A Prospective Longitudinal Analysis of Polygene by Environment Interactions for Alcohol Use Behaviors From Adolescence to Adulthood

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Introduction
- Alcohol use behaviors (AUB), including heavy drinking, drunkenness, and frequent consumption, are prevalent among adolescents and young adults.
- Genetic influences have been established through twin studies, with heritability estimates for alcohol dependence ranging from 50-60% (Dick, Prescott, & McGue, 2009).
- Genes also act in conjunction with environmental factors (gene-environment interaction; GxE); one environmental factor that has been shown to influence the association between genetic effects and AUB is peer substance use (e.g., Harden et al., 2008).
- However, there are several gaps in the gene-environment literature for AUB:
  1. Most studies of GxE use candidate genes, despite convincing evidence that genetic influences underlying complex phenotypes are likely polygenic (i.e., multiple genes of small effects)
  2. Few GxE studies have adopted developmental perspectives, despite evidence that the importance of genetic and environmental effects for AUB change across development (Dick, 2011)
- A developmental framework is needed to capture the dynamic nature of genetic influences across this period.
- We tested the interactive effects of polygene risk for trajectories of AUB and peer substance use from adolescence to young adulthood.

Methods
Participants
- European-American subsample of the Collaborative Study on the Genetics of Alcoholism (COGA) Prospective Study (n = 412; age 15-25)

Measures
Alcohol use behaviors (AUB):
- How often did you have 5 or more drinks in a 24-hour period?
- How often did you get drunk during the last 12 months?
- On how many days did you drink any beverages containing alcohol during the last 12 months?

Peer substance use:
- How many of the kids did you go to school with use alcohol?
- How many of the kids did you go to school with smoke cigarettes?
- How many of the kids did you go to school with smoke cannabis?
- How many of the kids did you go to school with use other illicit substances?

Polygenic score
- GWAS for alcohol dependence symptoms performed on a discovery sample (European-American adult subsample of COGA, n = 1,240)
- Genomic inflation factor was acceptable (λ = 1.01, S.E. = 1.02e-05)
- 587,378 SNPs analyzed in total, 279 SNPs met p-value threshold of .05
- Each SNP meeting this threshold was weighted by its effect size, and summed across all SNPs
- Controlling for sex and age, the polygenic score at p = .05 threshold explained 1.7% of variance in the initial status for AUB in the adolescent/young adult sample

Statistical Analyses
- Latent growth curve analysis (LGCA) used to analyze AUB, with all variables scaled by age
- Latent growth parameters regressed on polygene score, peer substance use, and interaction (Figure 2)

Results
- AUB was best characterized by a freely-estimated piecewise latent growth model (Chisq = 246.72, df = 94, p < .01, RMSEA = .06, CFI = .91, TLI = .88, SRMR = .09)

Gene-environment interaction analysis
- A significant three-way interaction between sex, polygene score, and peer substance use was detected (B = .22, p < .01)
  - Interaction between polygene score and peer substance use was only significant for girls (Bpolygene x peer use = .20, p < .05), not for boys (Bpolygene x peer use = .09, p = .21)
  - Girls with high polygenic scores had the steepest slopes at lowest level of peer substance use and the steepest slopes at moderately high levels of peer substance use (see Figure 3)

Discussion
- Polygenic scores interacted with peer substance use to predict trajectories of early AUB in girls.
- Results suggest that the magnitude of genetic and environmental effects (as well as their interactions) for AUB vary as a function of development (Dick, 2011; Kendler et al., 2008).
- High polygenic scores may be comprised of genes that not only confer additional risk for AUB, but also genes that foster psychopathology in one environment and offer protective effects in another, “for better or for worse” (Belsky & Pleuss, 2009).
- In the context of environmental influences, polygenic scores may potentially identify specific populations that may not only be a greater risk for developing pathology, but also benefit the most from interventions (Brody et al., 2009)

Figure 1: Structural model of the gene-environment interaction analysis

Figure 2: A UB trajectories; a) observed means; b) estimated means

Figure 3: Polygene score by peer substance use interaction on AUB for girls

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