Cytochrome P450 (CYP450) genotyping to predict response to antidepressant and antipsychotic medications

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Authors’ conclusions
Antidepressants and antipsychotics are used widely in the United States, with use having increased two to four times since the 1990s. Nearly all antidepressants and antipsychotics are metabolized by enzymes that belong to the cytochrome P450 (CYP) family. CYP enzymes are also responsible for metabolizing many endogenous and exogenous chemicals. Individuals may have differences in these genes (commonly referred to as polymorphisms, alleles, or sequence variants) that can affect the metabolism, efficacy, and side effects of antidepressant and antipsychotic medications. Further complicating the administration of these medications is that many of them also inhibit the CYP enzymes, resulting in drug interactions for some patients on polytherapy. While the potential for polymorphisms in the CYP genes to affect the efficacy of and side effects associated with antidepressants and antipsychotics is well known, the clinical relevance of these pharmacogenetic interactions remains less clear. The most relevant CYP genes that have polymorphisms that may affect the metabolism of antidepressants and antipsychotics are thought to be CYP1A2, CYP2C9, CYP2C19, and CYP2D6. The side effects that may be more common in patients with certain CYP polymorphisms are weight gain/metabolic syndrome, tardive dyskinesia (involuntary movements of the tongue, lips, face, trunk, and extremities), hyperprolactinemia (elevated serum prolactin), akathisia (a constant restless feeling), and serotonin syndrome (a potentially life-threatening adverse drug reaction leading to elevated serotonin). Sequence variants in other genes than those the CYP family may affect the metabolism and distribution of antidepressants and antipsychotics. Two genes that have been widely investigated for a relationship between use of these medications and response to treatment are HTR2A (5-hydroxytryptamine (serotonin) receptor 2A, G protein-coupled) and SCL6A4 (solute carrier family 6 (neurotransmitter transporter, serotonin), member 4).

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