Replication of Association of MEIS1, BTBD9 and MAP2K5/LBXCOR1 in Czech Austrian and Finnish Populations

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The prevalence of restless legs syndrome (RLS) in the Causacian population has been reported to be as high as 10%, and is one of the most common sleep disorders. There is a marked genetic component in its pathogenesis. To date, six linkage regions for RLS on chromosomes 2q, 9p, 12q, 14q, 19p and 20p, under a recessive or autosomal dominant model of inheritance have been identified. Recently the association of RLS with three intronic and intergenic variants of *MEIS1, BTBD9,* and *MAP5K/LBXCOR1* on chromosomes 2p, 6p and 15q was described by means of a genome-wide association study. The aim of our study was to investigate whether these variants are also relevant in RLS patients originating from the Czech Republic, Austria and Finland.

Our study population consisted of a total of 679 RLS patients and 1230 controls of Czech, Austrian and Finish origin, respectively. We tested the association using 10 single nucleotide polymorphism markers (SNP) by means of mass spectrometry (Sequenom MassArray system).

We replicated associations for all loci in the three samples combined (rs2300478 in *MEIS1,* P = 1.26×10^{-05}, odds ratio (OR) = 1.47, rs3923809 in *BTBD9,* p=4.11×10^{-05}, OR=1.58 and rs6494696 in *MAP5K/LBXCOR1*, p=0.04764, OR=1.27). Logistic regression showed no significant interaction with country for any SNP tested, and Breslow-Day test showed homogeneity ORs in all samples. The best models observed for individual loci are in agreement with previous findings. *BTBD9* among the known loci seems to be the most consistent in its effect to RLS across populations and also most independent of familial clustering. We conclude that the observed genetic determinants are risk factors for RLS in multiple populations.

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