Computational Identification of Deleterious SNPs in Migraine and Anxiety Regulatory Genes: A Pharmacogenomic Perspective

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Abstract

Migraine and anxiety are highly prevalent neuropsychiatric disorders with substantial biological overlap and comorbidity. Emerging evidence indicates that shared genetic determinants contribute to disease susceptibility, severity, and differential treatment response in both conditions. The present study employs a comprehensive *in silico* pharmacogenomics approach to investigate genetic variations in key regulatory genes associated with migraine and anxiety. SNP datasets for the target proteins BDNF, CGRP (CALCA), and HTR1B were retrieved from genomic repositories and analyzed using more than ten functional prediction tools including SIFT, PolyPhen, Panther, PredictSNP, and CADD to identify deleterious variants. Protein stability, evolutionary conservation, and structural alterations caused by high-impact SNPs were assessed using I-Mutant 3.0, MUpro, DynaMut2, ConSurf, and HOPE, while STRING was employed to analyze protein–protein interaction networks. Structural modeling and pathogenicity evaluation revealed that several missense variants induce significant conformational changes affecting protein stability, binding affinity, and downstream signaling. These functionally impactful SNPs potentially disrupt neurotransmission, vasoregulation, and stress-response pathways, suggesting a mechanistic basis for the comorbid presentation of migraine and anxiety. This study highlights the utility of integrating molecular modeling, variant impact prediction, and pharmacogenomic prioritization to identify potential biomarkers and therapeutic targets for comorbid neuropsychiatric disorders. While the findings provide strong computational evidence, experimental validation is necessary to confirm the pathogenic and functional consequences of the identified variants.

Keywords: Migraine, Anxiety, SNPs, Pharmacogenomics, BDNF, Missense variants