Pharmacogenetics of Cytochrome P450-Associated Drugs in Neuropsychiatry

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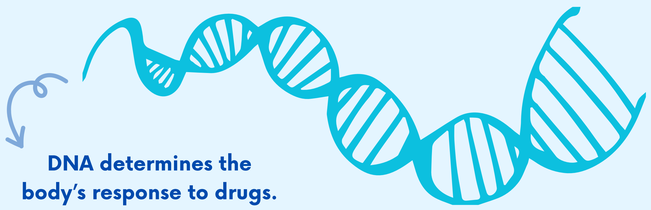
INTRODUCTION

It is widely understood that the proper management of medications of all kinds is vital to patient recovery and treatment. As a result of newly developing **pharmacogenetics**, the study of how **genetic variations can affect drug response and efficacy**, medicine management now has the potential to become personally tailored to each individual. In neuropsychiatry, this pharmacogenetic testing on the individual patient's genes focuses on a group of enzymes: **Cytochrome P450 (CYP)** enzymes. CYP enzymes are essential in catalyzing the metabolism of drugs. The testing of this group of enzymes thus can assist in determining the efficacy of drugs for each specific individual and their diagnoses, providing a more personalized treatment that may consequently be **more effective than a general prescription**. This research attempts to determine the value of pharmacogenetic testing and the impact it can have on a patient's treatment plan.



DNA determines the body's response to drugs.

METHODOLOGY

This study derived its results primarily from **Castle Biosciences' IDgenetix testing**, as well as patient medical charts and histories. The test results, which produced information on **patient-specific drug metabolism**, were compared to the patient's prescriptions before and after testing, as well as any changes made to the treatment plan as a result. From these data sets, conclusions were drawn on the **value** of pharmacogenetic testing in improving patient health, determining the **practicality** of pharmacogenetic testing as a whole.

However, it is worth noting the limitations of this research study. Since only three patients were able to be studied in close detail, there may exist many more possibilities in the realm of pharmacogenetic testing. Due to the nature of insurance coverage, the patients observed were only able to obtain this testing after having tried an average of 17 different medications.

RESULTS

UM
CYP1A2 Gene

PM
CYP3A5 Gene

IM
CYP2C9 Gene

EM
CYP2D6 Gene

UM: Ultra-Rapid Metabolizer
EM: Extensive Metabolizer (normal)
IM: Intermediate Metabolizer
PM: Poor Metabolizer

Gene	Star Allele Genotype/Diplotype	Metabolizer Phenotype PM/IM/EM/UM
ABCB1 [NM_000927.4:c.3435C>T]	C/T	N/A
ADRA2A -1291C>G [NM_000681.3:c.-1252G>C]	C/G	N/A
COMT [NM_000754.3:c.472G>A]	A/G	N/A
CYP1A2	*1F/*1F	UM
CYP2C19	*1/*17	UM
CYP2C9	*1/*2	IM

TEST SAMPLE

Use as Directed
Drug
quetiapine (SGA)
asenapine (SGA)
cariprazine (SGA)
lurasidone (SGA)
paliperidone (SGA)
ziprasidone (SGA)
loxapine (First Generation Antipsychotic)

Use With Caution and/or Increased Monitoring	
Drug	Dosing
clozapine	Consider dose adjustment or alternate drug. Use with caution: monitor for decreased effectiveness (CYP1A2 UM). Consider dose increase if necessary. (Drug Label)
olanzapine	Consider dose adjustment or alternate drug. Use with caution & monitor therapeutically. Increased dose may be required for response. (CYP1A2 UM)
aripiprazole*	Risk of metabolic interaction with celecoxib, fluoxetine
brexpiprazole*	Risk of metabolic interaction with celecoxib, fluoxetine
iloperidone*	Risk of metabolic interaction with celecoxib, fluoxetine
risperidone*	Risk of metabolic interaction with celecoxib, fluoxetine
chlorpromazine*	Risk of metabolic interaction with celecoxib, fluoxetine
haloperidol*	Risk of metabolic interaction with celecoxib, fluoxetine
perphenazine*	Risk of metabolic interaction with celecoxib, fluoxetine
thioridazine*	Risk of metabolic interaction with celecoxib, fluoxetine

Drugs under the **"Use as Directed"** category may be used according to the instructions on the standard packaging.

Drugs under the **"Use With Caution and/or Increased Monitoring"** category may have conflicts with other drugs or with metabolism. The patient is advised to consider an adjustment of dosage or an alternative drug entirely.

FINDINGS

Overall, the data indicates that although **pharmacogenetic testing** is just **one part** of a patient's extensive treatment plan, it can provide insight for providers to make improvements in **other aspects** of the patient's treatment. For example, for one patient, the results from the test indicated the need for **more specific genetic testing**, as the alleles tested by the targeted assay were not present. This opened the doors for more specific genetic testing to be **completed and covered by insurance**, improving the patient's treatment plan afterwards. For another patient, the results from the test gave the expected response– that the current medications were **not** effective. The test recommended the patient consider different medications that would not be covered by insurance, thus opening the opportunity for the patient to finally receive the **most effective** prescriptions for them **without** paying high costs out of pocket. The results of these tests have indicated that pharmacogenetic testing has a significant impact in **reducing personal patient costs**, as well as directing patients towards **other methods of genetic testing** to find the best, specifically tailored treatment plan possible. However, it is worth noting there is one marked instance of pharmacogenetic testing **contradicting** drug response in a patient. In this patient, the drugs marked as ineffective resulted in the **best response**, contrary to what the genetic profile read.

TESTS COST UP TO

$330

WITHOUT INSURANCE COVERAGE

NEXT STEPS

Currently, the value of pharmacogenetics as a **new field of study** in neuropsychiatry is **undetermined**. Therefore, this data could be utilized by physicians and patients to better understand the **importance** of pharmacogenetic testing in neuropsychiatry. Since testing is still locked behind financial barriers and insurance, emphasizing the importance of the testing would make it more **accessible** to patients. Utilizing pharmacogenetic testing more frequently in practice may also have the ability to take down **financial barriers**; patients would have a reason for insurance companies to cover medications that are genetically proven to be most effective, **reducing patient costs**.