Annals of General Psychiatry

BioMed Central

Poster presentation

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Haplotype analysis of the TPH gene and association with suicidal behaviour in Russian males and females

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from International Society on Brain and Behaviour: 2nd International Congress on Brain and Behaviour
Thessaloniki, Greece. 17–20 November 2005

Published: 28 February 2006

Annals of General Psychiatry 2006, **5**(Suppl 1):S213 doi:10.1186/1744-859X-5-S1-S213

Background

Abnormalities in functioning of the central serotonergic system are believed to be involved in the pathogenesis of depressive illness and suicidal behaviour. Tryptophan hydroxylase (TPH) is a rate-limiting enzyme in the biosynthesis of serotonin, so the TPH gene (11p15.3-p14) is a good candidate for association studies with suicide. Several polymorphisms in the TPH gene have been studied for association with suicidal behaviour, but the results are inconclusive. The aim of the present study is to determine whether the TPH gene is a susceptibility factor for suicidal behaviour in males and females, separately.

Materials and methods

Three SNPs (rs211105, rs1800532 and rs7933505) of the TPH gene were investigated using PCR-RFLP analysis in a case-control study included 116 individuals who had attempted suicide (41 males/78 females) and 219 controls (103 males/126 females) from Russian population, which belongs to Slavic group of Indo-European language family. Haplotype frequencies were estimated from genotypic data by the maximum-likelihood method using EH program. Comparison of the groups for the estimated frequencies of haplotypes was performed using the log-likelihood ratio test. Correction for multiple testing was carried using the Bonferroni procedure (the level of significance was set at 0.017).

Results

No significant differences in allele and genotype frequencies of any TPH polymorphisms were detected between suicide and control gtoups, neither for females nor for males. However, haplotype analysis revealed that one haplotype (GAG) was significantly more frequent among suicide cases than in normal controls both for females ($chi(2) = 6.43$, $df = 7$, $p = 0.01$) and males ($chi(2) = 6.29$, $df = 7$, $p = 0.013$), another haplotype (TAG) was more frequent in suicide females only ($chi(2) = 5.43$, $df = 7$, $p = 0.01$).

Discussion

This result suggests the involvement of the TPH gene in susceptibility to suicidal behaviour, both in Russian males and females. Haplotypic analysis, besides having stronger statistical power, could reveal the potential impact of the specific combination of polymorphic sites, as contrasted to single locus analysis. Further studies in larger samples are needed indeed.