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Evidence for Specificity of Transmission of Alcohol and Nicotine Dependence in an Offspring of Twins Sample

Heather E Volk MPH, Jeffrey F Scherrer PhD, Kathleen K Buchloz PhD, Andrew C Heath DPhil, Theodore Jacob PhD, William R True, PhD MPH
Background

• Alcohol dependence (AD) and nicotine dependence (ND) frequently co-occur
  – 22.8% of ND have alcohol use disorder\(^1\)
  – 34.5% with alcohol use disorder are ND\(^1\)

• AD and ND are both influenced by genes
  – 50-60% of risk for AD\(^2-4\)
  – 30-60% of risk for smoking initiation\(^2,5\)
  – 58-74% of risk for smoking persistence\(^2,6\)
Background

• AD and ND share genetic vulnerability
  – Genetic Correlation (r^A)
    \[ = 0.68 \text{ (95\%CI 0.61-0.74)} \]
  – Unique Environmental Correlation (r^E)
    \[ = 0.23 \text{ (95\%CI 0.14-0.32)^2} \]

• However, this overlap is incomplete. Risk may still be transmitted for AD only or ND only as well as for both substances together.

• Factors such as gender, age, and externalizing or internalizing disorders may moderate risk
Objective

• To test for specificity of transmission of AD and ND extending existing results on overlap of AD and ND using an offspring of twins design.
Methods (sample)

• Data from 2000-2002 study of adolescent and adult offspring of twin fathers sampled from the Vietnam Era Twin Registry
  – 730 twin fathers, 904 biologic and/or rearing mothers, 1,356 offspring
  – Lifetime diagnoses derived from structured diagnostic interview
Methods (measures)

- Twin father’s lifetime AD and ND diagnoses
- Offspring AD, ND, conduct disorder, panic attack, major depression, generalized anxiety disorder
- Maternal report of offspring attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD)
Methods (measures)

• Offspring disorders comorbid with AD or ND collapsed
  – Externalizing disorders: conduct disorder, ADHD, ODD
  – Internalizing disorders: panic attack, major depression, generalized anxiety disorder
Analysis

- Multinomial logistic regression to predict risk for comorbid AD and ND, AD only, or ND only
- 4 group offspring of twin design created for paternal AD and ND separately
  - Group 1: MZ/DZ affected
  - Group 2: MZ unaffected, cotwin affected
  - Group 3: DZ unaffected, cotwin affected
  - Group 4: MZ/DZ unaffected
Analysis

• Repeated multinomial logistic regression to examine effect of offspring gender, age, comorbid externalizing and internalizing psychopathology
## Results

Table 1: Multinomial Logistic Regression to Examine the Co-transmission of AD and ND due to Genetic Factors

<table>
<thead>
<tr>
<th></th>
<th>Comorbid AD and ND</th>
<th>AD</th>
<th>ND</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=116</td>
<td>N=100</td>
<td>N=196</td>
</tr>
<tr>
<td>MZ/DZ AD (Group 1)</td>
<td>1.79 (1.10-2.94)</td>
<td>2.09 (1.20-3.64)</td>
<td>1.06 (0.70-1.62)</td>
</tr>
<tr>
<td>MZ unaffected, cotwin AD (Group 2)</td>
<td>1.01 (0.40-2.57)</td>
<td>2.22 (1.08-4.53)</td>
<td>0.94 (0.50-1.78)</td>
</tr>
<tr>
<td>DZ unaffected, cotwin AD (Group 3)</td>
<td>1.25 (0.61-2.56)</td>
<td>1.64 (0.74-3.60)</td>
<td>0.69 (0.36-1.34)</td>
</tr>
<tr>
<td>MZ/DZ ND (Group 1)</td>
<td>1.93 (1.10-3.37)</td>
<td>0.79 (0.42-1.46)</td>
<td>2.56 (1.62-4.06)</td>
</tr>
<tr>
<td>MZ unaffected, cotwin ND (Group 2)</td>
<td>1.68 (0.72-3.93)</td>
<td>0.99 (0.50-1.98)</td>
<td>2.21 (1.25-3.92)</td>
</tr>
<tr>
<td>DZ unaffected, cotwin ND (Group 3)</td>
<td>1.65 (0.91-2.99)</td>
<td>0.83 (0.44-1.58)</td>
<td>1.33 (0.78-2.27)</td>
</tr>
</tbody>
</table>
Table 2: Multinomial Logistic Regression to Examine the Co-transmission of AD and ND due to Genetic Factors Adjusting for Covariates

<table>
<thead>
<tr>
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</tr>
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<td>MZ/DZ AD (Group 1)</td>
<td>1.54 (0.93-2.56)</td>
<td><strong>2.07 (1.17-3.68)</strong></td>
<td>0.96 (0.63-1.47)</td>
</tr>
<tr>
<td>MZ unaffected, cotwin AD (Group 2)</td>
<td>0.82 (0.32-2.12)</td>
<td><strong>2.24 (1.09-4.63)</strong></td>
<td>0.82 (0.42-1.63)</td>
</tr>
<tr>
<td>DZ unaffected, cotwin AD (Group 3)</td>
<td>1.28 (0.62-2.65)</td>
<td>1.73 (0.78-3.87)</td>
<td>0.72 (0.37-1.38)</td>
</tr>
<tr>
<td>MZ/DZ ND (Group 1)</td>
<td><strong>1.81 (1.01-3.25)</strong></td>
<td>0.77 (0.42-1.44)</td>
<td><strong>2.47 (1.57-3.90)</strong></td>
</tr>
<tr>
<td>MZ unaffected, cotwin ND (Group 2)</td>
<td>1.49 (0.63-3.52)</td>
<td>0.97 (0.48-1.98)</td>
<td><strong>2.04 (1.13-3.70)</strong></td>
</tr>
<tr>
<td>DZ unaffected, cotwin ND (Group 3)</td>
<td>1.32 (0.71-2.44)</td>
<td>0.79 (0.41-1.53)</td>
<td>1.14 (0.79-1.64)</td>
</tr>
<tr>
<td>Male Gender</td>
<td>1.10 (0.70-1.75)</td>
<td><strong>2.45 (1.53-3.92)</strong></td>
<td>1.14 (0.79-1.64)</td>
</tr>
<tr>
<td>Household Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;$50K/year</td>
<td>0.74 (0.45-1.23)</td>
<td>1.03 (0.62-1.72)</td>
<td>0.88 (0.59-1.32)</td>
</tr>
<tr>
<td>Age ≥18 years</td>
<td><strong>3.14 (1.81-5.46)</strong></td>
<td><strong>10.22 (4.82-21.64)</strong></td>
<td><strong>3.17 (2.04-4.92)</strong></td>
</tr>
<tr>
<td>Externalizing Disorders</td>
<td><strong>6.91 (4.33-11.02)</strong></td>
<td><strong>1.95 (1.17-3.24)</strong></td>
<td><strong>3.34 (2.33-4.78)</strong></td>
</tr>
<tr>
<td>Internalizing Disorders</td>
<td><strong>1.91 (1.21-3.02)</strong></td>
<td>0.98 (0.52-1.81)</td>
<td><strong>2.04 (1.39-2.99)</strong></td>
</tr>
</tbody>
</table>
Discussion

- Paternal AD and ND are associated with offspring AD and ND, respectively
- Paternal AD and ND predict comorbid AD and ND in offspring
- Specific genetic effects exist for transmission of AD and ND despite genetic correlation between the disorders
Discussion

• After controlling for genetic factors:
  – Age $> 18$ years and externalizing psychopathology increase risk for all outcomes
  – Internalizing disorders are associated with increased risk for comorbid AD and ND and ND alone
  – Male gender is associated with increased risk for AD alone
References


