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Evidence for Specificity of Transmission of Alcohol and Nicotine Dependence in an Offspring of Twins Sample

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Background

- Alcohol dependence (AD) and nicotine dependence (ND) frequently co-occur
 - 22.8% of ND have alcohol use disorder¹
 - 34.5% with alcohol use disorder are ND¹
- AD and ND are both influenced by genes
 - 50-60% of risk for AD²⁻⁴
 - 30-60% of risk for smoking initiation^{2,5}
 - 58-74% of risk for smoking persistence^{2,6}

Background

- AD and ND share genetic vulnerability
 - Genetic Correlation (r^A)
= 0.68 (95%CI 0.61-0.74)
 - Unique Environmental Correlation (r^E)
= 0.23 (95%CI 0.14-0.32)²
- However, this overlap is incomplete. Risk may still be transmitted for AD only or ND only as well as for both substances together.
- Factors such as gender, age, and externalizing or internalizing disorders may moderate risk

Objective

- To test for specificity of transmission of AD and ND extending existing results on overlap of AD and ND using an offspring of twins design.

Methods (sample)

- Data from 2000-2002 study of adolescent and adult offspring of twin fathers sampled from the Vietnam Era Twin Registry
 - 730 twin fathers, 904 biologic and/or rearing mothers, 1,356 offspring
 - Lifetime diagnoses derived from structured diagnostic interview

Methods (measures)

- Twin father's lifetime AD and ND diagnoses
- Offspring AD, ND, conduct disorder, panic attack, major depression, generalized anxiety disorder
- Maternal report of offspring attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD)

Methods (measures)

- Offspring disorders comorbid with AD or ND collapsed
 - Externalizing disorders: conduct disorder, ADHD, ODD
 - Internalizing disorders: panic attack, major depression, generalized anxiety disorder

Analysis

- Multinomial logistic regression to predict risk for comorbid AD and ND, AD only, or ND only
- 4 group offspring of twin design created for paternal AD and ND separately
 - Group 1: MZ/DZ affected
 - Group 2: MZ unaffected, cotwin affected
 - Group 3: DZ unaffected, cotwin affected
 - Group 4: MZ/DZ unaffected

Analysis

- Repeated multinomial logistic regression to examine effect of offspring gender, age, comorbid externalizing and internalizing psychopathology

Results

Table 1: Multinomial Logistic Regression to Examine the Co-transmission of AD and ND due to Genetic Factors

	Comorbid AD and ND N=116	AD N=100	ND N=196
MZ/DZ AD (Group 1)	1.79 (1.10-2.94)	2.09 (1.20-3.64)	1.06(0.70-1.62)
MZ unaffected, cotwin AD (Group 2)	1.01 (0.40-2.57)	2.22 (1.08-4.53)	0.94 (0.50-1.78)
DZ unaffected, cotwin AD (Group 3)	1.25 (0.61-2.56)	1.64 (0.74-3.60)	0.69 (0.36-1.34)
MZ/DZ ND (Group 1)	1.93 (1.10-3.37)	0.79 (0.42-1.46)	2.56 (1.62-4.06)
MZ unaffected, cotwin ND (Group 2)	1.68 (0.72-3.93)	0.99 (0.50-1.98)	2.21 (1.25-3.92)
DZ unaffected, cotwin ND (Group 3)	1.65 (0.91-2.99)	0.83 (0.44-1.58)	1.33 (0.78-2.27)

Table 2: Multinomial Logistic Regression to Examine the Co-transmission of AD and ND due to Genetic Factors Adjusting for Covariates

	Comorbid AD and ND N=116	AD N=100	ND N=196
MZ/DZ AD (Group 1)	1.54 (0.93-2.56)	2.07 (1.17-3.68)	0.96 (0.63-1.47)
MZ unaffected, cotwin AD (Group 2)	0.82 (0.32-2.12)	2.24 (1.09-4.63)	0.82 (0.42-1.63)
DZ unaffected, cotwin AD (Group 3)	1.28 (0.62-2.65)	1.73 (0.78-3.87)	0.72 (0.37-1.38)
MZ/DZ ND (Group 1)	1.81 (1.01-3.25)	0.77 (0.42-1.44)	2.47 (1.57-3.90)
MZ unaffected, cotwin ND (Group 2)	1.49 (0.63-3.52)	0.97 (0.48-1.98)	2.04 (1.13-3.70)
DZ unaffected, cotwin ND (Group 3)	1.32 (0.71-2.44)	0.79 (0.41-1.53)	1.14 (0.79-1.64)
Male Gender	1.10 (0.70-1.75)	2.45 (1.53-3.92)	1.14 (0.79-1.64)
Household Income >\$50K/year	0.74 (0.45-1.23)	1.03 (0.62-1.72)	0.88 (0.59-1.32)
Age \geq 18 years	3.14 (1.81-5.46)	10.22 (4.82-21.64)	3.17 (2.04-4.92)
Externalizing Disorders	6.91 (4.33-11.02)	1.95 (1.17-3.24)	3.34 (2.33-4.78)
Internalizing Disorders	1.91 (1.21-3.02)	0.98 (0.52-1.81)	2.04 (1.39-2.99)

Discussion

- Paternal AD and ND are associated with offspring AD and ND, respectively
- Paternal AD and ND predict comorbid AD and ND in offspring
- Specific genetic effects exist for transmission of AD and ND despite genetic correlation between the disorders

Discussion

- After controlling for genetic factors:
 - Age \geq 18 years and externalizing psychopathology increase risk for all outcomes
 - Internalizing disorders are associated with increased risk for comorbid AD and ND and ND alone
 - Male gender is associated with increased risk for AD alone

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