Genes and lifestyle factors in obesity: results from 12,462 subjects from MONICA/KORA.

Data from meta-analyses of genome-wide association studies provided evidence for an association of polymorphisms with body mass index (BMI), and gene expression results indicated a role of these variants in the hypothalamus. It was consecutively hypothesized that these associations might be evoked by a modulation of nutritional intake or energy expenditure. It was our aim to investigate the association of these genetic factors with BMI in a large homogenous population-based sample to explore the association of these polymorphisms with lifestyle factors related to nutritional intake or energy expenditure, and whether such lifestyle factors could be mediators of the detected single-nucleotide polymorphism (SNP)-association with BMI. It was a further aim to compare the proportion of BMI explained by genetic factors with the one explained by lifestyle factors. The association of seven polymorphisms in or near the genes NEGR1, TMEM18, MTCH2, FTO, MC4R, SH2B1 and KCTD15 was analyzed in 12,462 subjects from the population-based MONICA/KORA Augsburg study. Information on lifestyle factors was based on standardized questionnaires. For statistical analysis, regression-based models were used. The minor allele of polymorphism rs6548238 C>T (TMEM18) was associated with lower BMI (-0.418 kg m(-2), P=1.22 ×
and of polymorphisms rs9935401 G>A (FTO) and rs7498665 A>G (SH2B1) with increased BMI (0.290 kg m\(^{-2}\), \(P=2.85 \times 10^{-7}\) and 0.145 kg m\(^{-2}\), \(P=9.83 \times 10^{-3}\)). The other polymorphisms were not significantly associated. Lifestyle factors were correlated with BMI and explained 0.037\% of the BMI variance as compared with 0.006\% of explained variance by the associated genetic factors. The genetic variants associated with BMI were not significantly associated with lifestyle factors and there was no evidence of lifestyle factors mediating the SNP-BMI association. Our data first confirm the findings for TMEM18 with BMI in a single study on adults and also confirm the findings for FTO and SH2B1. There was no evidence for a direct SNP-lifestyle association.