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Genetic Basis for Comorbidity of Alcohol and Marijuana Dependence

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  • Dixie J. Statham, M.A.
INTRODUCTION

• Previous research has suggested that both alcohol dependence and marijuana dependence are heritable

• Furthermore, both clinical and general population studies have suggested a moderate to strong relationship between alcohol consumption and marijuana use

• Although it is plausible that the association is attributable to underlying risk factors shared by both alcohol and marijuana, little research has examined this possibility using a genetically informative design
RESEARCH QUESTIONS

• What are the relative contributions of genetic and environmental factors to marijuana dependence and DSM-IV alcohol dependence in young adults?

• To what extent are the genetic and environmental influences on marijuana and alcohol dependence the same?
SAMPLE

- 4955 individuals who completed a telephone diagnostic interview for the Australian Twin Study (“1989 cohort”)

- Both members of 2087 twin pairs:
  
  MZF=525  MZM=353
  DZF=415  DZM=296  DZO=498

- Mean age=29.5 years (range: 23-35)
MEASURES
Marijuana, part 1

- 2906 individuals had tried marijuana
- Mean age at first use = 18.9 years
- Number of times used:
  - Mean = 168.8
  - Median = 10
  - Mode = > 1000
  - 50.9% 10 or fewer times
  - 10.9% 1000 or more times
MEASURES
Marijuana, part 2

• Marijuana dependence was based on four criteria:
  • Used more often or in greater amounts than intended (13%; n=387)
  • Needed more to obtain same effect as had felt initially (16%; n=453)
  • Continued to use even though knew it caused emotional and/or psychological problems (17%; n=486)
  • Wanted to cut down on use 3+ times in life (15%; n=430)
MEASURES
Marijuana, part 3

- Total number of marijuana dependence symptoms (of those who had tried marijuana):
  - 71% had 0 Sx (n=2074)
  - 11% had 1 Sx (n=315)
  - 8% had 2 Sx (n=222)

- Marijuana dependence was defined as having three or four dependence symptoms

- 10% of users met dependence criteria (n=295)
MEASURES

Alcohol

• Only 25 of the 4955 participants (<1%) were lifelong alcohol abstainers

• 1070 respondents met DSM-IV criteria for alcohol dependence (3+ symptoms of 7 possible occurring within a 12-month period):

  • 28% had 0 Sx (n=1362)
  • 26% had 1 Sx (n=1263)
  • 22% had 2 Sx (n=1095)
  • 12% had 3 Sx (n=580)

  • 7% had 4 Sx (n=321)
  • 3% had 5 Sx (n=171)
  • 2% had 6 Sx (n=98)
  • 1% had 7 Sx (n=38)
RESULTS, 1

• Tetrachoric correlations provide an initial indication of familial influences on marijuana and alcohol dependence

• Because the MZ correlations are larger than the DZ correlations for both men and women (see **TABLE 1**), there is evidence of genetic influence on both measures

• Because the DZO correlations are similar in magnitude to the DZF and DZM correlations (see **TABLE 1**), there is not evidence of a gender difference in the genetic influences
**TABLE 1:**

**Tetrachoric Correlations**

**Marijuana Dependence**

<table>
<thead>
<tr>
<th></th>
<th>MZF=0.57* (0.30 – 0.77)</th>
<th>DZF=0.28 (-0.12 – 0.61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZF</td>
<td>0.57* (0.30 – 0.77)</td>
<td>DZF=0.28 (-0.12 – 0.61)</td>
</tr>
<tr>
<td>MZM</td>
<td>0.58* (0.30 – 0.78)</td>
<td>DZM=0.34* (0.03 – 0.60)</td>
</tr>
<tr>
<td></td>
<td>DZO=0.26 (-0.09 – 0.56)</td>
<td>DZM=0.34* (0.03 – 0.60)</td>
</tr>
</tbody>
</table>

**Alcohol Dependence**

<table>
<thead>
<tr>
<th></th>
<th>MZF=0.56* (0.39 – 0.69)</th>
<th>DZF=0.38* (0.19 – 0.56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZF</td>
<td>0.56* (0.39 – 0.69)</td>
<td>DZF=0.38* (0.19 – 0.56)</td>
</tr>
<tr>
<td>MZM</td>
<td>0.51* (0.35 – 0.65)</td>
<td>DZM=0.26* (0.07 – 0.44)</td>
</tr>
<tr>
<td></td>
<td>DZO=0.26* (0.09 – 0.41)</td>
<td>DZM=0.26* (0.07 – 0.44)</td>
</tr>
</tbody>
</table>

* Indicates p < .05
RESULTS, 2

- Structural equation modeling was used to assess the significance of genetic and environmental influences on marijuana and alcohol dependence, and to assess the extent of genetic and environmental overlap.

- The bivariate genetic model used to assess genetic and environmental overlap between alcohol and marijuana dependence is shown in FIGURE 1.

- There was significant genetic influence on both alcohol and marijuana dependence (see TABLE 2).

- The genetic overlap between alcohol and marijuana dependence was significant and substantial; environmental overlap was not significant (see TABLE 3).
FIGURE 1

A = additive genetics  
C = shared environment  
E = nonshared environment

$r_A$, $r_C$, and $r_E$ are the genetic, shared environmental, and nonshared environmental correlations respectively.
### TABLE 2: Proportions of Variance

<table>
<thead>
<tr>
<th></th>
<th>Alcohol Dependence</th>
<th>Marijuana Dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genetic</strong></td>
<td>0.46*</td>
<td>0.56*</td>
</tr>
<tr>
<td></td>
<td>(0.19 – 0.63)</td>
<td>(0.19 – 0.74)</td>
</tr>
<tr>
<td><strong>Shared Environmental</strong></td>
<td>0.07</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>(0.001 – 0.28)</td>
<td>(0.001 – 0.36)</td>
</tr>
<tr>
<td><strong>Nonshared Environmental</strong></td>
<td>0.46*</td>
<td>0.39*</td>
</tr>
<tr>
<td></td>
<td>(0.37 – 0.57)</td>
<td>(0.26 – 0.56)</td>
</tr>
</tbody>
</table>

* Indicates p < .05
<table>
<thead>
<tr>
<th></th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic</td>
<td>0.87*</td>
</tr>
<tr>
<td></td>
<td>(0.40 – 1.00)</td>
</tr>
<tr>
<td>Shared Environmental</td>
<td>-1.00</td>
</tr>
<tr>
<td></td>
<td>(-1.00 – 1.00)</td>
</tr>
<tr>
<td>Nonshared Environmental</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>(-0.09 – 0.37)</td>
</tr>
</tbody>
</table>

* Indicates $p < .05$
CONCLUSIONS

• Both marijuana dependence and DSM-IV alcohol dependence are influenced by genetic factors ($h^2=0.56$ and 0.46 respectively)

• There is evidence of substantial genetic overlap between marijuana and alcohol dependence ($r_A=0.87$)

• Nonshared environmental influences on marijuana and alcohol dependence do not appear to be correlated ($r_E=0.13$)