SEROTONIN TRANSPORTER 5HTTLPR POLYMORPHISM, CLINICAL VARIANTS AND SYMPTOM SEVERITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction. Gene expression of serotonin transporter (SERT) is modulated by a promoter polymorphism (44-base pair insertion/deletion; 5HTTLPR), which gives rise to long (L) and short (S) alleles. The S allele causes a decreased SERT expression with reduced efficiency of cellular serotonin reuptake, a condition which seems to play a significant role in psychiatric and peripheral disorders. This study was designed to evaluate possible associations of 5HTTLPR polymorphism with different clinical forms and symptom severity in irritable bowel syndrome (IBS). **Methods.** IBS patients were selected according to Rome II criteria, and subdivided into diarrhoea predominant (D-IBS), constipation predominant (C-IBS), and alternating bowel habit (A-IBS) groups. Symptom severity was estimated by the Francis-Whorwell score. Healthy volunteers were also enrolled. Genomic DNA was extracted from whole blood, and the SERT gene promoter region containing the 5HTTLPR polymorphism was amplified by polymerase chain reaction. **Results.** 152 IBS patients (38 males, 114 females; mean age 40.2 years; age range 18-75 years) and 109 healthy volunteers (38 males, 71 females; mean age 44.8 years; age range 22-84 years) were genotyped. All subjects were Italians of caucasian origin. Frequencies in IBS patients (L/L 32.2%, L/S 54.6%, S/S 13.2%) did not differ significantly from healthy volunteers (L/L 25.7%, L/S 54.1%, S/S 20.2%; Fisher's exact test: P=0.236), with a slightly lower prevalence of S/S genotype in the former group. When stratifying patients by clinical variants, the genotype distribution was: D-IBS (n=59), L/L 30.5%, L/S 50.8%, S/S 18.6%; C-IBS (n=57), L/L 38.6%, L/S 54.4%, S/S 7.0%; A-IBS (n=36), L/L 25%, L/S 61.1%, S/S 13.9%. Comparison of genotype frequencies in bowel habit subgroups versus healthy volunteers indicated a significant difference for C-IBS (P=0.041), but not for D-IBS or A-IBS patients. Mean symptom severity score values in IBS patients with L/L (256.4±68.2), L/S (275.1±68.8) and S/S (268.3±71.2) genotypes did not differ significantly (ANOVA: F=0.892, P=0.412). **Conclusions.** Previous reports have provided conflicting evidence about a possible involvement of 5HTTLPR polymorphism in the pathophysiology and/or clinical presentation of IBS. The present results indicate a slightly reduced prevalence of S/S genotype in an Italian cohort of IBS patients, and suggest a significant association between the C-IBS variant and 5HTTLPR polymorphism. No relationship appears to exist between 5HTTLPR genotypes and symptom severity in IBS patients.