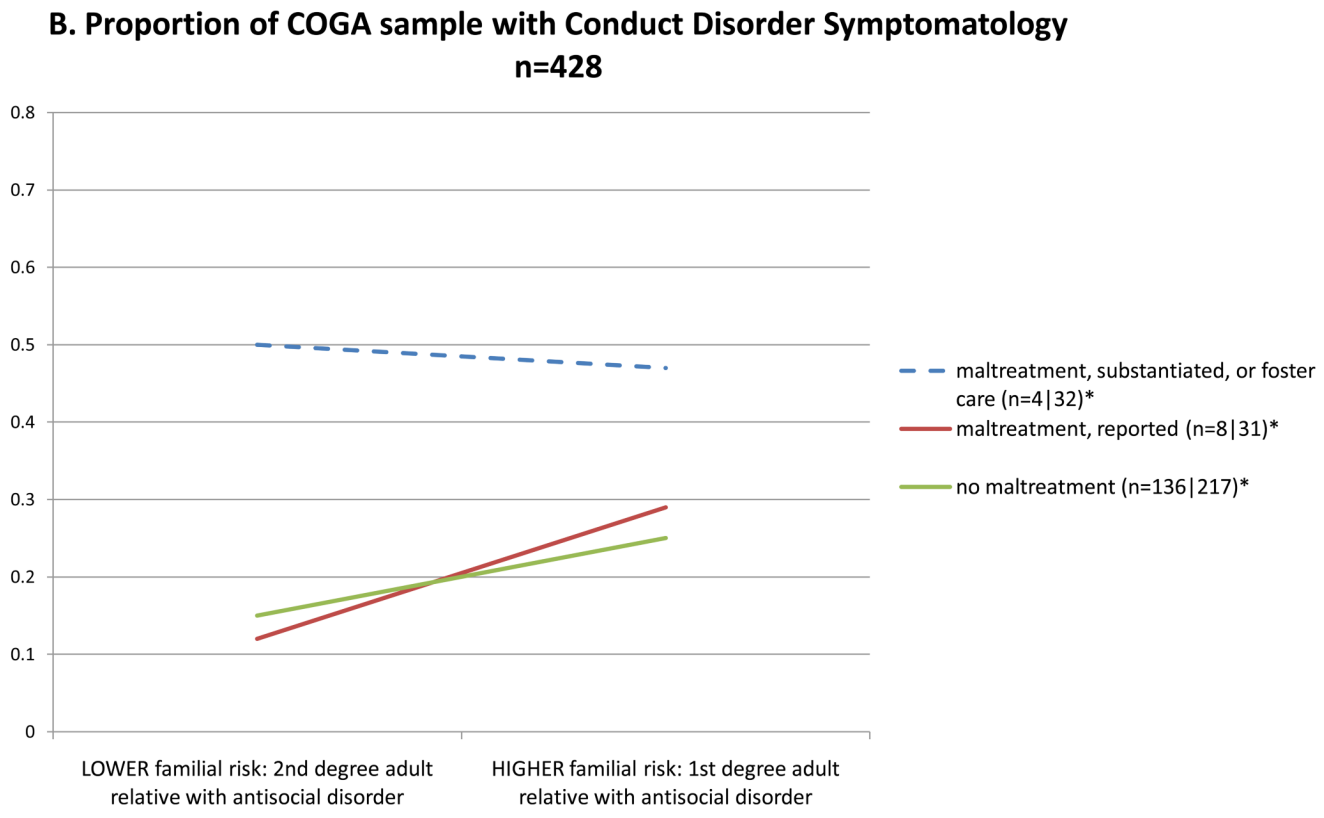


Figure 1.

(panel A. Missouri Twin Registry (MOTWIN) and B. Collaborative Study on the Genetics of Alcoholism (COGA)). Antisocial outcome as a function of maltreatment – including reported maltreatment (URM), substantiated maltreatment (SRM) and foster care (FC) -- and familial

liability. Actual numbers of children in each risk category are provided in the legend to the right of each respective plot.
CBCL = Child Behavior Checklist
MZ = Monozygotic
DZ = Dizygotic
EXT+ = child with externalizing behavior problems
EXT− = child without externalizing behavior problems

Table 1

a. Missouri Twin Registry (MOTWIN) data: Bivariate Association with Externalizing Behavior Outcome and Reports of Child Maltreatment

	N	% Externalizing Outcome (CBCL)	% Reported for Child Maltreatment (combined total of URM, SRM, FC)
Familial Risk			
MZ cotwin w/CBCL ext≥60T	201	59.7	23.4
DZ cotwin w/CBCL ext≥60T	463	38.4	19.0
DZ cotwin w/CBCL ext<60T	2483	11.5	7.2
MZ cotwin w/CBCL ext<60T	1285	6.3[1]	7.4
Race			
Non-white	347	17.9	20.5
White	4085	14.7	8.3
Gender			
Female	1725	13.7	10.0
Male	2707	15.8	9.0
Census Tract Income			
Below federal poverty level	250	24.8	18.4
Above federal poverty level	4182	14.4[1]	8.7
RPS[2]			
No Child Welfare contact	4082	13.69	
RPS	67	19.40	
Child Maltreatment			
No report	3956	12.9	
URM	283	32.5	
RM/FC	126	40.5[1]	

b. Collaborative Study on the Genetics of Alcoholism (COGA) data: Bivariate Association with Conduct Problem Outcome and Reports of Child Maltreatment

	N	% with Conduct Problem Outcome	% Reported for Child Maltreatment (combined total of URM, SRM, FC)
Familial Liability			
2nd deg.rel. antisocial disorder	148	15.5	8.1
1st deg.rel. antisocial disorder	280	28.2[3]	22.6
Race			
Non-white	114	35.1	37.7
White	314	19.7[3]	10.2

b. Collaborative Study on the Genetics of Alcoholism (COGA) data: Bivariate Association with Conduct Problem Outcome and Reports of Child Maltreatment

	N	% with Conduct Problem Outcome	% Reported for Child Maltreatment (combined total of URM, SRM, FC)
Gender			
Female	202	24.3	14.4
Male	226	23.4	20.4
Income			
Below federal poverty level	92	30.4	56.6
Above federal poverty level	336	22.0	6.9
RPS[2]			
No Child Welfare contact	345	20.8	
RPS	8	37.5	
Child Maltreatment			
No report	353	21.2	
URM	39	25.6	
SRM/FC	36	47.2[3]	

[1] = Mantel Haenzel chi-square <.0001

[2] RPS =referral for preventive services to the Missouri Department of Social Services. These referrals are for risk factors other than abuse or neglect. This row does not equal full sample because child welfare contact for maltreatment was excluded from the counts. Because of low frequency, RPS cases were deleted prior to multivariate analyses of COGA data.

[3] Mantel-Haenzel chi-square <.005

Foster Care (FC)

Substantiated Reports of Maltreatment (SRM)

Unsubstantiated Reports of Maltreatment (URM)

Referrals for Preventive Services (RPS)

CBCL = Child Behavior Checklist

MZ = Monozygotic

DZ = Dizygotic

Table 2

A. Missouri Twin Registry (MOTWIN): Logistic Regression Analysis, prediction of Externalizing Behavior problems, controlling for zip-code-level clustering and considering one twin per family selected at random (see text).

2 A. MOTWIN DATA	Model 1: Demographics Only		Model 2: Demographics + Child Welfare Contact (CWC)		Model 3: Demographics +Familial Liability (FL)		Model 4: Demographics + CWC + FL		Model 5: Full Model + FL × CWC interaction	
Variable	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***
DEMOGRAPHICS										
Gender (F v. M)	0.84	.08	0.84	.08	0.85	.08	0.85	.09	0.86	.10
Ethnicity (C v. non-C)	0.94	.71	1.13	.53	0.97	.83	1.09	.59	1.09	.56
Income (<v.>FPL)	1.91	.0005	1.74	.005	1.61	.0005	1.51	.005	1.50	.006
Birth Year	1.01	.53	0.99	.42	1.01	.65	0.99	.32	0.98	.28
	Wald χ^2 = 17.2; df=4; p=002; c= .54; r^2=.01									
MALTREATMENT										
(v. no report):										
(RPS*)			(1.62)	(.17)			(1.44)	(.31)	(1.45)	(.30)
URM			3.30	<.0001			2.52	<.0001	2.69	<.0001
SRM/FC			4.64	<.0001			3.31	<.0001	3.35	<.0001
			Wald χ^2 =112 .98, df=7; p<0001; c=.60; r^2=.05							
FAM. LIABILITY										
(v. MZ unaff):										
MZ aff					21.46	<.0001	19.59	<.0001	19.71	<.0001
DZ aff					9.23	<.0001	8.38	<.0001	8.52	<.0001
DZ unaff					1.94	<.0001	1.95	<.0001	1.92	<.0001
					Wald χ^2 =25 7.50, df=7. P<0001,c=.72; r^2=.18		Wald χ^2 =361 .64, df=10, P<0001,c=.74; r^2=.20			
FL × CWC										
URM										

2 A. MOTWIN DATA	Model 1: Demographics Only		Model 2: Demographics + Child Welfare Contact (CWC)		Model 3: Demographics +Familial Liability (FL)		Model 4: Demographics + CWC + FL		Model 5: Full Model + FL × CWC interaction	
Variable	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***
MZ aff									1.49	.40
DZ aff									0.78	.65
DZ unaff									1.11	.89
SRM/FC										
MZ aff									1.31	.70
DZ aff									1.16	.84
DZ unaff									0.79	.83
									Wald χ^2 =359.62, df=16, P<0001,c=.74; r^2=.20	

B. Collaborative Study on the Genetics of Alcoholism (COGA) Sample: Logistic Regression Analysis, prediction of Conduct Disorder symptomatology, controlling for family membership and zip-code-level clustering.

2 B.COGA DATA	Model 1: Demographics Only		Model 2: Demographics + Child Welfare Contact (CWC)		Model 3: Demographics + Familial Liability (FL)		Model 4: Demographics + CWC + FL		Model 5: Full Model + FL × CWC interaction	
Variable	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***
DEMOGRAPHICS										
Gender (F v. M)	1.06	.830	1.16	.570	1.15	.600	1.24	.420	1.25	.410
Ethnicity (C v. non-C)	0.41	.001	0.43	.004	0.40	.001	0.42	.003	0.42	.003
Income (<v.>FPL)	1.08	.780	0.65	.240	1.03	.920	0.66	.250	0.66	.250
Birth Year	0.90	.0005	0.88	.0001	0.89	.0004	0.88	.0001	0.88	.0001
	Wald χ^2 = 20 .1; df=4; p=0004; c=.6 5; r^2=.07									
MALTREATMENT										
(v. no report):										
RPS*			-----	-----			-----	-----	-----	------
URM			**1.87**	**.130**			1.67	.200	1.43	.440

B. Collaborative Study on the Genetics of Alcoholism (COGA) Sample: Logistic Regression Analysis, prediction of Conduct Disorder symptomatology, controlling for family membership and zip-code-level clustering.

2 B.COGA DATA	Model 1: Demographics Only		Model 2: Demographics + Child Welfare Contact (CWC)		Model 3: Demographics + Familial Liability (FL)		Model 4: Demographics + CWC + FL		Model 5: Full Model + FL × CWC interaction	
Variable	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***	**Odds Ratio**	***p***
SRM/FC			**4.01**	**.0009**			3.38	.004	3.69	.003
			Wald χ^2 =34. 4, df=6; p<0001; c=.67; r^2=.10							
FAM. LIABILITY										
1st degree rel. affected					2.16	.009	1.95	.026	1.92	.023
					Wald χ^2 =26. 6, df=5; p<0001; c=.6 7; r^2=.09		Wald χ^2 =37. 8, df=7; p<0001; c=69 ; r^2=.12			
FL × CWC INTERACTION										
RPS*									-----	-----
URM									2.14	.470
SRM/FC									0.68	.710
									Wald χ^2 =38. 9, df=9, P<0001,c=.6 9; r^2=.12	

* included in the analyses to explore as a possible moderating variable among non-maltreated subjects.

Between-Model Comparisons: For 3 df, critical value of χ^2 difference is 16.27 for p<.001; thus each successive model significantly improves on the preceding models, *except* for Model 5, depicting familial liability × maltreatment interaction.

Foster Care (FC)

Substantiated Reports of Maltreatment (SRM)

Unsubstantiated Reports of Maltreatment (URM)

Referrals for Preventive Services (RPS)

Familial Liability (FL)

Child Welfare Contact (CWC)

Federal Poverty Level (FPL)

Caucasian (C)

Monozygotic (MZ)

Dizygotic (DZ)

* too few cases to include in the analysis.

Between-Model Comparisons:

Model 2 versus Model 1: *improved*: critical value for difference in χ^2 is 13.82 (2 df), at p<.001 for difference.

Model 3 versus Model 1: *improved*: critical value for difference in χ^2 is 3.84 (1 df), at p<.05 for difference.

Model 4 versus Model 2: *difference is not significant.*

Model 4 versus Model 3: *improved*: critical value for difference in χ^2 is 9.21 (2 df), at p<.01 for difference.

Model 2 versus Model 1: *difference is not significant.*

Foster Care (FC),

Substantiated Reports of Maltreatment (SRM)

Unsubstantiated Reports of Maltreatment (URM)

Referrals for Preventive Services (RPS)

Caucasian (C)

Familial Liability (FL)

Child Welfare Contact (CWC)

Federal Poverty Level (FPL)