AN INTERACTION BETWEEN BTBD9 AND PTPRD VARIANTS INCREASES RISK OF RESTLESS LEG SYNDROME

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Study Objectives; Recent genome-wide association studies (GWAS) for Caucasians identified several allelic variants associated with increased risk of developing Restless Leg Syndrome (RLS), also known as Willis-Ekbom Disease. Although the pathogenic mechanisms of RLS are not entirely understood, it is becoming increasingly evident that many common human diseases such as RLS can be attributed to an epistasis. The aims of this study were to evaluate whether the associations of RLS with all loci determined in previous GWAS for Caucasians can be replicated significantly for the Korean population and to elucidate whether an epistasis plays a role in the pathogenesis of RLS.
Design, setting and participants: DNA from a total of 640 RLS patients (n=320) and age- and sex-matched controls (n=320) were genotyped for variants in the RLS loci.
Measurements and results: A significant association was found for rs3923809 and rs9296249 in BTBD9 ($p<0.0001$ and $p=0.001$, respectively); the OR for rs3923809 was 1.61 ($p<0.0001$) to 1.88 ($p<0.0001$) and the OR for rs9296249 was 1.44 ($p=0.001$) to 1.73 ($p=0.002$), according to the model of inheritance. The OR for the interaction between rs3923809 in BTBD9 and rs4626664 in PTPRD was 2.05 ($p<0.0001$) in the additive model, 1.80 ($p=0.002$) in the dominant model and 2.47 ($p=0.004$) in the recessive model. There was no significant association between genotypes of all tested SNPs and the mean value of serum iron parameters.
Conclusions: Our results suggest that the role of BTBD9 in pathogenesis of RLS would be more universal across populations than ever proved and more efforts should be focused on the role of epistasis in the genetic architecture of RLS.