Identification of Single Nucleotide Polymorphisms Associated With Genes Involved in Cocaine Dependence

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Addiction is a social disease that affects millions of people worldwide. It is a behavior driven by a response to increased reward stimuli paired with an impaired ability to regulate stimulus seeking-behavior. This is underlain by a condition in which structures and function of the dopaminergic signaling pathways are altered while the disease's underlying genetic mechanisms are complex and elusive and still not completely understood. The current study continues my previous analysis from last year that found 4 potentially druggable targets (CAMK2B, NEFL, GABRB3, and PRKCZ) that changed in the context of addiction in both rats and humans. To specifically investigate the single nucleotide polymorphisms of GABRB3 and PRKCZ specifically, we conducted a bioinformatic study analyzing data from several online databases, including gnomAD, and ClinVar. Through programs like PolyPhen2 and SIFT, we determined the probability of SNPs to cause functional damage to the protein for all SNPs of GABRB3 and PRKCZ. We then modeled the location of the damaging SNPs on each of the protein structures to determine whether or not these areas could be easily accessed. Ultimately, we found that PRKCZ and GABRB3 emerged as a high value candidates in which a variety of damaging single nucleotide polymorphisms may occur. Furthermore, some of these variants are located on highly accessible portions of the protein. Targeting these SNPs will augment our understanding of the intricacies of these altered protein sequences with the potential to improve our understanding of addicted individuals, and possibly offer effective methods of treatment.

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