Genome-wide association studies of the PR interval in African Americans.

Abstract:
The PR interval on the electrocardiogram reflects atrial and atrioventricular nodal conduction time. The PR interval is heritable, provides important information about arrhythmia risk, and has been suggested to differ among human races. Genome-wide association (GWA) studies have identified common genetic determinants of the PR interval in individuals of European and Asian ancestry, but there is a general paucity of GWA studies in individuals of African ancestry. We performed GWA studies in African American individuals from four cohorts (n = 6,247) to identify genetic variants associated with PR interval duration. Genotyping was performed using the Affymetrix 6.0 microarray. Imputation was performed for 2.8 million single nucleotide polymorphisms (SNPs) using combined YRI and CEU HapMap phase II panels. We observed a strong signal (rs3922844) within the gene encoding the cardiac sodium channel (SCN5A) with genome-wide significant association (p<2.5 x 10^-8) in two of the four cohorts and in the meta-analysis. The signal explained 2% of PR interval variability in African Americans (beta =
5.1 msec per minor allele, 95% CI = 4.1-6.1, p = 3 x 10^{-23}). This SNP was also associated with PR
interval (beta = 2.4 msec per minor allele, 95% CI = 1.8-3.0, p = 3 x 10^{-12}) in individuals of European
ancestry (n = 14,042), but with a smaller effect size (p for heterogeneity<0.001) and variability
explained (0.5%). Further meta-analysis of the four cohorts identified genome-wide significant
associations with SNPs in SCN10A (rs6798015), MEIS1 (rs10865355), and TBX5 (rs7312625) that
were highly correlated with SNPs identified in European and Asian GWA studies. African ancestry
was associated with increased PR duration (13.3 msec, p = 0.009) in one but not the other three
cohorts. Our findings demonstrate the relevance of common variants to African Americans at four loci
previously associated with PR interval in European and Asian samples and identify an association
signal at one of these loci that is more strongly associated with PR interval in African Americans than
in Europeans.