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The magnitude of genetic and environmental influences common to comorbid alcoholism and marijuana problem use is stable across diagnostic phenotypes

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- **Alcohol Dependence (AD) and Marijuana Dependence (MJD) are often co-morbid disorders**
 - **Previous analyses of Vietnam Era Twin Registry (VETR) data has suggested common genetic risk at the symptom level diagnoses**
 - **Past research has not investigated if the common genetic and environmental risks are similar for varying diagnostic phenotypes**
 - **Does the genetic architecture underlying alcohol and marijuana problem use vary by diagnostic phenotype?**

METHODS

■ Subjects and data collection

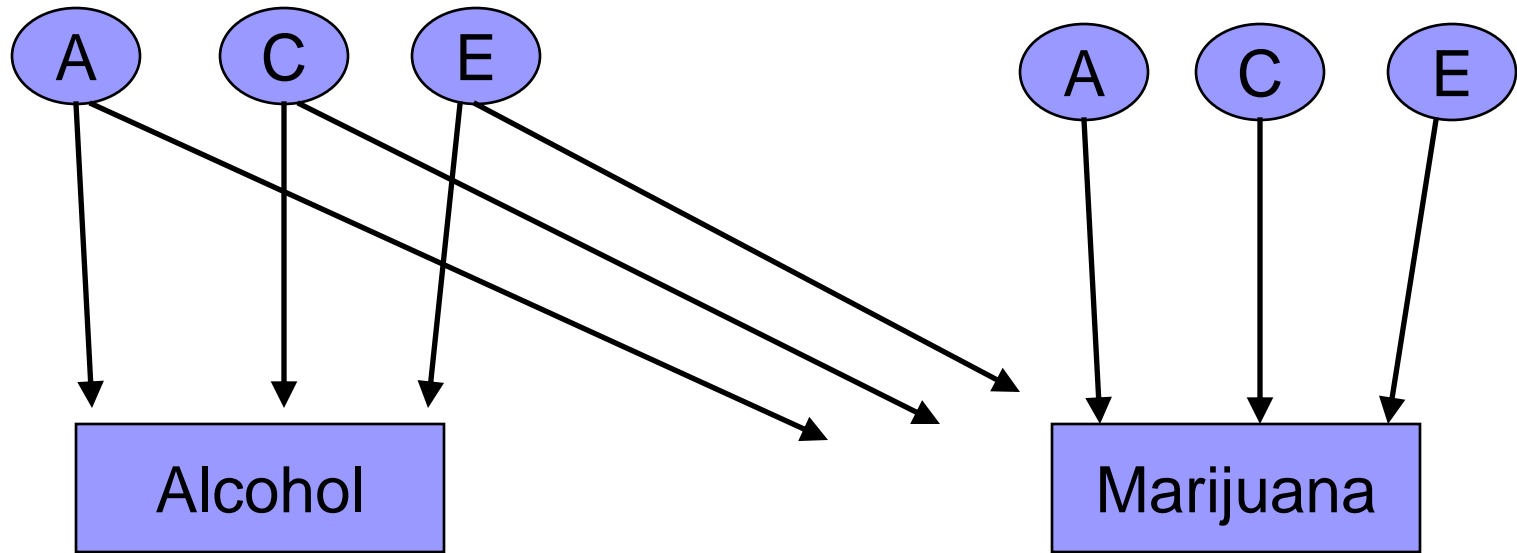
- **Male-Male twin pair members of the Vietnam Era Twin (VET) Registry**
- **Both twins served during Vietnam Era (1965-1975)**
- **6,711 twins answered questions about alcohol and marijuana use in 1992 administration of the Diagnostic Interview Schedule (DIS)**

- **Eligibility criteria for current study**
 - Participated in 1992 telephone admin. of DIS
 - Data available from both members of a twin pair
 - Data complete for alcohol and marijuana

■ Alcohol and Marijuana Phenotypes

- **dependence only**
- **abuse/dependence**
- **severity (unaffected, abuse only, dependence only)**

- **Genetic model fitting**
- **Bivariate Cholesky models**
- **Lisrel and MX software**





- **Prevalence of alcohol and marijuana phenotypes**

Alcohol abuse only	19.3%
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Alcohol dependence only	35.2%
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Alcohol abuse/dependence	54.5%
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Marijuana abuse only	0.6%
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Marijuana dependence only	6.6%
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Marijuana abuse/dependence	7.2%
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Distribution of Co-morbid Alcohol and Marijuana Abuse and Dependence

Marijuana

		Unaffected	Abuse	Dependence
Alcohol	Unaffected	2998 98.2%	6 0.2%	48 1.6%
	Abuse	1219 94.1%	7 0.5%	70 5.4%
	Dependence	2010 85.1%	27 1.1%	326 13.8%

Bivariate Model Fitting Results: Variance Component Estimates for Full and Best Fitting Models

1. Severity phenotype: full model

Alcohol unaffected/abuse/dep			Cannabis unaffected/abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-7.61
43.8%	9.0%	47.2%	14.8%	8.0%	5.3%	17.5%	21.6%	32.9%	

2. Severity phenotype: best reduced model

Alcohol unaffected/abuse/dep			Cannabis unaffected/abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-10.49
54.0%	--	46.0%	23.2%	--	4.5%	--	36.7%	35.6%	

1. Abuse/dependence phenotype: full model

Alcohol abuse/dependence			Cannabis abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-7.61
40.3%	12.8%	46.8%	27.0%	1.0%	4.7%	4.1%	29.7%	33.7%	

2. Abuse/dependence phenotype: best reduced model

Alcohol abuse/dependence			Cannabis abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-10.89
54.8%	--	45.2%	25.1%	--	4.4%	--	35.5%	35.0%	

1. Dependence phenotype: full model

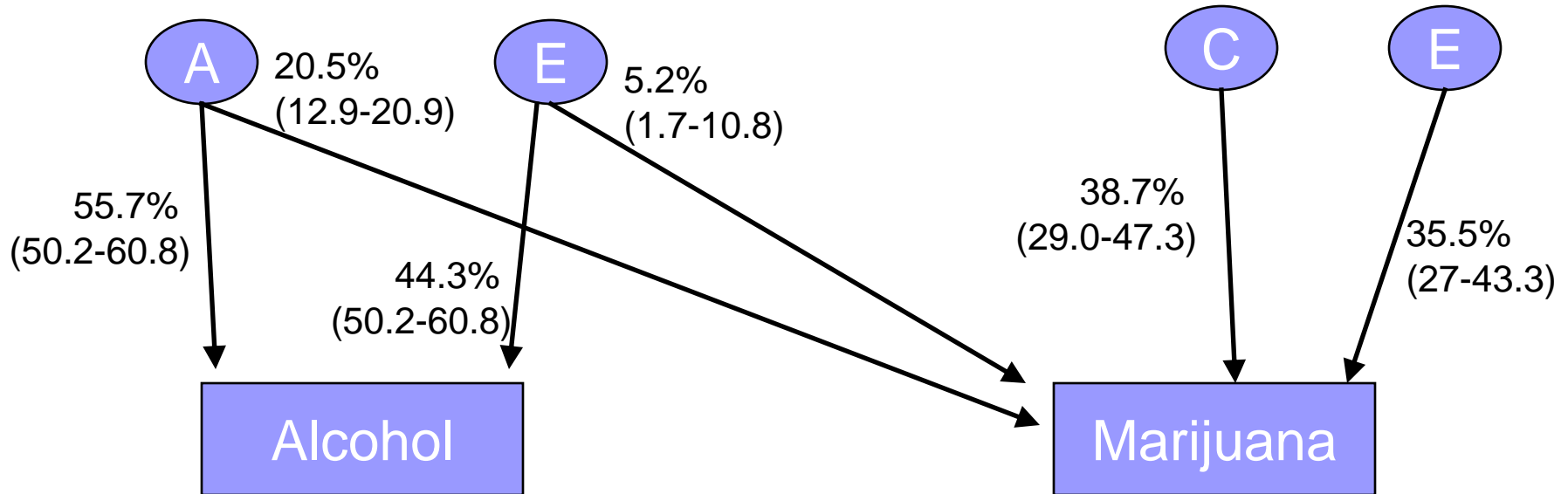
Alcohol dependence			Cannabis abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-4.66
51.6%	3.7%	44.7%	8.6%	0%	6.7%	23.7%	29.5%	31.6%	


2. Dependence phenotype: best reduced model

Alcohol dependence			Cannabis abuse/dependence						Model Fit
			Common			Specific			AIC
a ²	c ²	e ²	a ²	c ²	e ²	a ²	c ²	e ²	-8.06
55.7%	--	44.3%	20.5%	--	5.2%	--	38.7%	35.5%	

* **AIC: Akaike Information Criterion – measure of parsimony**

Path diagram for best fitting dependence model



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- Most co-morbidity accounted for by marijuana dependence among subjects with alcohol dependence
 - Genetic factors account for 20% and unique environmental factors account for 5% of marijuana dependence co-morbid with alcohol dependence
 - The genetic architecture was similar across phenotypes studied
 - Further research should consider diagnostic phenotypes outside limitations of DSM that may be derived from factor analyses or latent class analyses

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