

Genetic basis of the efficacy and tolerability of antipsychotic drugs: a review [abstract]. *Directions in Psychiatry* 2019;39(1):29-46.

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<p>Olanzapine is one of the most commonly used second-generation APDs with reports of association between its efficacy and DRD3 variant <i>D3Ser9Gly</i>, which has also been associated with antipsychotic efficacy of risperidone and clozapine.^{123, 124} However, this finding was not replicated in Indian patients¹²⁵ suggesting ethnic differences in response. Genetic variance in COMT were also associated with the efficacy of olanzapine,¹²⁶ as it was observed with other APDs pointing towards importance of dopamine levels in antipsychotic response. In terms of serotonergic mechanisms, L allele of the 5-HTT LPR¹²⁷ and several HTR6 polymorphisms¹²⁸ have been associated with olanzapine's efficacy. However, once again, this olanzapine response was not associated with HRT2A and HRT2C variants in the Indian population.^{124, 125} A differential response was also observed in another Asian study with olanzapine, showing haplotype variants rs723672 and rs1034936 associated with improvement in positive symptoms, haplotype variant rs2283271 associated with improvement in negative symptoms and haplotype variants rs10848635 and rs1016388 associated with improvement in general psychopathology.¹²⁹ These findings further suggest ethnic differences in olanzapine response. <i>Glutamate metabotropic receptor-3</i> (GRM3) polymorphism¹³⁰ and a calcium channel variant, CACNA1C, rs1006737 were also associated with better olanzapine response in schizophrenia patients.^{129, 131}</p>	<p>The efficacy of olanzapine, which is one of the most commonly used second-generation APDs, has been associated with the DRD3 variant <i>D3Ser9Gly</i>, which has also been associated with the antipsychotic efficacy of risperidone and clozapine.^{123, 124} This relationship has not been replicated in Indian patients,¹²⁵ however, which suggests differences in response among ethnic groups. Genetic variance in COMT has also been associated with the efficacy of olanzapine,¹²⁶ given the importance of dopamine levels in its antipsychotic response. Serotonin may also influence the efficacy of olanzapine, given that the L allele of 5-HTT LPR¹²⁷ and several HTR6 polymorphisms¹²⁸ have been associated with the efficacy of this drug. Once again, the olanzapine response was not associated with HRT2A or HRT2C variants in the Indian population.^{124, 125} A differential response was also observed in another Asian study with olanzapine, in which the haplotype variants rs723672 and rs1034936 were associated with improvement in positive symptoms, haplotype variant rs2283271 was associated with improvement in negative symptoms, and haplotype variants rs10848635 and rs1016388 were associated with improvement in general psychopathology.¹²⁹ These findings further suggest ethnic differences in the response to olanzapine. Patients with schizophrenia who had a <i>glutamate metabotropic receptor-3</i> (GRM3) polymorphism¹³⁰ and a calcium channel variant (CACNA1C, rs1006737) also exhibited a better response to this drug.^{129, 131}</p>	<p>The efficacy of olanzapine, which is one of the most commonly used second-generation APDs, has been associated with the DRD3 variant <i>D3Ser9Gly</i>, which has also been associated with the antipsychotic efficacy of risperidone and clozapine.^{123, 124} This relationship has not been replicated in Indian patients,¹²⁵ however, which suggests differences in response among ethnic groups. Genetic variance in COMT has also been associated with the efficacy of olanzapine,¹²⁶ given the importance of dopamine levels in its antipsychotic response. Serotonin may also influence the efficacy of olanzapine, given that the L allele of 5-HTT LPR¹²⁷ and several HTR6 polymorphisms¹²⁸ have been associated with the efficacy of this drug. Once again, the olanzapine response was not associated with HRT2A or HRT2C variants in the Indian population.^{124, 125} A differential response was also observed in another Asian study with olanzapine, in which the haplotype variants rs723672 and rs1034936 were associated with improvement in positive symptoms, haplotype variant rs2283271 was associated with improvement in negative symptoms, and haplotype variants rs10848635 and rs1016388 were associated with improvement in general psychopathology.¹²⁹ These findings further suggest ethnic differences in the response to olanzapine. Patients with schizophrenia who had a <i>glutamate metabotropic receptor-3</i> (GRM3) polymorphism¹³⁰ and a calcium channel variant (CACNA1C, rs1006737) also exhibited a better response to this drug.^{129, 131}</p>

