Genetic basis for comorbidity of alcohol and marijuana dependence

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Genetic Basis for Comorbidity of Alcohol and Marijuana Dependence

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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)
  - 6% had 3 Sx (n=183)
  - 4% had 4 Sx (n=112)
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>
<thead>
<tr>
<th></th>
<th>Marijuana Dependence</th>
<th>Alcohol Dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZF</td>
<td>$0.57^* (0.30 - 0.77)$</td>
<td>$0.56^* (0.39 - 0.69)$</td>
</tr>
<tr>
<td>MZM</td>
<td>$0.58^* (0.30 - 0.78)$</td>
<td>$0.51^* (0.35 - 0.65)$</td>
</tr>
<tr>
<td>DZF</td>
<td>$0.28 (-0.12 - 0.61)$</td>
<td>$0.38^* (0.19 - 0.56)$</td>
</tr>
<tr>
<td>DZM</td>
<td>$0.34^* (0.03 - 0.60)$</td>
<td>$0.26^* (0.07 - 0.44)$</td>
</tr>
<tr>
<td>DZO</td>
<td>$0.26 (-0.09 - 0.56)$</td>
<td>$0.26^* (0.09 - 0.41)$</td>
</tr>
</tbody>
</table>

* Indicates $p < .05$
RESULTS

• 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>
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<th></th>
<th>Alcohol Dependence</th>
<th>Marijuana Dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.46*</td>
<td>0.56*</td>
</tr>
<tr>
<td>Genetic</td>
<td>(0.19 – 0.63)</td>
<td>(0.19 – 0.74)</td>
</tr>
<tr>
<td>Shared Environmental</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>Nonshared Environmental</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

**TABLE 3:**
Correlations between Alcohol and Marijuana Dependence
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 ($r_E = 0.13$)