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ABSTRACT

Posttraumatic stress disorder (PTSD) is a debilitating anxiety disorder characterized by distressing symptoms that occur after experiencing or witnessing a traumatic event that includes an actual or perceived threat to the self or others (APA,1994). Genetic factors have been shown to explain a relevant proportion of the variance of PTSD and are assumed to moderate the vulnerability to the adverse effects of traumatic stress (Stein et al., 2002). The gene encoding the human serotonin transporter maps to chromosome17q11.1-12 (Ramamoorthy et al., 1993). It possesses several polymorphic loci that including a 44 base pair (bp) insertion/deletion polymorphism located in the promoter region (5-HTTLPR) producing the long (L) and short (S) allele respectively and a variable number of tandem repeats in the second intron (STin 2) (Lesch et al., 1994).

The sample for the first study comprised of 211 adult, male and female outpatients who met DSM-IV (American Psychiatric Association, 1994) criteria for a primary diagnosis of PTSD during the past 6 months. The normal control group included 211 randomly selected individuals visiting the hospital as attendants of the patients and who had witnessed at least one life threatening situation.

Genomic DNA was extracted from the lymphocytes of all the subjects and was subjected to PCR genotyping using high specificity primers for both the polymorphisms of the 5-HTT gene. The genotypic distribution of the controls was in accord with the Hardy-Weinberg equilibrium for both the polymorphisms. The comparative analysis of allelic and genotypic frequencies of 5-HTTLPR and STin 2 polymorphisms between the controls and the cases showed significant differences with a greater proportion of S/S genotype among PTSD patients compared to the S/L in control group. The distribution of the STin2 alleles also differed significantly between the two studied groups. An overrepresentation of 12 repeat allele was found in the PTSD patients. The haplotype analysis also showed an increased frequency of S12 haplotype in the PTSD patients as compared to the control group where an increase of L10 and S10 was observed.

In the second part of the study 226 PTSD patients were genotyped out of which 88 belonged to the L/L genotype, 95 to the S/S genotype with the remaining 43 belonging to the S/L genotype. After 12 weeks of treatment, the L/L group showed a better clinical improvement in the CAPS scale scores as compared to the S/S and S/L groups. The improvement was sharpest during the initial four weeks. Again a slightly better response on IES-R, CGI-S and CGI-I total scores was observed in the L/L group in comparison to the other two groups after 12 weeks of treatment.

In conclusion, the present findings support the existence of association between both the polymorphisms in the 5HTT gene and PTSD. Furthermore, our results also support an association between the 5-HTTLPR polymorphism and the treatment response to sertraline in PTSD patients.