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Gene-by-Intervention Effects on Alcohol Dependence Symptoms in Emerging Adulthood

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Background

- Alcohol use and dependence are influenced by both genes and environment, with heritability estimated at about 50% (Verhulst et al., 2015).
- Incorporating genetics into clinical studies may improve understanding of why prevention intervention programs are differentially effective (Belsky & van Ijzendoorn, 2015).
- Existing gene-by-intervention (GxI) studies have predominantly used candidate gene methods.
- Purpose: determine whether genome-wide polygenic risk moderates the effectiveness of an adolescent prevention program on alcohol dependence symptoms in young adulthood.

Method

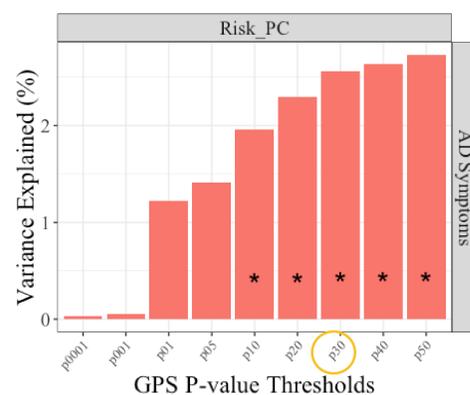
- Project Alliance: longitudinal study of 6th grade students recruited and randomized to a multi-component intervention to prevent substance use and deviant behaviors (Dishion, Nelson, & Kavanagh, 2003).
- 274 European Americans (EA) and 194 African Americans (AA)
- Alcohol dependence (AD) symptoms assessed with Composite International Diagnostic Interview at age 18-19.
- Genome-wide polygenic risk scores (GPS) derived using GWAS of four risky behaviors in 315,894 UK Biobank subjects (Linnér et al., 2019).
- Linear regression conducted separately in EA and AA subsamples, followed by analyses stratified by intervention condition.

Discussion

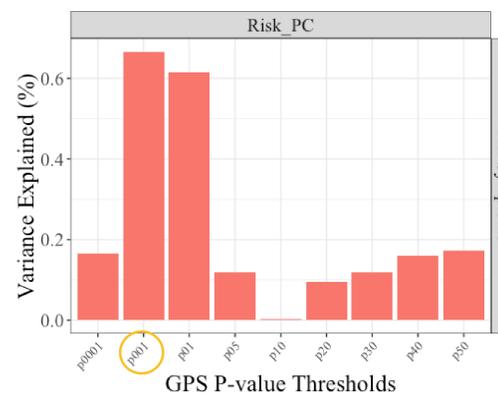
- GPS significantly predict AD symptoms at age 18-19 in European American. Stratified results suggest the intervention may diminish the impact of polygenic risk in EA, but there was no effect in AA.
- Null findings for AA subsample may be due to reduced power or population structure.
- Overall, there is modest evidence for differential effects of polygenic risk as a function of the intervention in a sample of EA young adults.

Intervention may reduce the effect of polygenic scores for risky behaviors on alcohol dependence symptoms.

GPS Threshold Determination in European Americans



GPS Threshold Determination in African Americans



Results of GxI Effects on Alcohol Dependence

	Estimate	Std. Error	t-value	p
European American Sample (n = 274)				
Intervention	.29	.19	1.51	.133
GPS for risky behavior	.23	.10	2.41	.016*
Gender	-.03	.03	-1.19	.236
Teacher report of child behavioral risk	.40	.14	2.73	.007**
PC1	.27	.19	1.4	.153
PC2	-.16	.13	-1.21	.228
GPSxIntervention	.09	.19	.04	.967
Adjusted R ² = .06, F(7, 236) = 3.35, p = .002				
African American Sample (n = 194)				
Intervention	.35	.20	1.76	.081
GPS for risky behavior	-.11	.10	-1.03	.305
Gender	-.04	.03	-1.42	.157
Teacher report of child behavioral risk	-.23	.13	-1.81	.073
PC1	.08	.12	.67	.503
PC2	-.05	.12	-.40	.689
GPSxIntervention	.05	.21	.26	.797
Adjusted R ² = .01, F(7, 163) = 1.48, p = .19				

GPS Effects on Alcohol Dependence Stratified by Intervention Condition in European Americans

	Estimate	Std. Error	t-value	p
Control Sample (n = 132)				
Gender	-.05	.04	-1.31	.192
Teacher report of child behavioral risk	.112	.07	.67	.507
PC1	1.50	.17	1.35	.179
PC2	-.37	-.213	-1.69	.095
GPS	.278	.22	2.39	.019*
Intervention Sample (n = 142)				
Gender	-.05	-.11	-1.179	.241
Teacher report of child behavioral risk	.81	.36	3.90	<.001**
PC1	.20	.10	1.04	.30
PC2	-.08	-.04	-.40	.689
GPS	.131	.08	.86	.392