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Next Section

Abstract

Background: Obesity is frequently associated with eating disorders, and evidence indicates that both conditions are influenced by genetic factors. However, little is known about the genes influencing eating behaviors.

Objective: The objective was to identify genes associated with eating behaviors.

Design: Three eating behaviors were assessed in 660 adults from the Québec Family Study with the use of the Three-Factor Eating Questionnaire. A genome-wide scan was conducted with a total of 471 genetic markers spanning the 22 autosomes to identify quantitative trait loci for eating behaviors. Body composition and macronutrient and energy intakes were also measured.

Results: Four quantitative trait loci were identified for disinhibition and susceptibility to hunger. Of these, the best evidence of linkage was found between a locus on chromosome 15q24-q25 and disinhibition ($P < 0.0058$) and susceptibility to hunger ($P < 0.0001$). After fine-mapping, the peak linkage was found between markers D15S206 and D15S201 surrounding the neuromedin β (NMB) gene. A missense mutation (p.P73T) located within the NMB gene showed significant associations with eating behaviors and obesity phenotypes. The T73T homozygotes were 2 times as likely to exhibit high levels of disinhibition (odds ratio: 1.8; 95% CI: 1.07, 2.89; $P = 0.03$) and susceptibility to hunger (odds ratio: 1.9; 95% CI: 1.15, 3.06; $P = 0.01$) as were the P73 allele carriers. Six-year follow-up data showed that the amount of body fat gain over time in T73T subjects was >2 times that than in P73P homozygotes (3.6 compared with 1.5 kg; $P < 0.05$).

Conclusion: The results suggest that NMB is a very strong candidate gene of eating behaviors and predisposition to obesity.

Background

Single nucleotide polymorphisms (SNPs) in genes encoding the components involved in the hypothalamic pathway may influence weight gain and dietary factors may modify their effects.

Aim

We conducted a case-cohort study to investigate the associations of SNPs in candidate genes with weight change during an average of 6.8 years of follow-up and to examine the potential effect modification by glycemic index (GI) and protein intake.

Methods and Findings

Participants, aged 20–60 years at baseline, came from five European countries. Cases ('weight gainers') were selected from the total eligible cohort (n = 50,293) as those with the greatest unexplained annual weight gain (n = 5,584). A random subcohort (n = 6,566) was drawn with the intention to obtain an equal number of cases and noncases (n = 5,507). We genotyped 134 SNPs that captured all common genetic variation across the 15 candidate genes; 123 met the quality control criteria. Each SNP was tested for association with the risk of being a 'weight gainer' (logistic regression models) in the case-noncase data and with weight gain (linear regression models) in the random subcohort data. After accounting for multiple testing, none of the SNPs was significantly associated with weight change. Furthermore, we observed no significant effect modification by dietary factors, except for SNP rs7180849 in the neuromedin β gene (NMB). Carriers of the minor allele had a more pronounced weight gain at a higher GI ($P = 2\times10-7$).

Conclusions

We found no evidence of association between SNPs in the studied hypothalamic genes with weight change. The interaction between GI and NMB SNP rs7180849 needs further confirmation.