AN OVERVIEW OF GENETIC TESTING IN PSYCHIATRY

Genetic testing is a new tool introduced in the practice of psychiatry to learn more about patients, medications, and treatment options. Since its introduction, genetic testing in psychiatry has gained both positive and negative views. The primary purpose of this material is to educate readers about the basic concepts of gene and how it can influence our health and response towards medication.

DEFINITIONS:

To understand genetic testing, it is important to define the key players involved: Chromosomes, Genes, DNA, and Pharmacogenomics.

- **Chromosomes**: Our body is made up of trillions of cells and every cell has 46 packed materials in the nucleus called chromosomes. These 46 chromosomes are inherited - 23 from your mother and the other 23 from your father. Every chromosome has many units called genes.

- **Genes**: Genes are the basic units that make up who we are. Genes hold information about our body functions, what we look like, our talents, and the reason for why we react differently towards different diseases and medications.

- **DNA**: Genes are made up of proteins known as DNA (Deoxyribonucleic acid).

- **Pharmacogenomics**: Pharmacogenomics is the study of how gene influences the response of a patient towards a medication.
  
  Pharmaco = Medication; Genomics = Study of genes

IMPORTANCE OF UNDERSTANDING GENETICS:

Genetic testing opens the world of psychiatry to increase understanding about patients and treatment. With genetic testing, doctors can better understand the reasons, factors, and risks associated with individuals including medication reactions and predicting successful outcomes.

- Predict medication reactions: Medications used in psychiatry work differently in different people. It is possible for the same biological members to have different sets of genes. In other words, we cannot always assume that a medication that worked for one family member will work for another even if it is used for the same problem. According to the Centers for Disease Control and Prevention, negative reactions towards medication cause over 700,000 emergency department visits each year. With genetic testing, medication is prescribed based on the genetic makeup of an individual. This is known as individualized medicine or personalized medicine. This approach acknowledges the fact that “one size does not fit all.”

- Predicting the most efficient treatment: Psychiatric illnesses can be chronic and may require treatment for a long time. Understanding the factors that lead to various responses towards medication is extremely important. This is referred to as “efficacy,” the ability to produce a favorable treatment effect.
In order to learn good and bad responses towards medication, it is important to understand two key concepts:

Concept 1: **Metabolism**, or what the body does to the medication.

Concept 2: **Drug action**, or what the medication does to the body.

**CONCEPT 1 – METABOLISM:**

Most of the medications used for treating depression, anxiety disorder, schizophrenia, and bipolar disorder go to the liver for metabolism.

Patient takes the medication by mouth

The medication is absorbed in the gastrointestinal system, then goes to the bloodstream

The medication is taken to the liver for metabolism.

The liver uses a special system (known as the Cytochrome P450 enzymes) to metabolize most medications. These enzymes influence the effectiveness of a medication.

We have 18 types of Cytochrome P450 enzymes that influence the metabolism of drugs and the interactions between medications.

In Psychiatry, the Cytochrome P450 enzymes that are involved in the metabolism of psychiatric drugs are:

- Cytochrome P450 1A2 enzyme.
- Cytochrome P450 2C19 enzyme.
- Cytochrome P450 2C9 enzyme.
- Cytochrome P450 2D6 enzyme.
- Cytochrome P450 3A4 enzyme.
- Cytochrome P450 2B6 enzyme.

Since people can have different Cytochrome P450, they can exhibit different drug responses. The traditional classification of metabolic responses are:

- Ultra-rapid metabolizer
- Extensive or normal metabolizer
- Intermediate metabolizer
- Poor metabolizer

To keep things simple, let’s call these types as normal, slow, and fast.

- **Normal metabolizer**: If your Cytochrome P450 metabolizes the standard dosage of medication recommended by the FDA normally and maintains an adequate level in the body for a therapeutic response, you have a normal metabolizer.
• Fast metabolizer: If your Cytochrome P450 metabolizes the medication faster than normal, the level of medication in the body becomes lower than the standard recommended dosage, and there is little or no response.

For example, if we need to prescribe an antidepressant for a patient whose 3A4 enzyme has been identified as a fast metabolizer, then we’ll have to prescribe a different antidepressant medication that will not go through their 3A4 enzyme but will go through any or all of the other enzymes (1A2, 2C19, 2D6, 2B6 or 2C9) that have a normal metabolizing rate.

• Slow metabolizer: If your Cytochrome P450 metabolizes the medication slower than normal, the level of psychiatric medication in the body becomes high even with a small dosage.

Scientifically, we can identify these groups by looking at the genes that control the Cytochrome P450 enzymes. This way we can know in advance how a person will respond towards some medications.

CONCEPT 2 - DRUG ACTION:

In addition to metabolism, drug action is the other determining factor in your response towards medication. When the psychiatric medication goes to the brain through the bloodstream, it works at its site of action in the brain. The site of action can be a:

1) **Receptor**, involving Serotonin, Dopamine, and/or Norepinephrine receptor genes
2) **Brain enzyme**, the Catechol-O-methyltransferase gene (COMT)
3) **Brain chemical** transporter involving Serotonin, Dopamine, and/or Norepinephrine transporter genes

Despite the level of medication in the body being sufficient, we still see poor clinical response towards the medication. This can be understood by identifying abnormalities at the site of action through genetic testing.

LIMITATIONS OF GENETIC TESTING:

Although this concept is both helpful and reassuring to both patients and doctors, it is important to understand that genetic testing is still in the developmental stages. Some discourage testing, such as a workgroup at the Centers for Disease Control and Prevention (CDC) who discouraged the use of Cytochrome P450 testing for the most commonly prescribed antidepressants. However, some experts feel that the methodology used by the CDC to evaluate the application of genetic testing was inappropriate.

Despite these limitations, experts consider pharmacogenomics a highly promising aspect of psychiatric care and a step towards individualized medicine. Clinicians consider genetic testing a valuable tool in some treatment-resistant cases, or for patients who are on multiple psychiatric medications with low responses, or for patients who have failed multiple trials of medications due to side effects.
GENETIC TESTS:

The tests are done through blood draw or oral swabs. These tests are approved by the Food and Drug Administration and with the development of new techniques, costs have moved significantly lower. Most public and private insurance cover pharmacogenomics testing in psychiatry. For more information on reimbursement coverage, talk to your insurance provider.

REFERENCES:


