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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)

  - 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)

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

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)

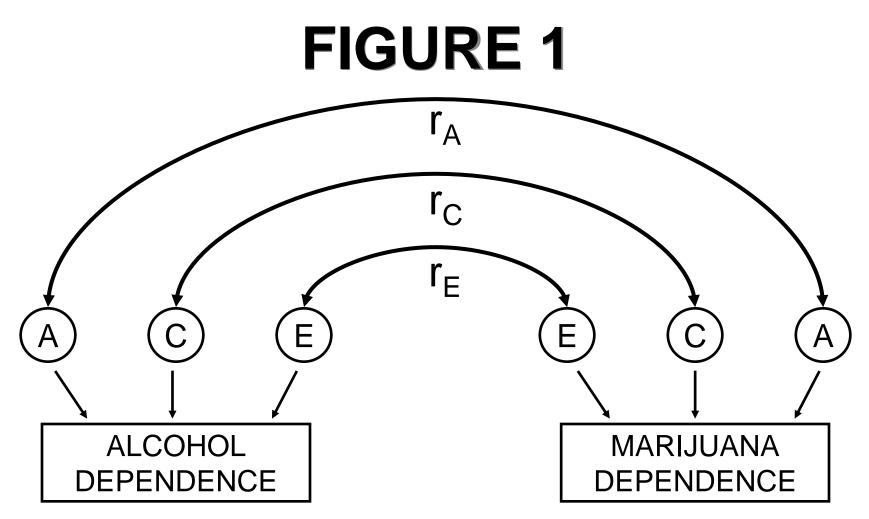   DZO=0.26* (0.09 – 0.41)

* Indicates p < .05

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**)
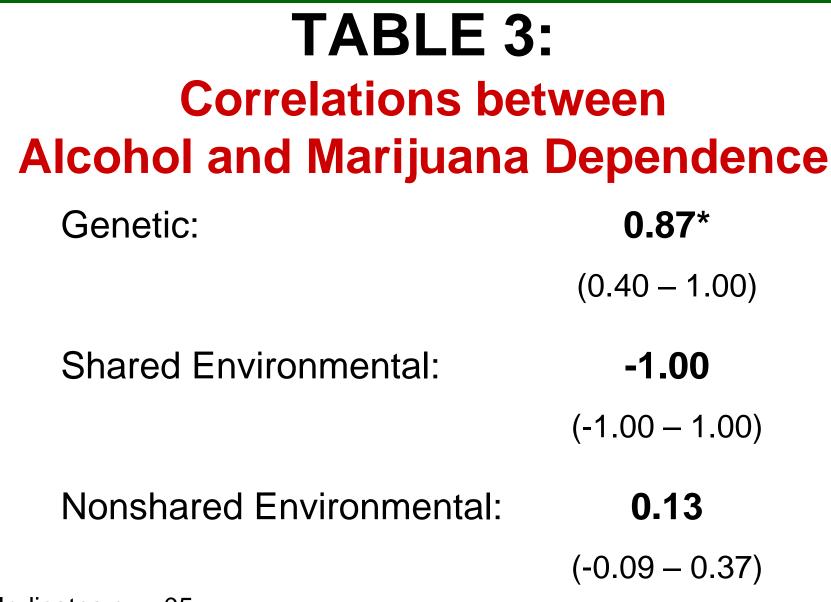
FIGURE 1

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

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

* Indicates p < .05

TABLE 3:

Correlations between
Alcohol and Marijuana Dependence

Genetic: **0.87***

                                  (0.40 – 1.00)

Shared Environmental: **-1.00**

                                  (-1.00 – 1.00)

Nonshared Environmental: **0.13**

                                  (-0.09 – 0.37)

* 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 be correlated (r_E=0.13)