2009

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Genetic and Environmental Influences on Change and Stability of Alcohol Consumption

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Abstract

Past research using behavior genetic methodology (i.e., studies of twins) has found estimates of the heritability (the proportion of total phenotypic variance accounted for by genetic variance) of alcohol consumption around .40-.60. The purpose of the current study was to examine the heritability of alcohol consumption over time and to examine genetic and environmental influences on change and stability in alcohol consumption over time. Male twins from the Vietnam Era Twin Registry were assessed with quantity-frequency measures (QFI) of alcohol consumption in 1987 (when approximately age 38), 1992 (age 42), and 2000 (age 50). High concordance rates for both MZ and DZ twins were found for abstinence, revealing large environmental effects. For QFI scores, however, MZ twin pairs were much more similar than DZ twin pairs, revealing genetic influences. A trivariate Cholesky biometric model was used to estimate genetic and shared environmental influences on QFI. The AE model fit the data best, with heritabilities at all three assessments around .35. There was no significant change in heritability over time. The modeling results also supported the hypotheses that stability in QFI scores across time was primarily accounted for by genetic effects, the change in scores at subsequent time points was primarily environmental.

Background

- Heritability estimates (proportion of total phenotypic/ behavioral variance accounted for by genetic variance) for alcohol abuse and dependence are around .45-.60 (Dick & Bierut, 2006; Heath, et al., 1997; McGue, 1999; Prescott & Kendler, 1999)

- Studies have also found that different aspects of alcohol use behavior may be differentially influenced by genes and environment.

  - For instance, the initiation of substances and abstinence are more environmentally influenced than problem use and consumption (Heath, Meyer, Jardine, & Martin, 1991; Rhee, et al., 2003)

- Measures of alcohol consumption (frequency and quantity of use) have been shown to have heritabilities around .40-.60 (Hansell et al., 2008; Heath, 1995; Reed, et al., 1994; Swan, Carmelli, & Cardon, 1996)
- The purpose of the current study was to examine the heritability of alcohol consumption over time in a sample of twins in midlife and to examine genetic and environmental influences on change and stability in alcohol consumption

Hypotheses

- It was hypothesized that
  - (1) twin concordance rates for abstinence for both MZ (monozygotic) and DZ (dizygotic) twins would be similar, indicating large shared environmental effects on drinking initiation
  - (2) correlations for alcohol consumption levels would be higher for MZ twins than DZ twins, indicating a genetic effect
  - (3) there would be little residual genetic effect for successive time points of QFI measurement, showing strong genetic influences on stability in consumption but not on change in consumption
    - Non-shared environmental effects were hypothesized to influence change in consumption levels over time

Methods

- Participants: 1295 Male twins from the Vietnam Era Twin Registry
  - 671 MZ twins (280 full pairs)
  - 624 DZ twins (253 full pairs)
- Procedure: assessed at three time points for quantity-frequency measures (QFI) of alcohol consumption
  - 1987 Survey of Health, mailed survey
    - Mean age = 38.9, SD = 2.6, range 30-45
  - 1992 Harvard Drug Study, phone interview
    - Mean age = 41.6, SD = 2.5, range 34-49
  - 2000 Family Twin Study, phone interview, using Lifetime Drinking History (LDH)
    - Mean age = 50.9, SD = 2.8, range 43-63
  - 99.2% of the mean have quantity-frequency data at all three time points

- Measures:
  - Abstinence = QFI scores of zero at all three assessments *and* report of no regular drinking on the LDH
  - QFI score = number of drinks per month
    - Maximum score cut off at 360, scores log-transformed to reduce skew
- Analyses:
  - Phenotypic correlations across time
  - MZ and DZ concordance rates for abstinence
  - MZ and DZ correlations for QFI scores
  - Trivariate Cholesky model to estimate A, C, and E components of variance, for drinking sample. See Figure 1.

Results

- Phenotypic correlations across time:
  - Rank-order stability was high
    - Correlations between .50 - .65 for entire sample
    - Correlations between .38 - .61 for drinking subsample (twin pairs who were both drinkers)

- MZ and DZ concordance rates for abstinence: Table 1
  - 158 twins categorized as abstinent, 77 (of 671) MZ twins and 81 (of 624) DZ twins
  - Large shared environmental effects for abstinence, as DZ twins were equally concordant as MZ twins (6.3% & 4.3%)

- MZ and DZ correlations for QFI scores: Table 2
  - MZ correlations higher than DZ correlations across all time points, thus showing genetic effect

- Trivariate Cholesky model to estimate A, C, and E components of variance: Table 3 and Figure 1
  - Model fitting:
    - The AE model fit the data better than the full ACE model (change in -2LL of 1.2 on 6 df, $p > .05$, AIC = -10.84)
    - The CE model also fit the data better than the full ACE model (change in -2LL of 7.95 on 6 df, $p > .05$, AIC = -4.05), but it did not fit better than the AE model
  - Estimates:
    - Total heritability around .35 at each assessment
    - At each successive timepoint, most of the genetic variance was shared with the genetic variance from previous assessments
    - Environmental variance was unique (residual) to each assessment
    - Genetic correlations were large, showing the same genes are influencing QFI at each time point

Table 1. Number (and Percent) of Twin Pairs Concordant and Discordant for Abstinence.

| | MZ pairs (N=280) | | DZ pairs (N=253) | |
	Abstainer	Drinker	Abstainer	Drinker
Abstainer	12 (4.3%)		16 (6.3%)	
Drinker	40 (14.3%)	228 (81.4%)	34 (13.4%)	203 (80.2%)

Table 2. Intraclass Correlations for MZ and DZ Twins on QFI Scores for the Entire Sample and the Subsample of Drinking Twin Pairs.

| | Entire Sample | | Drinking Pairs | |
Assessment	MZ	DZ	MZ	DZ
1987	.44** N=276	.23** N=251	.40** N=225	.12* N=202
1995	.38** N=280	.27** N=253	.36** N=228	.18** N=203
2000	.36** N=279	.27** N=251	.32** N=227	.18** N=202

Table 3. Standardized Variance Estimates (and 95% Confidence Intervals) and Genetic/Environmental Correlations for QFI Scores in the Drinking Sample.

Assessment	Paths	Standardized Variance		Correlation	
		A	E	A	E
1987	Residual (a_1 and e_1)	.36 (.25-.46)	.64 (.54-.75)		
1992	Due to 1987 (a_{21} and e_{21})	.30 (.20-.41)	.13 (.07-.19)	.92 (.81-1.0)	.44 (.35-.52)
	Residual (a_2 and e_2)	.05 (.003-.12)	.52 (.45-.59)		
2000	Due to 1987 (a_{31} and e_{31})	.16 (.08-.27)	.03 (.01-.07)	.72 (.51-.93)	.20 (.09-.31)
	Due to 1992 (a_{32} and e_{32})	.15 (.03-.26)	.02 (.004-.05)	.93 (.79-1.0)	.24 (.15-.33)
	Residual (a_3 and e_3)	.00 (.00-.10)	.64 (.55-.73)		

Figure 1. Trivariate Cholesky Model

A = additive genetic effect, E = nonshared environmental effect.

Conclusions

- All hypotheses were supported:
  - There were large shared environmental influences on drinking initiation/abstinence
  - There was genetic influence on QFI scores ($a^2 \approx .35$)
    - No evidence for a change in the heritability of consumption with age in our sample of men in midlife
  - There were large genetic correlations between QFI assessments, showing that stability in scores was due to genetic effects. Residual variance was due to non-shared environmental influences, which influence change in QFI over time.
- More research should be done examining the environmental influences on change in alcohol use, as possible mechanisms for treatment.

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