Detecting Underlying Mechanisms of the Comorbidity between Alcohol Dependence and Suicidality

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Project Goals

- It is well-established that alcohol dependence and suicidality are co-occurring more often than expected by chance.
- The mechanisms of this comorbidity are poorly researched.
- This analysis is to understand how genetic and environmental risk factors influence the comorbidity of alcohol dependence and suicidality.
Description

- The Vietnam Era Twin Registry (VETR), N=7,369 male-male twin pairs, assembled from computerized Department of Defense databases in the 1980s.
  - Monozygotic twins: 53.5%; dizygotic twins: 43.8%; indeterminate zygosity: 2.7%.

- A total of 3,360 complete twin pairs from the Harvard Twin Study of Substance Abuse and Dependence surveyed by telephone in 1992.
  - the overall pairwise response rate: 66.1%
  - individual response rate: 79.7%.

Description

- The mean age at interview:
  - 42.0 years (SD +2.7, range 33-52 years)

- Ethnicity:
  - 93.8% non-Hispanic white
  - 5.8% African American
  - <1% Hispanic
  - 0.3% other

- Education:
  - 33.3% high school graduates
  - 38.7% college graduates

- Employment:
  - 98.2% full-time
  - 1.8% part-time
Statistical Analysis

• Assessment
  − Main outcomes
    • Lifetime DSM III-R alcohol dependence, determined using a computerized telephone version of the Diagnostic Interview Schedule, Version 3, Revised (DIS3R).
    • Suicidality, a composite variable - suicide attempt, suicidal ideation only, and neither.
  − Other covariates
    • Lifetime DSM III-R nicotine dependence, illicit drug dependence, major depression, panic disorder, posttraumatic stress disorder, antisocial personality disorder, race, education, marital status, employment, and combat exposure.

• Biometric Model
  − Liability to a phenotype or trait is assumed to be continuous and normally distributed in the population, with individuals who exceed a theoretical threshold expressing the outcomes, so-called a standard normal liability-threshold model.
  − Structural equation modeling was used to decompose the phenotypic correlation between two traits into additive genetic (AG), share environmental (SE) and nonshared environmental (NE) correlation components.
Statistical Analysis

• Biometric Model
  - Two types of bivariate correlation models were fitted to the raw data by the maximum likelihood method using Mx (Neale, 1999). One model estimated genetic and environmental correlations without adjusting for the confounding effects. The other one re-estimated those correlation after adjusting for other major psychiatric disorders and sociodemographic variables.
  - A goodness-of-fit chi-square test was used to assess the fit of a submodel. \( p \)-value >0.05 indicates a good fit.

Results

• Figure 1. Genetic and environmental variances and correlations of DSM-III-R alcohol dependence and suicidality. Chi-square test \( p=0.98 \)
Results

- Figure 2. Genetic and environmental variances and correlations of DSM-IIIR alcohol dependence and suicidality after controlling for sociodemographic and other psychiatric disorders. Chi-square test $p=0.96$

<table>
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<tr>
<th>AG$_1$</th>
<th>AG$_2$</th>
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<th>SE$_1$</th>
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<td>0%</td>
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<table>
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<th>NE$_1$</th>
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<td>44.6%</td>
<td>64.8%</td>
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<td>0.21 (0.11 – 0.31)</td>
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Summary

- The genetic, shared environmental and nonshared environmental correlation between liabilities to alcohol dependence and suicidality was 0.45, 0.0, and 0.23, respectively.

- Genetic factors accounted for approximately two thirds of the phenotypic correlation between alcohol dependence and suicidality.

- After controlling for other psychiatric disorders and sociodemographic variables, the above correlations became 0.21, 0.0, and 0.12, respectively.
Conclusions

- The comorbidity of alcohol dependence and suicidality can be explained by common genetic and nonshared environmental risk factors.
- Genetic risk factors are the main causes of the comorbidity.
- Moreover, approximately half of the common risks are mediated by genetic and nonshared environmental risk factors responsible for other major psychiatric disorder.