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Selective serotonin reuptake inhibitors in depression: the influence of 5-HTTLPR and STin2 on treatment effect

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Background

Genetic variation in the serotonin transporter gene has been proposed as a possible explanation for inter-individual differences in treatment effects of selective serotonin reuptake inhibitors (SSRIs) in major depression [1-3]. Assessment of these genetic influences is necessary in order to decide whether genetic testing in psychiatric practice prior to antidepressant prescription could be useful [3]. This study evaluates the influence of two polymorphisms in the serotonin transporter gene (5-HTTLPR and STin2) on SSRI treatment outcome in major depression.

Materials and methods

For this study, 50 known non-responders to SSRIs (cases) and 164 referent patients meeting the DSM-IV criteria for major depressive disorder and using a SSRI for at least 6 weeks were included in the analyses. Blood samples or buccal swabs were taken from all participants to determine the 5-HTTLPR an STin2 genotype. Additional information was gathered through interviews. The association between the serotonin transporter genotype and SSRI response was assessed by use of logistic regression.

Results

Patients with the 5-HTTLPR s-allele and the STin2 10-allele appeared to have a non-significantly increased risk of developing SSRI non-response; Odds Ratio (OR) = 1.51 (95% CI: 0.68–3.33) for 5-HTTLPR and OR = 1.42 (95% CI: 0.60–3.39) for STin2. After stratification for gender, the 5-HTTLPR effect appeared to be stronger in female patients (OR = 3.05, 95% CI: 1.06–8.79) whereas the STin2 effect tended to be stronger in male patients (OR = 2.21, 95% CI: 0.44–11.09). In addition, an age- dependent effect of 5-HTTLPR and STin2 on treatment outcome was observed; patients under 42 years old had a non-significantly increased risk on SSRI non-response (OR = 2.55, 95% CI 0.75–8.61 for 5-HTTLPR and OR = 2.13, 95% CI 0.54–8.43 for STin2).

Discussion

Our findings indicate that women with the 5-HTTLPR genotype and men with the STin2 10/10 genotype have a less favourable response to SSRI treatment in major depressive disorder. To our knowledge, these findings have not been reported in studies on the influence of serotonin transporter polymorphisms on treatment effect up till now. More research is needed, particularly in subgroups of depressive patients, before the implementation of genetic testing in psychiatric practice can be recommended.

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