

## The Catechol-O-Methyl Transferase Val/met Polymorphism and Bipolar Disorder

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**Introduction:** Genetic factors have long been implicated in the etiology of bipolar disorder, but little is known about the mode of inheritance. Catechol-O-methyltransferase (COMT) is a metabolizing enzyme of catecholamines that is polymorphic for activity; Val allele is four times more active than Met allele. Among the reported neurobehavioral associations with the COMT Val<sup>108/158</sup>Met polymorphism, some findings appear inconsistent, raising questions about both phenotype definitions and the mechanisms by which this polymorphism exerts its effects.

**Objective:** To assess the COMT Val<sup>108/158</sup>Met genotype in bipolar disorder type I patients and its relationship with clinical response to pharmacological treatment with Olanzapine and Lithium.

**Method:** Forty-two patients with DSM-IV diagnosis of Bipolar I disorder, manic or mixed state, were treated with Olanzapine (10mg/day for the first four days and 20mg/ day during the next four weeks); Lithium was added the 8<sup>th</sup> day (until a lithemia of 0.6-1.2 mEq/L was achieved). Clinical outcome during treatment was periodically evaluated with the YOUNG scale for mania (YRSM), the Scale for the Assessment of Positive Symptoms (SAPS) and the global clinical impression (ICG). Plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) and cortisol concentrations were assessed. Clinical and biochemical measures were done on the same days. COMT genotype was also determined.

**Results and Discussion:** A total of 19 women and 23 men were studied. The proportion of psychotic patients (34 psychotic and 8 non-psychotic patients) was very high due to the characteristics of our hospital.

Genotype distributions were: Val/Met 18 psychotics and 4 non-psychotic; Met-Met 7 psychotics and 3 non-psychotics; and Val-Val 9 psychotics and 1 non-psychotic. Patients do not differ significantly in the genotypic or allelic frequency from the general population.

We have not found an association between the COMT genotypes and the severity of the illness before treatment or the clinical response to treatment.

A significant positive correlation was found between clinical outcome and the concentration MHPG in plasma before treatment.

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