Parental Alcoholism and Offspring Behavior Problems: Findings in Australian Children of Twins

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Abstract

We examine the impact of rearing by an alcoholic parent on risk for child behavior problems using data on 2492 offspring drawn from two ongoing studies of children of female and male same- and opposite-sex twin pairs. Results of regression models predicting child behavior problems from parental and co-twin lifetime history of alcohol use disorder (AUD) provide support for genetic but not environmental transmission of externalizing and a measure of total problem behaviors. Results for internalizing behavior were inconclusive with respect to transmission of risk.

Children of alcoholics (COAs) are at increased risk for a range of externalizing difficulties, notably conduct-disordered and other "acting out" behaviors (Kuperman, Schlosser, Lidral, & Reich, 1999; Sher, Walitzer, Wood, & Brent, 1991; Reich, Earls, Frankel, & Shakya, 1993), with similar risks observed for early and problem substance use (Chassin, Rogosch, & Barrerra, 1991; Lieb, Merkinagas, Hofler, Pfister, Isensee, & Wittchen, 2002; Schuckit & Smith, 1996; Sher et al., 1991). Although the magnitude of effects is somewhat reduced for internalizing compared to externalizing outcomes, associations between parental alcoholism and depressive and anxious behaviors are also reported (Chassin, Pitts, DeLucia & Todd, 1999; Kuperman et al., 1999; Sher et al., 1991). With approximately one-quarter of children exposed to alcoholism in the family (Grant, 2000), increased understanding of mechanisms underlying risks to COAs is critical for targeted preventive and intervention efforts.

Distinguishing among causal and correlated risks for problem behavior is an increasing focus of much theoretical and empirical work, and this is especially true of research on COAs (see Sher, 1991; Windle & Searles, 1990). Although widely believed, it was until recently difficult to demonstrate a causal effect of growing up in an alcoholic home. Family studies consistently document a range of adversities associated with rearing by an alcoholic parent, but leave heritable influences uncontrolled. For biological offspring, exposure to parental alcoholism is confounded with genetic risks associated with problem and dependent drinking (for reviews, see Heath, 1995; McGue, 1999). Thus, it is impossible to determine from family studies alone whether risk to COAs is due to shared genes or exposure to alcoholic environments. Because genetic effects and gene by environment interaction (GxE) are confounded in classical twin designs (Eaves, Last, Martin, & Jinks, 1977), estimates of shared environment from twin studies include only those influences that do not interact with shared genes. Adoption designs in theory should be ideal for demonstrating environmental effects, while controlling for genetic

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influences. However, selection for high risk genetic backgrounds but reduced environmental risk is a critical limitation, resulting in restriction of the range of environmental adversity to which adoptive offspring are exposed (Stoolmiller, 1999).

The goal of this study is to examine whether being raised by a parent with history of alcohol use disorder (AUD) increases risk of child behavioral problems, over and above genetic influences. We use a Children-of-Twins (COT) design (Gotteman and Bertelson (1989; Heath, Kendler, Eaves, & Markell, 1985; Nance & Corely, 1976), in which genetic and environmental risks are inferred from parent and co-twin history of AUD. By comparing outcomes of biological offspring of an alcoholic parent to biological offspring of the unaffected co-twin of the alcoholic parent, the COT design combines the advantages of both adoption and classical twin studies, while minimizing their respective limitations. In COT studies, outcomes of offspring from a minimum of four groups are compared, each with varying degrees of genetic risk and environmental exposure. In the context of the present study, these groups include: offspring whose parent is alcoholic (Group 1); offspring of an unaffected parent whose monozygotic (MZ) co-twin is alcoholic (Group 2); offspring of an unaffected parent whose dizygotic (DZ) co-twin is alcoholic (Group 3); and offspring from control families, where neither parent nor co-twin, regardless of zygosity, is alcoholic (Group 4).

Following from quantitative genetic theory, assumptions regarding environmental, genetic, and GxE risks to offspring are summarized in Table 1, separately by risk group. If the association between parental alcoholism and child behavior problems results from exposure to alcoholic environments, i.e., environmental transmission, offspring reared by an alcoholic parent should exhibit more behavior problems than offspring of unaffected parents (Group 1 > Groups 2–4), regardless of genetic risk. If the association results from genes shared between parents and their children, i.e., genetic transmission, offspring at high genetic risk should exhibit more behavior problems than offspring at intermediate genetic risk (Groups 1 and 2 > Group 3), regardless of environmental risk. Offspring at intermediate genetic risk in turn should exhibit more problems than offspring at low genetic risk (Group 3 > Group 4). A pattern consistent with GxE is evident if offspring reared by an alcoholic parent exhibit more behavior problems compared to offspring of unaffected parents, with offspring of an unaffected parent whose co-twin is also unaffected exhibiting the fewest problems (Group 1 > Group 2 > Group 3 > Group 4).

To date, a handful of studies have capitalized on the COT design to examine causal consequences of exposure to a range of putative environmental risks, including parental alcoholism. Taken together, this research largely supports genetic over environmental transmission underlying the association between parental alcoholism and conduct disorder symptoms (Haber, Jacob & Heath, 2005) and both diagnostic and symptom-count measures of ADHD (Knopik, Heath, Jacob, Slutske, Bucholz et al., 2006; Knopik, Jacob, Haber, Swenson & Howell, 2009), despite attenuation in models adjusting for important correlates, such as parental comorbid psychopathology and prenatal alcohol or nicotine exposure. For AUD assessed in older offspring, evidence of environmental transmission from parental alcoholism has been shown in some reports (Duncan, Scherrer, Fu, Bucholz, Heath et al., 2006; Jacob, Waterman, Heath, True, Bucholz et al., 2003), but not all (Slutske, D'Onofrio, Turkheimer, Emery, Harden, et al., 2008). Fewer COT studies of parental alcoholism and internalizing outcomes are available. The single report of offspring suicidal behavior was inconclusive with respect to the role of environmental, genetic or GxE risks associated with paternal alcoholism (Glowinski, Jacob, Bucholz, Scherrer, True & Heath, 2004), but likely suffered from limited power associated with low prevalence outcomes. The present study extends this growing body of work by using a COT design to examine associations between parental alcoholism and offspring internalizing as well as externalizing behavior during childhood.

METHODS

Participants

Participants were drawn from ongoing studies of Australian children of twins selected from two broadly representative Australian volunteer twin panels maintained by the Australian National Health and Medical Research Council (NHMRC). The older panel (Cohort I) was born between 1893 and 1964 and ascertained as adults (Heath, Bucholz, Madden, Dinwiddie, Slutske et al., 1997). The younger panel (Cohort II) was born between 1964 and 1971 and ascertained as children through their parents in response to flyers distributed throughout Australian schools (Heath, Howells, Kirk, Madden, Bucholz et al., 2001; Knopik, Heath, Madden, Bucholz, Slutske et al., 2004). Twins in both cohorts are of primarily European decent reflecting the predominantly Caucasian Australian population from which they were ascertained. Detailed characterization of each panel is described elsewhere (see Heath et al., 1997; Heath et al., 2001).

All twins completed diagnostic telephone interviews between 1992–1994 (Cohort I) or 1997–2002 (Cohort II). Twins in the current study were selected based on lifetime history of alcohol use disorder (AUD). Pairs where at least one twin had biological children ages 7– 24 and one twin met DSM-IV criteria for AUD [operationalized for this study as alcohol dependence (AD) in male twins and either AD or alcohol abuse (AB) in female twins] were recruited for participation in one of two children of twins studies with coordinated assessment: Mothers And Their Children (MATCH) and Parental Alcoholism & Child Environmental Risk (PACER). A random sample of control pairs, where at least one twin had biological children ages 7– 24, but neither twin met criteria for AUD, was also recruited.

Twins from the MATCH study were selected from female same-sex pairs from both cohorts. PACER twins were selected from male same- and opposite-sex pairs from Cohort II. Reassessment of twin parents and co-twins by telephone interview and self-report questionnaire began in 2000 and 2005 for MATCH and PACER studies, respectively. The present analyses are based on questionnaire data from 874 MATCH twins (from 337 MZ and 280 DZ pairs) reporting on 1643 offspring, and 411 PACER twins (from 116 MZ, 87 same-sex DZ, and 171 opposite-sex DZ pairs), of whom 367 provided reports on 756 offspring and 44 biological co-parents (mothers in the case of twin fathers) reported on 93 offspring. In all, questionnaire data were available from 1285 parents reporting on 2492 offspring. Combined samples sizes by risk group are shown in Table 2, with sample characteristics provided in Table 3. Average age of parents was 42.01 ($\underline{SD} = 4.08$), ranging from 32 to 65 years. The average age of offspring was 14.14 years ($\underline{SD} = 3.77$), with roughly equal proportion of male (51%) and female (49%) offspring.

Measures

Twins completed adaptations of the Semi-Structured Assessment of the Genetics of Alcoholism (SSAGA; Bucholz, Cadoret, Cloninger, Dinwiddie, Hesselbrock, et al., 1994; Hesselbrock, Easton, Bucholz, Schuckit, & Hesselbrock, 1999), which was developed for the Collaborative Study on the Genetics of Alcoholism (COGA) to assess physical, psychological, and social manifestations of alcoholism and related psychiatric disorders in adults. All interviews, both initial and follow-up, were administered by trained interviewers, who were supervised by a project coordinator and clinical psychologist. Interviews were tape-recorded, with a random sampling of tapes reviewed for quality control and coding inconsistencies. Informed consent was obtained from all participants using procedures approved by the institutional review boards at both Washington University School of Medicine and Queensland Institute of Medical Research.

Much of the original SSAGA was retained at reassessment, with additional items from the Family History Assessment Module (FHAM; Rice, Reich, Bucholz, Neuman, Fishman et al., 1995) included to assess biological co-parent history of conduct problems, adult antisocial behavior, and alcohol and other substance use or disorder. To assess rearing history and offspring psychopathology, parent-report items adapted from the Diagnostic Interview for Children and Adolescents (DICA; Herjanic & Reich, 1982) and the Child SSAGA (C-SSAGA-P; Kuperman, Schlosser, Kramer, JBucholz, Hesselbrock et al., 2001) were also incorporated. In addition, twins with age-eligible offspring completed a brief self-report questionnaire (SRQ), which included assessments of offspring medical history, school and neighborhood characteristics, parenting behaviors, parent-child relationship quality, and partner conflict. Included with the SRQ was the parent report form of the Child Behavior Checklist for Ages 6–18 (CBCL; Achenbach, 2001).

Parental alcohol use disorder (AUD)—For Cohort I, lifetime history of AD and AB were coded from DSM-IV symptoms based on a DSM-III-R assessment. The SSAGA administered to Cohort I predates DSM-IV; however, we applied an approximate algorithm for DSM-IV criteria without clustering that was developed by Heath and colleagues (see Heath, Whitfield, Madden, Bucholz, Dinwiddie et al., 2001). Consistent with other reports (Grant, Heath, Bucholz, Madden, Agrawal et al., 2007; Knopik et al., 2006; Waldron, Heath, Bucholz, Madden, & Martin, 2008), twins in Cohort I were diagnosed with AD if they endorsed three or more DSM-IV AD symptoms. Female twins were diagnosed with AB if they reported at least one symptom of DSM-IV AB. For Cohort II, DSM-IV AD was directly assessed, as was DSM-IV AB for female twins.

Offspring behavior problems—Twin parents or biological co-parents completed the Child Behavior Checklist for Ages 6–18 (CBCL; Achenbach, 2001) reporting on up to three age-eligible offspring. The CBCL is a widely used parent report measure of child behavior problems, with well-established psychometrics (Achenbach & Rescorla, 2001; Achenbach, 1991). Parents reported whether a given behavior described his or her child's behavior within the previous six months using a likert rating of 0 = "not true", 1 = "somewhat or sometimes true," or 2 = "very true or often true" for each item. For offspring ages 19–24, parents provided a retrospective report of offspring behavior at age 18. Scores from underlining internalizing and externalizing scales of the CBCL were analyzed. Internalizing consists of items from anxious/depressed, withdrawn/depressed, and somatic complaints subscales, with rule-breaking and aggressive behavior subscales comprising externalizing. Scores from a combined index of problem behavior, total problems, were also analyzed and include items from all subscales, including social problems, thought problems, and attention problems subscales. Given significant positive skew observed of raw CBCL scores, log-transformations of internalizing, externalizing, and total problems scales were analyzed. Consistent with Achenbach and Rescorla (2001), data were considered valid if fewer than 8 items were missing, excluding open-ended items. Valid mother and twin father reports were both available for 16 of 411 PACER families; for these families, mother report was used.

Analytic Strategy

Regression models predicting CBCL internalizing, externalizing, and total problems scores from parent and co-twin AUD were conducted in STATA (StataCorp, 2005), with post-hoc tests for group differences. All models included three dummy variables coding for offspring at both high genetic and high environmental risk (Group 1: parent AUD+), offspring at high genetic risk but reduced environmental risk (Group 2: parent AUD-, MZ co-twin AUD+), and offspring at intermediate genetic risk but reduced environmental risk (Group 3: parent AUD−, DZ co-twin AUD+). Control families, where offspring are at low genetic and low environmental risk (Group 4: parent and co-twin AUD−), comprised the reference group.

Analyses were conducted first without and then with adjustment for offspring age and gender. The Huber-White robust variance estimator option in Stata was used to correct for non-independence of twin-family data.

RESULTS

Preliminary analyses indicate significant differences in parental age by risk status, $\underline{F}$ (3, 1281) = 10.82, $\underline{p}$ < .0001. Differences in offspring age by risk status were also significant, $\underline{F}$ (3, 2488) = 6.30, $\underline{p}$ < .001. Results of post-hoc tests suggest that parents from control families (Group 4) are older on average than parents from families where either the parent or parent's MZ or DZ co-twin is AUD+ (Groups 1, 2 and 3). Although offspring in Group 4 are also older than offspring whose parent is AUD+ (Group 1), both groups are indistinguishable from offspring whose parent's MZ or DZ co-twin is AUD+ (Groups 2 and 3).

At the phenotypic level, parental AUD accounted for modest variation in offspring behavior problems. Associations between parental AUD and internalizing ($\underline{r}$ = .09, $\underline{p}$ < .0001), externalizing (r = .11, $\underline{p}$ < .0001) and total problems ($\underline{r}$ = .10, $\underline{p}$ < .0001) were of similarly small magnitude. The strength of these associations did not differ as a function of maternal versus paternal AUD, nor offspring gender (all $\underline{p\text{-levels}}$ > .30).

Results of regression models predicting internalizing, externalizing, and total problems from parent and co-twin AUD are shown in Tables 4–6, respectively. Means and standard deviations of raw scores are also shown. Offspring of an affected parent (Group 1) scored higher on internalizing compared to offspring from control families (Group 4). Differences between Group 4 and offspring of an unaffected parent with an alcoholic MZ or DZ co-twin (Groups 2 and 3) were non-significant. Differences between Group 1 and either of Groups 2 or 3 were also non-significant. This pattern was observed regardless of adjustment for offspring age and sex.

For externalizing problems, compared to offspring from control families (Group 4), offspring of an affected parent (Group 1) had higher scores, as did offspring of an unaffected parent with an alcoholic MZ co-twin (Group 2). Furthermore, Groups 1 and 2 did not differ in overall level of externalizing, with both groups differing significantly from offspring of an unaffected parent with an alcoholic DZ co-twin (Group 3). This pattern of Groups 1 and 2 > Groups 3 and 4 held in models without and with adjustment for offspring age and sex. The same pattern was observed for total problems: Groups 1 and 2 > Groups 3 and 4, regardless of covariate adjustment.

DISCUSSION

We examined whether being raised by an alcoholic parent increases risk of offspring behavioral problems. Using data from two ongoing studies of children of twins, we compared internalizing and externalizing behaviors of offspring, with genetic and environmental risks inferred from parent and co-twin history of alcohol use disorder (AUD). Consistent with previous research, results provide little evidence of environmental transmission of risk from parental alcoholism for internalizing, externalizing, or a measure of total problem behavior. In contrast, there was strong support for genetic transmission for externalizing and total problem behavior. Findings regarding genetic risks for internalizing behavior were inconclusive.

Although the pattern of internalizing scores by risk group was consistent with expectations assuming genetic transmission from parental alcoholism, differences between groups were small and mostly nonsignificant. Compared to offspring of control twins, offspring of an alcoholic parent exhibited greater internalizing behavior; however, offspring of an alcoholic parent were indistinguishable from offspring at low environmental risk but high or intermediate

genetic risk, who were in turn indistinguishable from offspring of control twins. In contrast, offspring of an alcoholic parent and offspring of an unaffected parent at high genetic risk exhibited similar levels of externalizing, with both groups exhibiting greater externalizing than offspring at intermediate genetic risk or offspring of control twins. The same pattern was observed for a measure of total problem behavior.

Together, results are highly suggestive of genetic but not environmental transmission of risk from parental AUD for externalizing and total problem behaviors, but there are several limitations of the present study to warrant cautious interpretation. First, the sample was drawn from predominantly Causation twin panels in Australia. Given reported differences by race in risk of alcohol use and disorder (Grant, 1997; Hasin, Stinson, & Grant, 2007), it is possible that observed patterns differ for other racial or ethnic groups. Observed patterns might also differ cross-nationally, further restricting generalizability. Another limitation pertains to sample ascertainment, with well-educated individuals over-represented in both panels (see Heath et al., 2001; Heath, Madden, & Martin, 1998).

Perhaps most importantly, proximal causal mechanisms remain unknown. Behaviors or conditions genetically correlated with AUD and not parental AUD per se, may explain the association between parental alcoholism and externalizing and total problem behaviors. Likely candidates include comorbid parental psychopathology, such as antisociality and depressive disorders, both of which show moderate to high genetic variation, and are strongly correlated with AUD (Fu, Heath, Bucholz, Nelson, Goldber et al., 2002; Prescott, Aggen, & Kendler, 2000; Slutske, Heath, Dinwiddie, Madden, Bucholz et al., 1998; Slutske, Heath, Madden, Bucholz, Statham, & Martin, 2002). A related limitation concerns transmission of risks associated with co-parent AUD, which was unmeasured in the present analysis. To the extent that co-parent AUD, including co-parent comorbid psychopathology, are not included in COT models, this model-misspecification may lead to false inference (see Eaves, Sliberg, & Maes, 2005).

Capitalizing on coordinated ascertainment and assessment protocols, we combined samples of offspring of maternal and paternal alcoholics and their co-twins. As a result, we are unable to examine separately the effects of maternal versus paternal alcoholism on offspring outcome within the COT design, owing largely to reduced statistical power from analyzing each sample separately. This is especially true for internalizing, where combined samples lack statistical power necessary to distinguish among genetic and environmental risks. In addition, we used mother report of offspring behavior problems if valid CBCL data were available from both a biological mother and twin father. Although reports from both parents were available from only a handful of families, using a structural equation modeling rather than regression-based framework for data-analysis would enable incorporation of data from both parents, while allowing for potential rater biases associated with parental psychopathology.

Conclusion

Overall, this study adds to a growing body of work using innovative research designs to address issues of causation in alcoholic families. Despite methodological limitations, the present findings offer important insight into risk mechanisms underlying the association between parental alcoholism and offspring behavior problems. Continued research on causal processes is necessary, including a more comprehensive analysis of the role of other correlated but yet unmeasured genetic and environmental risks. Co-parent history of AUD and comorbid psychopathology in both parents as well as offspring will be especially important to examine to ensure specificity of observed effects, but also to identify potential mechanisms of mediation or risk moderation.

Acknowledgments

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Table 1

Risk group by environmental, genetic, and GxE risks

Risk Group	Environmental Risk	Genetic Risk	GxE Risk
1. Parent AUD+	high	high	high
2. Parent AUD− and MZ co-twin AUD+	low	high	low
3. Parent AUD− and DZ co-twin AUD+	low	intermediate	low
4. Parent and co-twin AUD−	low	low	very low

Note. AUD = Alcohol Use Disorder.

Table 2

Available data by risk group: Combined MATCH and PACER samples

Risk group	n parents	n offspring
1. Parent AUD+	327	604
2. MZ co-twin AUD+	94	167
3. DZ co-twin AUD+	131	246
4. Parent and co-twin AUD−	733	1475

Table 3

Sample characteristics by risk group

Risk Group	Parent Age <u>M(SD)</u>	Child Age <u>M(SD)</u>	Child Sex (<u>%</u>Male)
1. Parent AUD+	41.30 (3.99)[a]	13.67 (3.64)[a]	52
2. MZ co-twin AUD+	41.05 (4.28)[a]	13.94 (3.47)[a,b]	49
3. DZ co-twin AUD+	41.36 (4.30)[a]	13.80 (3.81)[a,b]	52
4. Parent and co-twin AUD−	42.59 (3.98)[b]	14.40 (3.82)[b]	51

<u>Note</u>: Means with different superscripts are significantly different from each other.

Table 4

Regression of risk status predicting internalizing behavior

		Unadjusted			Adjusted		
	M(SD)	Coef	SE	p	Coef	SE	p
Parent AUD+	4.62 (5.76)	.21[a]	.06	.001	.21[a]	.06	.001
MZ co-twin AUD+	4.59(6.19)	.18[a]	.10	.07	.18[a]	.10	.07
DZ co-twin AUD+	3.34 (3.76)	.04[a]	.08	.59	.04[a]	.08	.57
Parent and co-twin AUD− (constant)	3.29 (4.22)	1.08	.03	.00	1.13	.09	.00

Note. Coefficients with different superscripts are significantly different from each other.

Table 5

Regression of risk status predicting externalizing behavior

	M(SD)	Unadjusted			Adjusted		
		Coef	SE	p	Coef	SE	p
Parent AUD+	5.79 (6.74)	.27[a]	.06	.00	.27[a]	.06	.00
MZ co-twin AUD+	5.58 (6.20)	.28[a]	.10	.005	.28[a]	.10	.004
DZ co-twin AUD+	3.88 (4.20)	.05[b]	.07	.481	.05[b]	.07	.48
Parent and co-twin AUD− (constant)	4.14(5.77)	1.22	.03	.00	1.09	.09	.00

Note. Coefficients with different superscripts are significantly different from each other.

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Table 6

Regression of risk status predicting total problems

	M(SD)	Unadjusted			Adjusted		
		Coef	SE	p	Coef	SE	p
Parent AUD+	19.98 (20.75)	.28[a]	.07	.00	.27[a]	.07	.00
MZ co-twin AUD+	19.51 (20.09)	.32[a]	.11	.005	.31[a]	.11	.006
DZ co-twin AUD+	13.61 (12.45)	.06[b]	.08	.50	.04[b]	.08	.60
Parent and co-twin AUD− (constant)	14.45 (16.36)	2.25	.04	.00	2.40	.11	.00

Note. Coefficients with different superscripts are significantly different from each other.