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## The association between catechol-o-methyltransferase (COMT) Val158Met polymorphism and treatment response in schizophrenic patients treated with risperidone or olanzapine

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Schizophrenia is a serious psychiatric disorder affecting 0.7% to 1.4% of the population worldwide with estimated heritability of around 83%. Patients' symptoms are strongly associated with dopaminergic system dysregulation. Catechol-o-methyltransferase (COMT) is an enzyme responsible for dopamine catabolism. In *COMT* gene a functional single nucleotide polymorphism (SNP) was found. This COMT Val158Met (rs4680) polymorphism affects COMT activity in a way that Val allele encodes a protein with greater enzymatic activity than the Met allele. Risperidone and olanzapine are atypical antipsychotic drugs used to treat schizophrenia and other psychiatric disorders. The hypothesis of this study was that COMT Val158Met polymorphism will affect treatment response in schizophrenic patients, treated with risperidone or olanzapine. The study included 272 (230 men and 42 women) patients with schizophrenia (diagnosis made according to Structured Clinical Interview for DSM-IV) treated with risperidone (mean dose = 3.4 ± 0.8 mg/day, range 3-6 mg/day) and/or olanzapine (mean dose = 17.7 ± 2.8 mg/day, range 10-20 mg/day) for 36 weeks. Psychotic symptoms were evaluated using the Positive and negative syndrome scale (PANSS). A late treatment response was evaluated after 8-weeks of treatment, and positive treatment response was defined as a 30% reduction in the PANSS total, positive, negative, and general psychopathology subscale scores. A remission was defined as a reduction of the scores on the particular PANSS items (positive items P1, P2, P3, general psychopathology items G5, G9, and negative items N1, N4 and N6) to a score of 3 or less. COMT Val158Met was determined using the TaqMan SNP Genotyping Assay. Results were evaluated with a $\chi^2$ test and a logistic regression. Since logistic regression showed significant sex related differences in the treatment response, all patients were subdivided according to gender, COMT genotype, treatment response and remission. In male, but not in female patients, the frequency of the COMT genotypes differed significantly between patients with and without positive late treatment response, defined according to the total PANSS scores ($\chi^2$=6.01; df=2; P=0.049), positive PANSS scores ($\chi^2$=6.04; df=2, P=0.049), and negative PANSS scores ($\chi^2$=7.18; df=2; P=0.028). No significant differences were found in the frequency of the COMT genotypes between male or female patients with and without positive late treatment response, defined according to the general PANSS scores. COMT genotypes frequencies differed significant between male, but not female patients, with and without remission ($\chi^2$=9.86; df=2; P=0.007). Absence of any significant association between COMT Val158Met and treatment response or remission in female patients might be explained by a relatively small sample for this subgroup, and that is a limitation of this study. In conclusion, COMT Val158Met polymorphism affects late treatment response and remission in male patients with schizophrenia treated with risperidone and/or olanzapine, and if confirmed, these results could indicate that COMT Val158Met polymorphism might be used to differentiate responders and non-responders in schizophrenia.