Evidence of sexual dimorphism of HTR1B gene on major adult ADHD comorbidities


Journal of Psychiatric Research, 2017
DOI: https://doi.org/10.1016/j.jpsychires.2017.09.011

Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a very common psychiatric disorder across the life cycle and frequently presents comorbidities. Since ADHD is highly heritable, several studies have focused on the underlying genetic factors involved in its etiology. One of the major challenges in this search is the phenotypic heterogeneity, which could be partly attributable to the sexual dimorphism frequently seen in psychiatric disorders. Taking into account the well-known sexual dimorphic effect observed in serotonergic system characteristics, we differentially tested the influence of HTR1B SNPs (rs11568817, rs130058, rs6296 and rs13212041) on ADHD susceptibility and on its major comorbidities according to sex. The sample comprised 564 adults with ADHD diagnosed according to DSM-IV criteria and 635 controls. There was no association of any HTR1B SNPs tested in relation to ADHD susceptibility. As for the comorbidities evaluated, after correction for multiple tests, significant associations were observed for both rs11568817 and rs130058 with substance use disorders (Pcorr = 0.009 and Pcorr = 0.018, respectively) and for rs11568817 with nicotine dependence (Pcorr = 0.025) in men with ADHD. In women with ADHD, the same rs11568817 was associated with generalized anxiety disorder (Pcorr = 0.031). The observed effects of rs11568817 G allele presence conferring risk to either substance use disorders or generalized anxiety disorder according to sex, suggest an overall scenario where a higher transcriptional activity of HTR1B, resulting from the presence of this allele, is related to externalizing behaviors in men and internalizing behaviors in women. These results are consistent with and expand previous evidence of sexual dimorphism of the serotoninergic system.