

**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.<sup>123, 124</sup> However, this finding was not replicated in Indian patients<sup>125</sup> suggesting ethnic differences in response. Genetic variance in COMT were also associated with the efficacy of olanzapine,<sup>126</sup> 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 <i>5-HTT LPR</i><sup>127</sup> and several <i>HTR6</i> polymorphisms<sup>128</sup> have been associated with olanzapine's efficacy. However, once again, this olanzapine response was not associated with <i>HRT2A</i> and <i>HRT2C</i> variants in the Indian population.<sup>124, 125</sup> A differential response was also observed in another Asian study with olanzapine, showing haplotype variants <i>rs723672</i> and <i>rs1034936</i> associated with improvement in positive symptoms, haplotype variant <i>rs2283271</i> associated with improvement in negative symptoms and haplotype variants <i>rs10848635</i> and <i>rs1016388</i> associated with improvement in general psychopathology.<sup>129</sup> These findings further suggest ethnic differences in olanzapine response. <i>Glutamate metabotropic receptor-3</i> (<i>GRM3</i>) polymorphism<sup>130</sup> and a calcium channel variant, <i>CACNA1C</i>, <i>rs1006737</i> were also associated with better olanzapine response in schizophrenia patients.<sup>129, 131</sup></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.<sup>123, 124</sup> This relationship has not been replicated in Indian patients,<sup>125</sup> however, which suggests differences in response among ethnic groups. Genetic variance in COMT has also been associated with the efficacy of olanzapine,<sup>126</sup> given the importance of dopamine levels in its antipsychotic response. Serotonin may also influence the efficacy of olanzapine, given that the L allele of <i>5-HTT LPR</i><sup>127</sup> and several <i>HTR6</i> polymorphisms<sup>128</sup> have been associated with the efficacy of this drug. Once again, the olanzapine response was not associated with <i>HRT2A</i> or <i>HRT2C</i> variants in the Indian population.<sup>124, 125</sup> A differential response was also observed in another Asian study with olanzapine, in which the haplotype variants <i>rs723672</i> and <i>rs1034936</i> were associated with improvement in positive symptoms, haplotype variant <i>rs2283271</i> was associated with improvement in negative symptoms, and haplotype variants <i>rs10848635</i> and <i>rs1016388</i> were associated with improvement in general psychopathology.<sup>129</sup> These findings further suggest ethnic differences in the response to olanzapine. Patients with schizophrenia who had a <i>glutamate metabotropic receptor-3</i> (<i>GRM3</i>) polymorphism<sup>130</sup> and a calcium channel variant (<i>CACNA1C</i>, <i>rs1006737</i>) also exhibited a better response to this drug.<sup>129, 131</sup></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.<sup>123, 124</sup> This relationship has not been replicated in Indian patients,<sup>125</sup> however, which suggests differences in response among ethnic groups. Genetic variance in COMT has also been associated with the efficacy of olanzapine,<sup>126</sup> given the importance of dopamine levels in its antipsychotic response. Serotonin may also influence the efficacy of olanzapine, given that the L allele of <i>5-HTT LPR</i><sup>127</sup> and several <i>HTR6</i> polymorphisms<sup>128</sup> have been associated with the efficacy of this drug. Once again, the olanzapine response was not associated with <i>HRT2A</i> or <i>HRT2C</i> variants in the Indian population.<sup>124, 125</sup> A differential response was also observed in another Asian study with olanzapine, in which the haplotype variants <i>rs723672</i> and <i>rs1034936</i> were associated with improvement in positive symptoms, haplotype variant <i>rs2283271</i> was associated with improvement in negative symptoms, and haplotype variants <i>rs10848635</i> and <i>rs1016388</i> were associated with improvement in general psychopathology.<sup>129</sup> These findings further suggest ethnic differences in the response to olanzapine. Patients with schizophrenia who had a <i>glutamate metabotropic receptor-3</i> (<i>GRM3</i>) polymorphism<sup>130</sup> and a calcium channel variant (<i>CACNA1C</i>, <i>rs1006737</i>) also exhibited a better response to this drug.<sup>129, 131</sup></p>

