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.