GWAS Identifies 14 Polymorphisms Associated with Motion Sickness

Introduction

Roughly one in three individuals is highly susceptible to motion sickness, and yet the underlying etiology of this condition is not well understood. One theory suggests that motion sickness results from contradictory information the brain receives from the vestibular system of the inner ear, which senses motion and influences balance. Signals "moving" to the brain, while the eye signals "not moving" because the vehicle appears stationary relative to the viewer. Twin studies on motion sickness suggest high heritability (57-70%), but no genetic factors have been significantly associated with motion sickness to date. We conducted the first genome-wide association study on this condition in over 36,572 individuals.

About Motion Sickness

Stilt hurling. Traveling in cars, boats, planes, and spacecraft; amusement park rides; skiing; riding on camels; virtual reality environments.

Symptoms. Dizziness, nausea, vomiting, headache, pallor, sweating, drowsiness, increased salivation, hyperventilation, emotional distress.

Comorbidities. Migraine, vertigo, postoperative nausea and vomiting (PONV), chemotherapy-induced nausea and vomiting (CINV), morning sickness.

Risk Factors. Younger age, female, Asian, physiological factors.

Methods

We performed a GWAS in 36,572 individuals with European ancestry from the customer base of 23andMe. Inc. Motion sickness was assessed by online self-report. Participants responded to questions about their degree of motion sickness during travel: these questions were combined into a motion sickness score of 0 (never), 1 (occasionally), 2 (sometimes), or 3 (frequently) (Figure 1). Participants were genotyped using 890,916 to 1,008,948 SNPs on Illumina-based BeadChip. We imputed 8,058,452 SNPs; 7,087,609 met our thresholds of 0.05 MAF and P > 0.3. We also investigated comorbidities with motion sickness within the 23andMe database by looking at the association of 1667 different phenotypes with motion sickness. All analyses were controlled for age, sex, and five principal components.

Results

GWAS Identifies 14 Polymorphisms (

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<th>Allele MAF</th>
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Figure 2. Cohort Statistics

Motion sickness was more severe in women than men. Motion sickness also decreased with advancing age.

Figure 3. Manhattan Plot of GWAS Results

Negative log p-values for SNPs by genome position. Genome-wide significant SNPs are shown in red.

Table 1. SNPs Associated with Motion Sickness

SNPs with p < 1e-6. Genomic positions are given with respect to NCBI build 37.0. Parentheses mark SNPs in genes; for integers, nearby genes are listed. Alleles are listed as major/minor and are specified for the forward strand. r2 is a measure of the imputation quality. Beta is the effect per copy of the minor allele. P-values were adjusted for the inflation factor.

Table 2. Phenotypic Associations

Under our threshold of significance (Bonferroni-corrected p-value < 0.001 with 3334 tests), 38 phenotypes were associated with motion sickness. Associations include known syndromes or comorbidities of motion sickness (blue) and gastrointestinal (GI) phenotypes (green). For case control (CC), the effect is for cases; for quantitative traits (QT), the effect is per SD change in the phenotype.

Conclusions

We report 14 novel genome-wide significant associations for motion sickness and nine others with suggestive evidence. Associated regions appear to be involved in eye and eye development, neurological processes including synaptic formation and balance, and insulin/glucose homeostasis. Two regions contain hypoxia-inducible genes. We also provide evidence that motion sickness is significantly associated with numerous conditions and traits. Our phenotypic analysis confirmed associations with known comorbidities including vertigo, migraine, and postoperative nausea and vomiting (PONV) and suggested novel associations with poor circulation and altitude sickness. Together, these findings provide clues about the etiology of motion sickness.

Acknowledgments

We thank 23andMe’s customers who consented to participate in research for enabling this study. We also thank the employees of 23andMe who contributed to the generation of the infrastructure that made this research possible.

References


Figure 4. Genes in Significant Regions Categorized by Biological Process

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