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COMT IN MAJOR DEPRESSION - UK CANDIDATE GENE ASSOCIATION STUDY

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Catechol-O-methyltransferase (COMT) has a central role in brain dopamine, noradrenalin and adrenalin signaling, and has been suggested to be involved in the pathogenesis and pharmacological treatment of affective disorders. The functional single nucleotide polymorphism (SNP) in exon 4 (Val^{158}Met, rs4680) influences the COMT enzyme activity. The Val^{158}Met polymorphism is a commonly studied variant in psychiatric genetics, and initial studies in schizophrenia and bipolar disorder presented evidence for association with the Met allele. In unipolar depression, while some of the investigations point at an association between the Met/Met genotype and others have found a link between the Val/Val genotype and depression, most of the studies cannot detect any difference in Val^{158}Met allele frequency between depressed individuals and controls.

In the present study, we further elucidated the impact of COMT polymorphisms including the Val^{158}Met in MDD. We investigated 1,250 subjects with DSM-IV and/or ICD-10 diagnosis of major depression (MDD), and 1,589 control subjects from UK. A total of 24 SNPs spanning the COMT gene were successfully genotyped using the Illumina HumaHap610-Quad Beadchip (22 SNPs), SNPlex^{TM} genotyping system (1 SNP), and Sequenom MassARRAY® iPLEX Gold (1 SNP). Statistical analyses were implemented using PASW Statistics18, FINETTI (http://ihg.gsf.de/cgi-bin/hw/hwa1.pl), UNPHASED version 3.0.10 program and Haploview 4.0 program.

Neither single-marker nor haplotypic association was found with the functional Val^{158}Met polymorphism or with any of the other SNPs genotyped. Our findings do not provide evidence that COMT plays a role in MDD or that this gene explains part of the genetic overlap with bipolar disorder.

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