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Genetic and Environmental Contributions to Post-traumatic Stress Disorder and Alcohol Dependence in Young Women

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ALCOHOLISM
MIDWEST RESEARCH CENTER

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Background

- Rates of alcohol dependence (AD) are elevated in individuals who meet criteria for post-traumatic stress disorder (PTSD).

- Twin studies have consistently produced evidence for substantial genetic contributions both to PTSD and to AD.

- The majority of genetically-informative studies of PTSD have focused exclusively on males, yet the prevalence of PTSD (and co-occurrence with AD) in women is comparable to that in men.

- ***The current study explored common genetic and environmental contributions to PTSD and AD in young women.***

Participants

- Twins born between 1975 and 1985 recruited into the Missouri Adolescent Female Twin Study (MOAFTS)

- MOAFTS is a longitudinal study of alcohol use disorders and related psychopathology in female adolescents and young adults, with 5 waves of data collection (PI: Heath).

- The sample for the current study consisted of all Wave 4 participants (n=3,787).

- 85.4% self-identified as Caucasian, 14.6% as African-American.

Participants

- Data were drawn from all waves where lifetime (vs. past 12- or 24-month) histories were assessed: 1, 3, and 4.

- Respondents ranged in age from:
  - ❖ 12 - 23 at Wave 1
  - ❖ 15 - 23 at Wave 3
  - ❖ 18 - 29 at Wave 4

- The sample was comprised of:
  - ❖ 954 monozygotic (MZ) twin pairs
  - ❖ 819 dizygotic (DZ) twin pairs
  - ❖ 135 twins whose co-twins did not participate

Assessment Protocol

The Semi-Structured Assessment for the Genetics of Alcoholism was adapted for telephone administration and used to gather psychiatric histories, including:

- **Traumatic event exposures**
- **DSM-IV Alcohol dependence**
- **DSM-IV Post-traumatic stress disorder (PTSD)**

PTSD Criteria

A. Experienced or witnessed an event involving threat to life or personal integrity that induced feelings of fear, horror, or helplessness

B. Re-experiencing symptoms (1+): 1) intrusive memories 2) distressing dreams 3) re-living of event 4) intense psychological distress when exposed to reminders 5) physiological reactivity when exposed to reminders

C. Avoidance symptoms (3+): 1) avoidance of thoughts or feelings associated with traumatic event 2) avoidance of people, places, or activities that arouse recollections of event 3) inability to recall important aspects of event 4) diminished interest in significant activities 5) detachment from others 6) restricted range of affect 7) sense of foreshortened future

D. Arousal symptoms (2+): 1) sleep difficulties 2) irritability or angry outbursts 3) difficulty concentrating 4) hypervigilance 5) exaggerated startle response

E. Symptom duration of 1 month or longer

F. Clinically significant distress or impairment in functioning

Events Identified as Most Distressing
('Nominated Events' in PTSD assessment)

Event	All who endorsed an event (n=1,673)	PTSD + (n=138)
Natural disaster	18.9%	0%
Life-threatening accident	16.8%	8.0%
Witnessed death/serious injury	17.6%	8.0%
Raped	11.2%	31.2%
Sexually molested	12.0%	30.0%
Physically abused as child	6.6%	6.5%
Seriously physically attacked	4.0%	7.3%
Seriously neglected as child	1.6%	3.6%
Threatened w/weapon or kidnapped	5.7%	5.8%
Other	5.6%	0.7%

PTSD and AD

- Mean age at PTSD onset: 13.8 years (SD=5.2)

- Mean age at AD onset: 17.8 years (SD=2.4)

- Prevalence of AD *

  - ❖ PTSD **-** : 11.3%

  - ❖ PTSD **+** : 33.3%

- Proportion of PTSD+/AD+ cases meeting PTSD criteria:

  - ❖ Prior to/same age as AD onset: 69.6%

  - ❖ Following AD onset: 30.4%

* $\chi 2$ = 60.51, p<.001

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Genetic Modeling

Standard genetic analyses were conducted in the structural equation modeling program Mx to partition variance into 3 components:
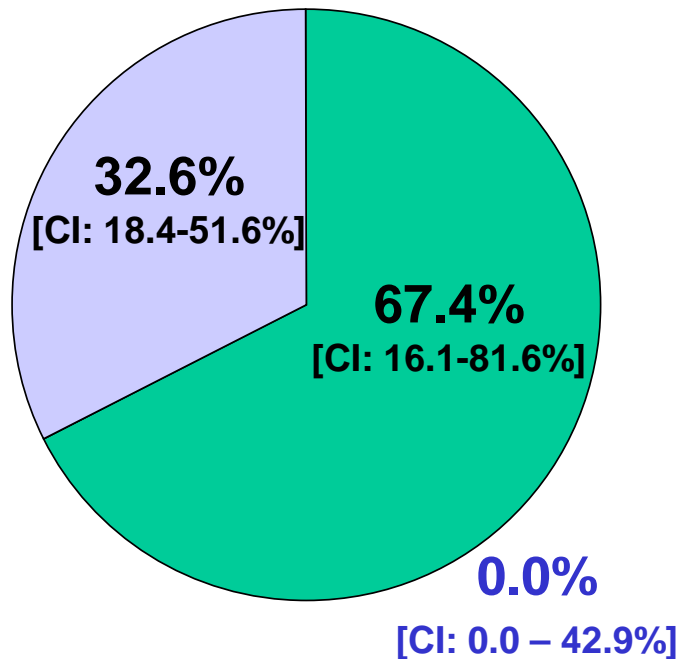
A: Additive Genetic
C: Shared Environmental
E: Unique Environmental

Models were adjusted for age at time of PTSD report (Wave 4) and age at time of AD report (Wave 1, 3, or 4).
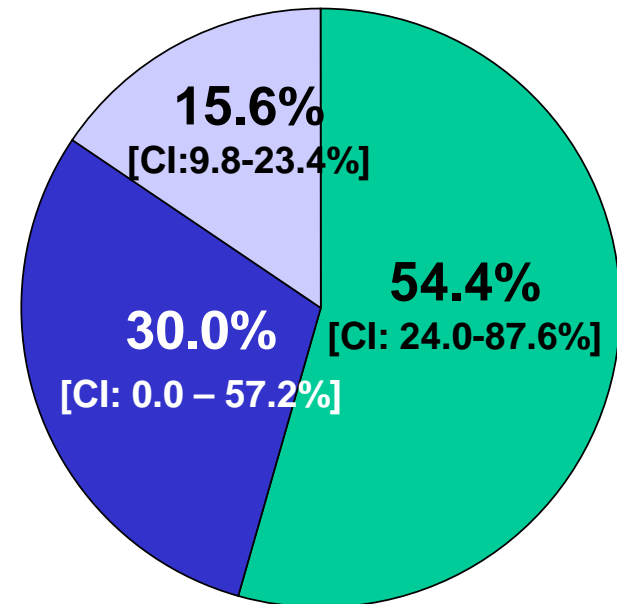
Univariate Models
Proportion of Variance Attributable to A, C, E

PTSD

Alcohol Dependence

32.6%
[CI: 18.4-51.6%]

67.4%
[CI: 16.1-81.6%]

0.0%
[CI: 0.0 – 42.9%]

A
C
E

15.6%
[CI:9.8-23.4%]

54.4%
[CI: 24.0-87.6%]

30.0%
[CI: 0.0 – 57.2%]

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Best-Fitting Bivariate Model
Proportion of Variance Attributable to A, C, E

	A	C	E
PTSD	0.694 [CI: 0.533-0.757]	-------	0.306 [CI: 0.175-0.486]
AD	0.722 [CI: 0.634-0.736]	-------	0.278 [CI: 0.249-0.366]

Genetic correlation between PTSD & AD
$(r_g) = $ 0.496 [CI: 0.351-0.637]

PTSD and Alcohol Dependence
Bivariate Cholesky Decomposition*

$a_{21} = 0.421$

$a_{11} = 0.833$

$a_{22} = 0.738$

A_1

A_2

PTSD

Alcohol Dependence

$e_{11} = 0.554$

$e_{22} = 0.527$

E_1

E_2
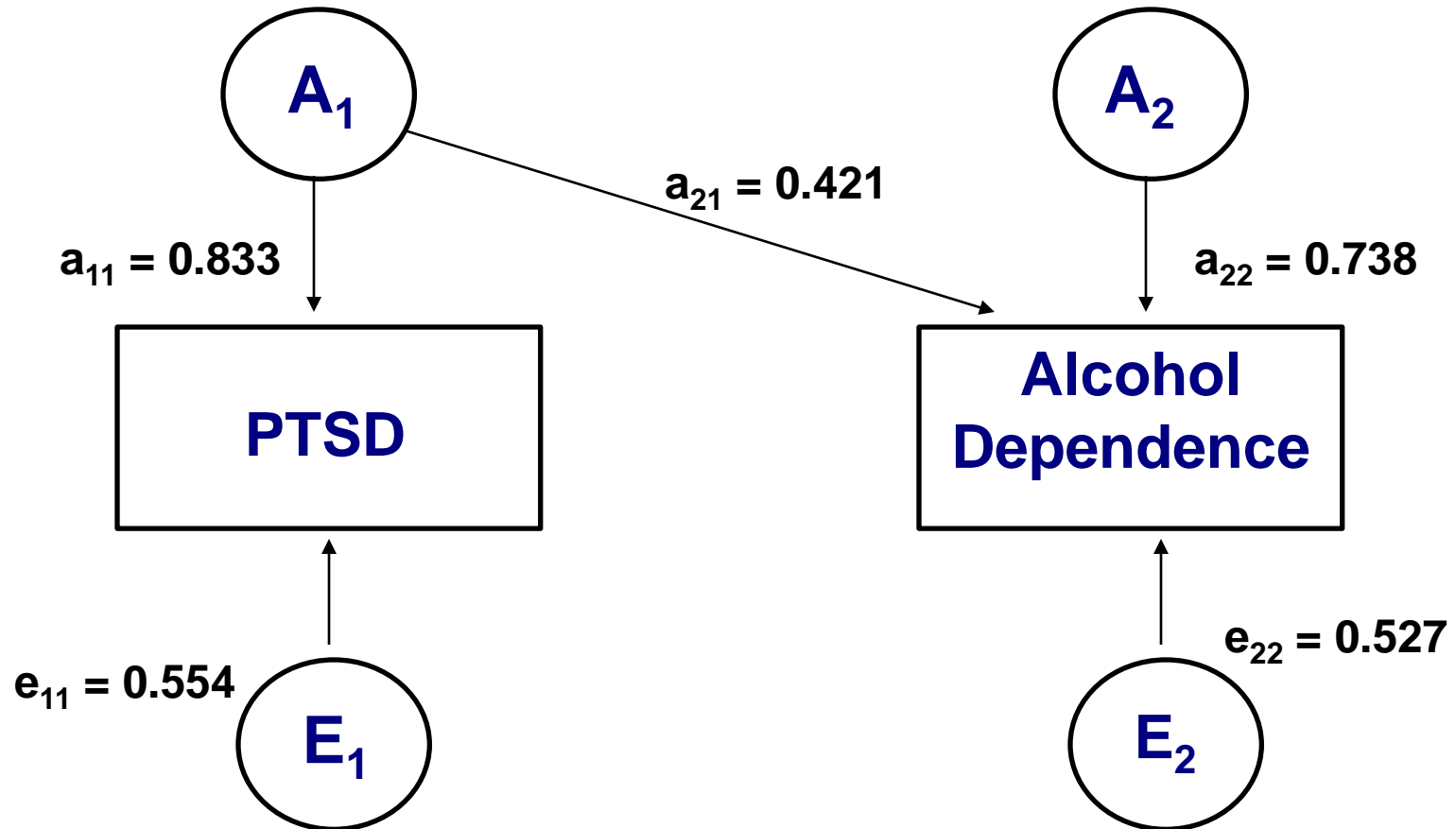
* shown with unstandardized path coefficients

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Results

- The most common nominated events for women who met PTSD criteria were rape (31.2%) and sexual molestation (30.0%).

- The rate of AD in women who met PTSD criteria was 3 times that of women who did not meet PTSD criteria.

- Additive genetic influences accounted for 69.4% of variance in PTSD and 72.2% of variance in AD.

- Shared environmental influences were non-significant for both PTSD and AD.

- Common genetic factors accounted for 24.6% of heritable influences on the two disorders.

Conclusions

- Results provide further support for the strong association between PTSD and AD in women.

- Heritability for AD was somewhat higher than the 50-60% range estimated in prior reports (including other MOAFTS studies*).

- Genetic influences on PTSD were also higher than reports from previous twin studies of PTSD - *all but one of which was based on the all-male Vietnam Era Twin Registry, for whom combat was the primary traumatic event.*

* likely due in part to the incorporation of AD data from prior waves of data, which produced a higher prevalence of AD than Wave 4 data alone.

Limitations and Future Directions

- The heritability estimate for PTSD may also reflect genetic liability to traits associated with traumatic event exposure, such as neuroticism and risk-taking (i.e., a gene-environment correlation).

- In one of the few studies addressing PTSD and trauma exposure that included females, Stein et al. (2002) found evidence for additive genetic contributions to exposure to assaultive trauma.

Limitations and Future Directions

- Twin correlations conducted in the current sample revealed higher rates of concordance among MZ vs. DZ twins for exposure to any trauma (0.636 vs. 0.495).

- The present investigation will be extended to include formal modeling of genetic and environmental contributions to trauma exposure (as a 3-level variable: *no trauma, non-assaultive trauma, and assaultive trauma*) to determine whether it (partially) mediates the genetic association between PTSD and AD.