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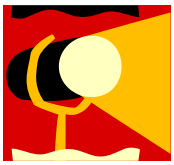
## Spotlight on COMT MET/MET and atypical antipsychotics: Response rate and cognition



The *COMT* gene is the next topic in our Spotlight series. *COMT* is a pharmacodynamic gene coding for catechol-O-methyltransferase, an enzyme which is the primary means of dopamine degradation in the prefrontal cortex. The Genecept Assay® tests for the Val108/158Met variant of the *COMT* gene. We have previously addressed the variant's effect on efficacy of *COMT* inhibitors like tolcapone, however an individual's *COMT* genotype may also influence the response to treatment with atypical (second generation) antipsychotics.

Bertolino et al. demonstrated in 2004 that individuals with the Met/Met genotype experienced a greater improvement in working memory performance when treated with olanzapine, as compared to their Val/Val counterparts.[1] This finding was replicated by Weickert et al. in patients treated with various antipsychotics (mostly atypical antipsychotics); schizophrenia patients with the Met/Met genotype experienced working memory improvement on these drugs, but Val allele carriers did not improve.[2]

Similar findings have been demonstrated when treatment-naive schizophrenia patients were treated with clozapine; after 6 months of treatment, Met allele carriers (homozygous and heterozygous) experienced greater improvement in attention and verbal fluency measures compared to the Val/Val group.[3] A 2013, two year study of bipolar patients suggests that the Val allele is associated with detrimental effects of antipsychotics on cognitive function.[4] A twin study of schizophrenia patients further supports this, demonstrating an interaction between drug dose and *COMT* genotype on verbal IQ and working memory. Val/Val patients on higher doses of various antipsychotic chlorpromazine dose equivalents had lower verbal IQ and working memory scores than Met/Met patients.[5]

Huang et al. published a meta-analysis in 2016 of ten schizophrenia studies with a total sample size of 1,416 individuals. Those with the Met/Met genotype were more likely to respond to treatment with antipsychotics overall ($p=0.039$, OR Met/Met = 1.37, 95% CI: 1.02–1.85). Upon separate analysis of 1,207 individuals who were treated with atypical antipsychotics, the Met/Met genotype showed an even stronger likelihood of response ($p=0.0098$, OR = 1.54, 95% CI: 1.11–2.14).[6]

In summary, there are several data points relating the *COMT* Met/Met genotype with improved response rates to antipsychotics as well as increases in some cognitive functioning, secondary to these medications. Knowledge of a patient's *COMT* genotype can be informative for selection of optimal treatment, leading to a better approach to holistic patient care.

**References**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