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Local Ancestry-Aware Meta-Analysis of Genome-Wide Association Studies for Substance Use Traits in Latin American Populations

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Genome-wide association studies (GWAS) have made substantial progress in understanding the genetic liability of alcohol consumption. However, efforts modeling ancestry-specific effects in GWAS studies in admixed populations, like the Latin American (LA) population, has been minimal. LAs are highly admixed with a mosaic of different proportions of European, Amerindigenous (AMR), and African (AFR) descent, which could be difficult to model in GWAS analysis. However, innovative approaches have been recently developed using local ancestry information. Here, we analyzed local ancestry-specific effects for alcohol consumption in admixed LA populations. We conducted a meta-analysis of local ancestry-aware GWAS of alcohol consumption in 11,655 individuals of LA descent. We identified associations with rs1874323 (p-value = 2.5760e-08) in the MAGI1 gene, rs6833926 (p-value = 3.0010e-08) in the ARAP2 gene, two in the SLIT3 gene (rs73805262, p-value = 9.9540e-09; rs115143510; z = p-value = 1.2250e-08), and one intergenic variant (rs3929849, p-value = 2.3930e-09) in those individuals where the section of the genome comes from AFR descent. We also identified intergenic variants in those where the region is of AMR descent (rs4130378, p-value = 9.673e-09; rs536315876 p-value = 4.3640e-09; rs115675116, p-value = 4.3190e-09). Our study significantly contributes to the ongoing efforts to understand the ancestry-specific genetic architecture of alcohol consumption in Latin American populations. The novel genetic associations identified in highly admixed Latin American individuals highlight the importance of conducting ancestry-aware GWAS to identify potential ancestry-specific loci.