Predicting Offspring Conduct Disorder Using Parental Alcohol and Drug Dependence

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Abstract

• Introduction: Previous research has shown that the offspring of parents having a history of alcohol dependence (AD) are at increased risk for conduct disorder (CD), results that support the contention that common genes may underlie both AD and CD (Haber, Jacob, & Heath, 2005). This study further examines these findings to consider both AD and drug dependence (DD) as simultaneous predictors of offspring CD using the offspring of twins research design.

• Methods: Participants were male monozygotic (MZ) and dizygotic (DZ) twins from the Vietnam Era Twin Registry obtained for two parallel studies: The Children of Alcoholics (COA) and the Twins as Parents (TAP) studies. Families included twin fathers, their offspring, and the mothers of those offspring. Twin fathers were concordant or discordant for alcohol and/or drug dependence. Offspring risk of CD was examined as a function of both genetic risk (due to paternal and co-twin substance dependence diagnoses) and environmental risk (due to being reared by a father with a substance dependence diagnosis).

• Results: After controlling for potentially confounding variables, the offspring of both AD and DD fathers were significantly more likely to exhibit CD symptoms than were offspring of non substance-dependent fathers, thus indicating diagnostic crossover in generational family transmission patterns. Comparing offspring at various levels of genetic and environmental risk indicated that genetic factors were responsible for both the paternal AD/offspring CD and the paternal DD/offspring CD associations, while there was little evidence of environmental effects.

• Conclusions: Results demonstrated diagnostic crossover from parental AD to offspring CD and indicated genetic factors to be the dominant mechanism accounting for CD outcomes, findings that provide further support for the common genes hypothesis.
Introduction

• There is an overrepresentation of children with conduct disorder (CD) symptoms in families with an alcoholic parent (McGue, 1997; Sher et al., 1991).

• Over 70% of the association between alcohol dependence (AD) and CD can be attributed to genetics (Slutske et al., 1998).

• Paternal alcohol abuse (AA)/dependence (AD) predicts offspring AA/AD. Both genetic and environmental effects have been implicated in this association (Jacob et al., 2003).

• Genetic influences associated with paternal alcoholism are associated with higher CD symptom counts in offspring (Haber, Jacob, & Heath, 2005).

Methods

• Sample:
  – 1,917 male and female offspring aged 13-26 and their Vietnam Era Twin (VET) fathers and biological mothers were selected for the Children of Alcoholics (COA) and Twins as Parents (TAP) studies.

• Assessment Variables:
  – IV: Paternal twin and cotwin AD and drug dependence (DD) status and MZ/DZ zygosity were used to construct 7 risk status categories
  – DV: Offspring CD defined dichotomously as having 3+ CD symptoms or not
  – Covariates:
    • Father: Psychiatric diagnosis (Panic Disorder, Generalized Anxiety Disorder, PTSD, Dysphoria, Major Depression, and Antisocial Personality Disorder), full-time employment status, level of education attained
    • Mother: Substance use diagnoses (AD & MJ), Major Depression diagnosis, Antisocial Personality diagnosis
    • Offspring: Gender, Age, Marital status of biological parents
4 Group Design with DD and AD Cross-Classification

• Group 1:
  – Group D1 = Father meets criteria for DD, with or without AD
  – Group A1 = Father meets criteria for AD without DD

• Group 2:
  – Group D2 = Father does not meet criteria for DD or AD, but MZ cotwin meets criteria for DD with or without AD
  – Group A2 = Father does not meet criteria for DD or AD, but MZ cotwin meets criteria for AD only

• Group 3:
  – Group D3 = Father does not meet criteria for DD or AD, but DZ cotwin meets criteria for DD with or without AD
  – Group A3 = Father does not meet criteria for DD or AD, but DZ cotwin meets criteria for AD only

• Group 4:
  – Neither father nor cotwin meet either DD or AD criteria

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Genetic Risk</th>
<th>Environment Risk</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
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Data Analysis Approach

- **Basic Model:**
  - DV (offspring CD) regressed on 7 cross-classified IV (paternal DD and AD risk status)
    - G1 - DD, G2 - DD, G3 - DD, G4 - Control (unaffected)
    - G1 - AD, G2 - AD, G3 - AD
  - Determine whether G1-DD and G1-AD are equivalent predictors of offspring CD. Equivalence allows combining groups.
    - Similarly consider G2 and G3
  - Adjusted Model: Using combined groups where justified, add covariates. Analyze group differences.

Data Analysis

- **Analytic Approaches used:**
  - Linear Regression on CD symptom counts
  - Linear Regression on square root and log transformed CD symptom counts (to normalize the DV distribution)
  - Logistic Regression on a binary symptom variable based on having 3 or more AD or DD symptoms (3+ Sx= 1)
  - Final analyses used Logistic Regression to examine a binary CD variable (3+ Sx) regressed on paternal AD and DD risk categories alone, and then with covariates
  - Results were checked with a model that controlled for twin similarity using STATA data software.
Results of Step 1: Basic Model of Cross-Classified DD-AD Groups

Results:

Group 2 and Group 3 can be combined

- Analyses testing equivalence of DD and AD groups to determine whether groups can be combined:
  - Binary Model: Drug & Alcohol Group Means (w/o covariates)
    - Group D1 vs. Group A1: $p = .03$
      - D1 and D2 are significant so hold as separate variables
    - Group D2 vs. Group A2: $p = .81$
      - No significant difference so collapse D2 and A2
    - Group D3 vs. Group A3: $p = .12$
      - No significant difference so collapse D3 and A3
Adjusted Model:
G1 modeled with DD risk and AD risk as separate

Summary of Results:

Adjusted Model

- Binary CD: Group Means (w/o Covariates)
  - Group D1 vs. Group 4: p = .000
    - Family risk associated with paternal DD (both genetic and environmental) is significant
  - Group A1 vs. Group 4: p = .015
    - Family risk associated with paternal AD (both genetic and environmental) is significant
  - Group 2 vs. Group 4: p = .216
  - Group 3 vs. Group 4: p = .176
Results: Adjusted Model

Summary of Main and Contrast effects

• Group D1 vs. Group 4:  \( p = .009 \)
• Group A1 vs. Group 4:  \( p = .01 \)
• Group 2 vs. Group 4:  \( p = .09 \)
• Group 3 vs. Group 4:  \( p = .18 \)
• Group D1 vs. Group A1:  \( p = .51 \)
• Group D1 vs. Group 2:  \( p = .24 \)
• Group A1 vs. Group 2:  \( p = .72 \)
• Group 2 vs. Group 3:  \( p = .009 \)
Interpretation of Results

Contrast D1 vs. Group 4:  p = .009
  - Implication: Family effects evident for DD risk

• Contrast A1 vs. Group 4:  p = .01
  - Implication: Family effects evident for AD risk

• Contrast Group 2 vs. Group 4:  p = .09
  - Implication: Little possible environmental effect

• Contrast Group 3 vs. Group 4:  p = .18
  - Implication: No genetic effect

• Contrast D1 vs. A1:  p = .51
  - Implications: Group 1 DD and AD risks are not equal

• Contrast D1 vs. Group 2:  p = .24
  - Implications: No environmental effect

• Contrast A1 vs. Group 2:  p = .72
  - Implication: No environmental effect

• Contrast Group 2 vs. Group 3:  p = .009
  - Implication: Genetic effects are evident

Discussion

• Both the Drug Group 1 and Alcohol Group 1 are significantly different from normal controls, indicating a strong family effect. Therefore, just as paternal drug or alcohol risk predicts offspring AD symptoms, both predict offspring CD symptoms as well.

• Group 2 (MZ twins without environmental risk) is significantly different from Group 3 (DZ twins without environmental risk), providing strong evidence for genetic effects.

• Since neither D1 or A1 is different from Group 2, and since Group 2 is close to significantly different from Group 4, there is very little evidence of environmental influences.

• All analytic approaches reach the same conclusion: genetic effects are most important in the transmission of risk from paternal history of both DD and AD to offspring CD outcomes.
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