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## 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
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# 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?
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# 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)
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# 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)
    - 6% had 3 Sx (n=183)
    - 4% had 4 Sx (n=112)
  - Marijuana dependence was defined as having three or four dependence symptoms
  - 10% of users met dependence criteria (n=295)
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# 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)
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# 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
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# TABLE 1:

## Tetrachoric Correlations

### Marijuana Dependence

MZF=0.57\* (0.30 – 0.77)

DZF=0.28 (-0.12 – 0.61)

MZM=0.58\* (0.30 – 0.78)

DZM=0.34\* (0.03 – 0.60)

DZO=0.26 (-0.09 – 0.56)

### Alcohol Dependence

MZF=0.56\* (0.39 – 0.69)

DZF=0.38\* (0.19 – 0.56)

MZM=0.51\* (0.35 – 0.65)

DZM=0.26\* (0.07 – 0.44)

DZO=0.26\* (0.09 – 0.41)

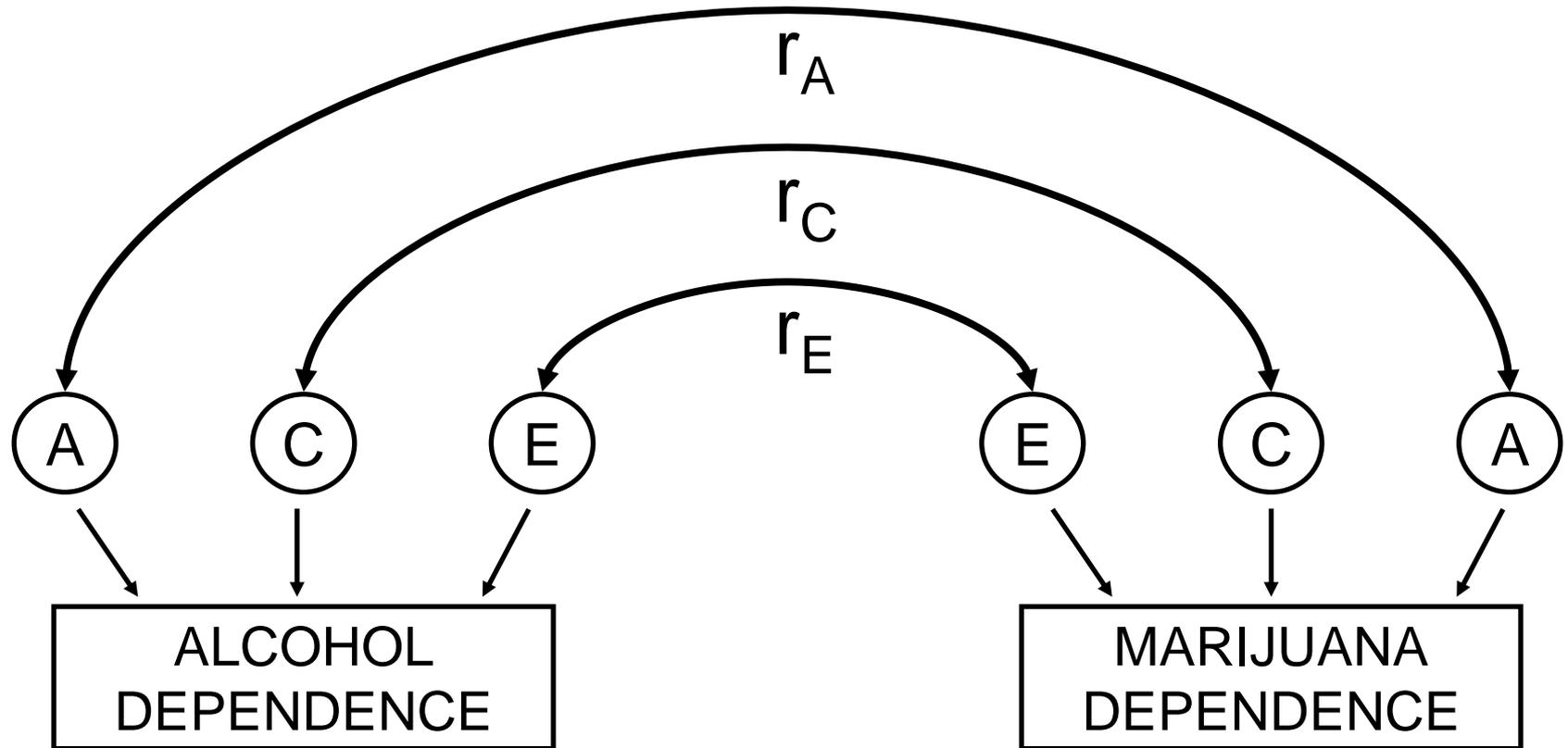
\* Indicates  $p < .05$

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# 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**)
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# 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

	Alcohol Dependence	Marijuana Dependence
Genetic	<b>0.46*</b> (0.19 – 0.63)	<b>0.56*</b> (0.19 – 0.74)
Shared Environmental	<b>0.07</b> (0.001 – 0.28)	<b>0.04</b> (0.001 – 0.36)
Nonshared Environmental	<b>0.46*</b> (0.37 – 0.57)	<b>0.39*</b> (0.26 – 0.56)

\* Indicates  $p < .05$

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# TABLE 3:

## Correlations between Alcohol and Marijuana Dependence

Genetic:	<b>0.87*</b> (0.40 – 1.00)
Shared Environmental:	<b>-1.00</b> (-1.00 – 1.00)
Nonshared Environmental:	<b>0.13</b> (-0.09 – 0.37)

\* Indicates  $p < .05$

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# 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 be correlated ( $r_E=0.13$ )
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