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CONDUCT DISORDER IN CHILDREN AT HIGH RISK FOR ALCOHOL USE DISORDERS

C. E. Sartor, J. R. Haber, T. Jacob, & W. R. True



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ABSTRACT

Objective: To clarify the roles of genetic and environmental factors in the development of Conduct Disorder (CD) among offspring at high genetic and/or environmental risk for alcohol use disorders (AUDs).

Method: Alcohol-related behaviors and psychiatric status were assessed in 1213 male twin members of the Vietnam Era Twin Registry (VETR), 1270 offspring, and 862 mothers of offspring. Through the use of an offspring-of-twins design, rates of CD were compared among four groups of offspring with varying genetic and environmental risk for AUDs.

Results: Only offspring at both high genetic and high environmental risk for AUDs evidenced elevated rates of CD.

Conclusions: Findings supported the common genes hypothesis, while maintaining that this genetic influence is conditional upon environmental factors that promote externalizing behaviors. Results are discussed in terms of Zucker's "nesting hypothesis" (2002).

BACKGROUND LITERATURE

Studies of both genetic and environmental factors associated with CD provide evidence that the disorder occurs at higher rates among children of alcoholics (COAs). Family and social contexts associated with externalizing behaviors have been linked to alcohol use disorders (AUDs) later in life and CD is known to co-occur with alcohol abuse in adolescence ((Jacob & Johnson, 1997). The question remains, however, whether the source of this association is a genetic link between the disorders, an environmental factor present in alcoholic families that promotes externalizing behaviors in children, or a combination of the two (i.e. gene-environment interaction).

The current study attempted, through the use of an offspring-of-twins design, to determine the relative contribution of genetic and environmental factors in the expression of CD in children at high risk for developing AUDs. Research questions were posed within the framework of a “latent externalizing factor model” (Krueger, Hicks, Patrick, Carlson, Iacone, & McGue, 2000), which posits that CD, adolescent antisocial behavior, Alcohol Dependence (AD), and illicit substance dependence are derived from a common genetic factor. It was hypothesized that environmental factors (i.e. being raised by an alcoholic parent) increase risk for the development of externalizing symptoms beyond the genetic risk posed from being the biological offspring of parents with AUDs.

HYPOTHESES

- Offspring of AD fathers were expected to evidence higher rates of CD than offspring of unaffected fathers whose monozygotic (MZ) or dizygotic (DZ) cotwins are also unaffected (i.e. control group).
- Offspring of unaffected fathers whose MZ cotwins are positive for AD were not expected to evidence as high rates of CD as offspring of AD fathers. That is, the highest rates of CD were expected to be among the offspring of AD fathers who are at high genetic and high environmental risk. Rates were expected to be lower among offspring with high genetic but low environmental risk.

METHODS

Participants

Male twins were recruited through the Vietnam Era Twin Registry (VETR). Twins, offspring and mothers of offspring participated in the study.

- 1213 male twins (mean age: 50.73)
- 862 mothers (mean age: 47.50)
- 1270 offspring (mean age: 20.10; range: 12-28 years)

Design

Participants were offspring of

- 1) fathers of any twin status with a history of AD
(high genetic, high environmental risk)
- 2) unaffected fathers with AD MZ co-twins
(high genetic, low environmental risk)
- 3) unaffected fathers with AD DZ co-twins
(moderate genetic, low environmental risk)
- 4) unaffected fathers with unaffected co-twins
(low genetic, low environmental risk)

METHODS (2)

Assessment

Alcohol-Related Behaviors

Alcohol dependence and alcohol abuse
Lifetime drinking history
Family history of alcohol abuse/dependence
Nicotine dependence, cannabis dependence
and substance abuse

Psychiatric Status

Major depression and mania
Anxiety disorders
Antisocial personality disorder
Conduct disorder
Oppositional defiant disorder

Analyses controlled for the following covariates:

- Paternal CD, antisociality, drug abuse, depression, dysthymia, generalized anxiety disorder, panic disorder, and post-traumatic stress disorder
- Maternal AD, alcohol abuse, and depression

RESULTS

A logistic regression analysis testing the association between paternal AD and offspring CD yielded the following findings (see Table 2):

- Offspring of MZ and DZ twins with a history of AD (Group 1) were significantly more likely to exhibit CD than offspring of unaffected control fathers (Group 4)
- Offspring of unaffected fathers whose MZ cotwins are positive for AD (Group 2) were not significantly more likely to exhibit CD than Group 4
- After controlling for family risk (i.e. group) status, several demographics were associated with elevated rates of CD: parental divorce, age > 17, and male gender

TABLE 1. Offspring CD by Age Group, Gender, and Family Risk Status

	Age 12 – 17 (n=430)		Age 18 – 26 (n=644)	
	Male (n=228)	Female (n=202)	Male (n=292)	Female (n=352)
Father AD Status				
□ AD	10.53% (24)	2.48% (5)	16.78% (49)	5.40% (19)
□ Unaffected, AD MZ Cotwin	.88% (2)	0% (0)	2.05% (6)	.28% (1)
□ Unaffected, AD DZ Cotwin	1.32% (3)	.99% (2)	0.34% (1)	0.57% (2)
□ Unaffected, Cotwin Unaffected (Control)	0% (0)	1.98% (4)	2.40% (7)	.85% (3)

TABLE 2. Relative Risk Ratios (95% confidence intervals) for Offspring CD as a Function of Family Risk Status and Pertinent Covariates

	Conduct Disorder
Group 4: Offspring of MZ and DZ control	1.00 (Reference)
Group 1: Offspring of AD fathers (MZ and DZ)	1.80 (1.00-3.22)*
Group 2: Offspring of unaffected father with AD MZ cotwin	1.43 (0.64-3.16)
Group 3: Offspring of unaffected father with AD DZ cotwin	0.89 (0.37-2.15)
Maternal alcohol dependence	0.99 (0.52-1.85)
Maternal alcohol abuse	0.79 (0.40-1.58)
Maternal depression	1.19 (0.75-1.88)
Paternal illicit drug abuse/dependence	1.61 (0.93-2.78)
Paternal psychiatric disorder^a	0.73 (0.46-1.15)
Offspring age 18+	1.84 (1.22-2.77)**
Offspring male	4.51 (2.97-6.84)**
Father education > high school	1.43 (0.96-2.13)
Father employed full-time	0.75 (0.38-1.50)
Parental marital status: divorced	2.40 (1.52-3.78)**

^a major depression, antisocial personality disorder and/or CD* p<.05; ** p<.01

DISCUSSION

- Rates of CD among offspring of AD fathers (Group 1) compared with those of normal controls (Group 4) were elevated, providing support for the notion of a broadband genetic factor that links the two disorders
- Inclusion of Group 2, offspring of unaffected fathers whose MZ cotwins are positive for AD, allowed for the examination of environmental risk separately from genetic risk. Results indicated that when environmental risk was minimal, the association between paternal AD and offspring CD was non-significant; prevalence rates equaled those of normal controls. High genetic risk only resulted in manifestation of CD when interacting with a high risk environment.
- These findings can be best understood in the context of “nesting”. Nesting refers to the idea that genetically-based behavioral undercontrol personality traits, when coupled with an environmental structure that facilitates development of these temperamental attributes (in this case, parental alcoholism), culminates in antisocial personality and a reinforcing deviant peer network (Zucker, 2002).

DISCUSSION (2)

Limitations of the study

- CD has a low prevalence; low sample power limited consideration of finer group distinctions.
- Results are limited in only addressing two diagnoses with the externalizing domain. Future research efforts will examine a broader array of psychiatric disorders reflective of behavioral undercontrol.

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