Pleiotropic effects of MEIS1 in insomnia and restless legs syndrome

Konrad Oexle

Institute of Neurogenomics, Helmholtz Zentrum München, Germany

Genome-wide association studies (GWAS) on restless legs syndrome (RLS) in populations of European origin have shown that the minor allele (T) of low-frequency SNP rs113851554 (MAF = 0.07), located within a putative regulatory element of *MEIS1*, is the strongest (OR = 2.2) genetic risk factor of RLS (Schormair et al 2017). The same SNP has been identified as the leading genetic risk factor for insomnia complaints (OR = 1.2) reported by 33% of the women and 24% of the men in the UK Biobank database (Hammerschlag et al 2017). This might be due to overrepresentation of RLS among people with insomnia complaints. For a precise evaluation, the expected proportions of RLS in the UK Biobank insomnia cases and controls were calculated using data on age-specific RLS prevalence and on the RLS sensitivity and specificity of the question used by the UK Biobank when assessing insomnia. The two proportions and the reported rs113851554 effect size in RLS were then used to predict the P value of the association of rs113851554 with insomnia complaints under the assumption that the RLS contamination alone drives this association. It turned out that the predicted signal (P = 2 × 10E−04, 95% CI 0.056 to 1.1 × 10E−11) was much weaker than the signal actually observed (2 × 10E−18). This finding indicated that the effect of *MEIS1* on insomnia complaints can be explained only in part by overrepresentation of RLS among UK Biobank insomnia cases. Consequently, there might be subclinical RLS among insomnia patients or pleiotropy of *MEIS1,* influencing independently both RLS and insomnia.