ESTIMATION OF THE GENOMEWIDE ADDITIVE GENETIC COVARIANCE ACROSS SUBJECTS OF EUROPEAN AND AFRICAN ANCESTRY: AN EXAMPLE USING ALCOHOL DEPENDENCE

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ACKNOWLEDGEMENTS:

This body of work was supported by a grant from the National Institute on Alcohol Abuse and Alcoholism (K01AA021113 awarded to Rohan Palmer).

PURPOSE: A major challenge to the field of addiction genetics is genetic heterogeneity as only a handful of studies have attempted to simultaneously understand the relationship between genetic variation within different ethnic groups and addiction outcomes, and whether these observed effects differ between samples from different ancestral backgrounds. Given our recent demonstration of genetic homogeneity across the DSM-IV indicators of alcohol dependence, w leveraged the increased power of mixed linear model association analysis to examine the genetic architecture on AD across subjects of European and African ancestry (EA/AA, respectively). The goal of this study was to identify convergent genomewide evidence for polygenic effects.

METHODS: Data (N=11,140) from a pooled sample of alcohol and other drug using individuals were used to identify and characterize the genomewide SNP-heritability and co-heritability of ADs. Unrelated EAs (N=6515) and AAs (N=2196) were confirmed using a combination of principal component analysis and multidimensional scaling with reference samples obtained from the 1000 genomes project. Phenotypes were derived using FIML factor analysis in MPlus. SNP-heritability estimates were characterized using Genomic Relatedness Restricted Maximum Likelihood and BayesR. Gene loci identified as significant contributors to the SNP-heritability of the traits are described and contrasted across populations.

RESULTS: Factor scores for AD were observed across both ethnicities, but loadings were not invariant across the two groups. Additive genetic effects on AD were similar across EAs (h^2_{SNP}=0.21[SE=0.05], p<0.001) and AAs (h^2_{SNP}=0.30[SE=0.14], p=0.001) and largely overlapped ($r_{G\text{-}SNP}$=0.76[0.45], p=0.030). Notably, withing AAs, an additional 7% genetic variance was indicated.

CONCLUSION: Within this pooled sample of substance using individuals, the evidence suggests that similar genetic factors influence AD in EAs and AAs and additional genetic variance that can be captured using AAs. Given the importance of genetic background and diversity in genetics research, additional studies are needed to determine whether these observations generalize to other substances of abuse.