**Genetic Vulnerability Factors**

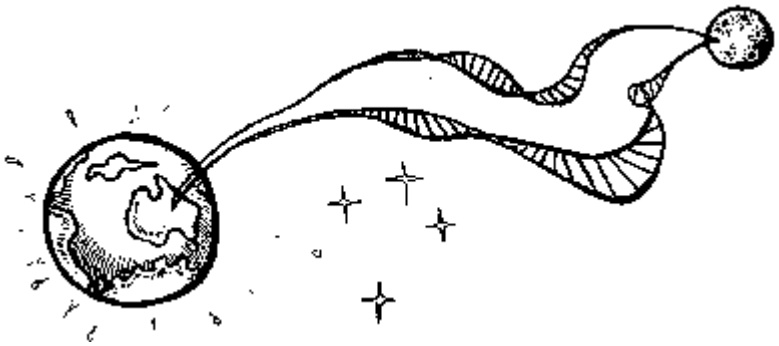
To properly understand what the genetic vulnerability factors are, we need to start at the beginning and make sure that we are clear that we know the answers to questions like: What is DNA? What is a chromosome? What is a gene?

***What is DNA?***

DNA stands for deoxyribonucleic acid. This complicated name just describes the chemical structure of the molecule. DNA is made up 4 types of smaller unit called nucleotides. These 4 types of DNA unit (the nucleotides) each have a letter, they are A C G and T. The DNA in each cell of our bodies contains 6 billion (6,000,000,000) of these units, A, C, G and T!

To get an idea of how much that is, imagine that you are typing out the letters. You can probably get about 1500 letters on a page, so if you were to make a book every time you had 400 of these pages, you would need 5,000 books for all the letters in one cell!

DNA is found in almost every cell in our bodies. Inside each of our cells, we have 6 feet of DNA! If you were to lay out all the DNA in your body, from every cell, from end to end, it would stretch 9 million kilometres! That is enough to reach to



the moon and back 13 times!

***What is a chromosome?***

This much DNA needs to be carefully and tightly packaged so that it can fit into the cell.

So, inside our cells, DNA is tightly packaged up as chromosomes. Most types of cell in the body have 23 pairs of chromosomes – 46 in all.

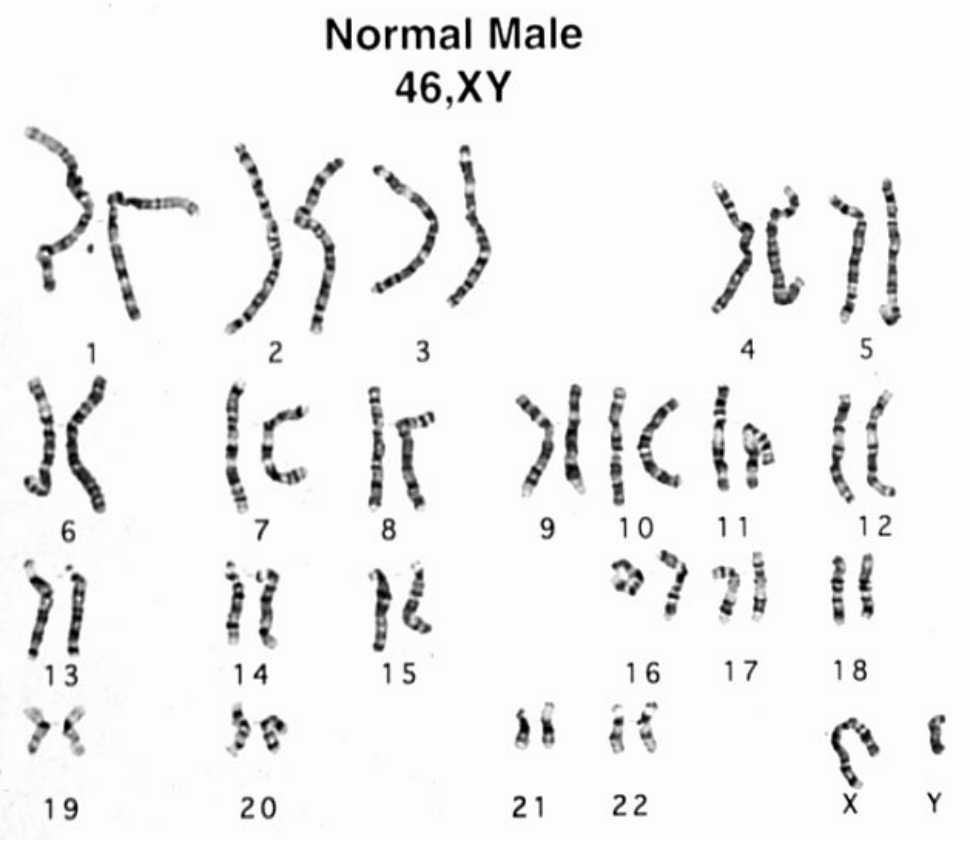
The only type of cells that don't have 46 chromosomes are the egg and the sperm cells, these cells each have just one copy of 23 chromosomes. This is so that when the egg and the sperm cell meet to make a new embryo, the new embryo now has 23 pairs of chromosomes – 46 in all.

So, we each get one copy of each chromosome from our mothers and one copy of each chromosome from our fathers.

The first 22 pairs of chromosomes have numbers (1-22) and are called the autosomes. The last pair of chromosomes are called the sex chromosomes, males have an X chromosome and a Y chromosome, while females have no Y and instead have 2 copies of the X chromosome.

The different chromosomes can be distinguished from each other by their size, and by the particular pattern of light and dark bands that can be seen when they are treated with a special stain.

The picture below shows the chromosomes of a normal male.



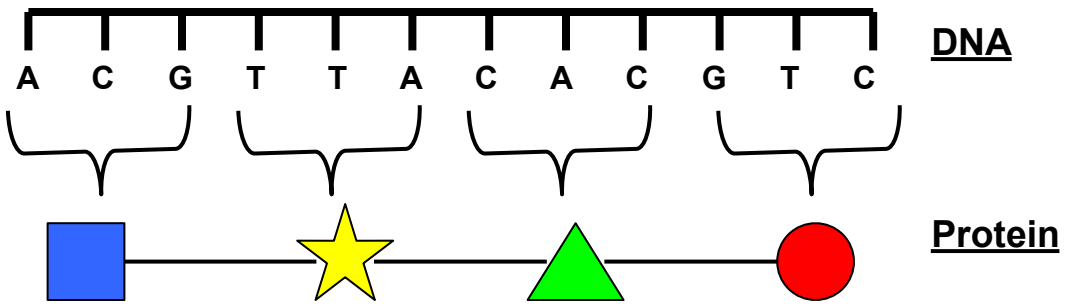

***What is a gene?***

A gene is a special section of DNA that makes a protein. Proteins are the building blocks that make up every cell of our bodies. By making proteins, genes tell our bodies how to grow and develop. Every chromosome has lots of these special sections of DNA, or genes.

The genes are the instructions that tell the body whether to make proteins for black or blonde hair, and proteins for brown or blue eyes and whether to make proteins for A, B, or O type blood.

The genes are also the instructions that tell our bodies how to make proteins which are different components of the brain, like the chemicals that transmit signals from one brain cell to another (neurotransmitters), and the special receptors for these signals that are found on the surface of brain cells.

Within a gene, each set of three DNA subunits (e.g. ACC or GTA), corresponds to a different protein subunit (or amino acid). So, when the sequence of letters in the gene is read, the body knows what amino acids to put together to make the proper protein.




It is estimated that humans have about 25,000 genes.

Each set of 23 chromosomes has a single copy of each of the 25,000 genes. So, we have two copies of each of these 25,000 genes, as we have 2 copies of every chromosome.

So, because we inherit 23 chromosomes from our mothers and 23 chromosomes from our fathers, we also inherit genes (the instructions telling out bodies how to grow and develop) from both our mothers and our fathers. This explains how we have characteristics of both of our parents!

**Summary so far…**

**DNA is packaged inside the cell as 46 chromosomes. Genes are the special sections of that DNA that contain the instructions to the body about how to make a protein**

***How do genes cause diseases?***

Genes can have mistakes in them. This is quite common and everyone will have at least some genes with mistakes in them. However, in some people, these mistakes can sometimes cause health problems. We call these genetic mistakes mutations.

Mutations can cause health problems because they can change the instructions for making a protein contained within the gene. A mutation may make the genes instructions incorrect, or it might make the instructions make no sense. This is shown below.

As you remember from above, genes are read in groups of 3 letters (like ACG, or TGA), and each group of 3 letters corresponds to an amino acid, which the body then assembles to make a protein. So, imagine this is a gene:

theoldmansat → the old man sat

Reading it in groups of 3 letters it makes sense, and so if this were a gene, the protein would be made correctly. However, if we make a difference in the gene (and there are a number of ways in which this can happen, shown below) reading in groups of 3 letters no longer makes sense, and then the protein would not be made correctly.

**1)** A letter in the gene can be changed:

thdoldmansat → thd old man sat

1) Or a letter in the gene can be lost:

theoldansat → the old ans at

2) Or a letter in the gene can be gained:

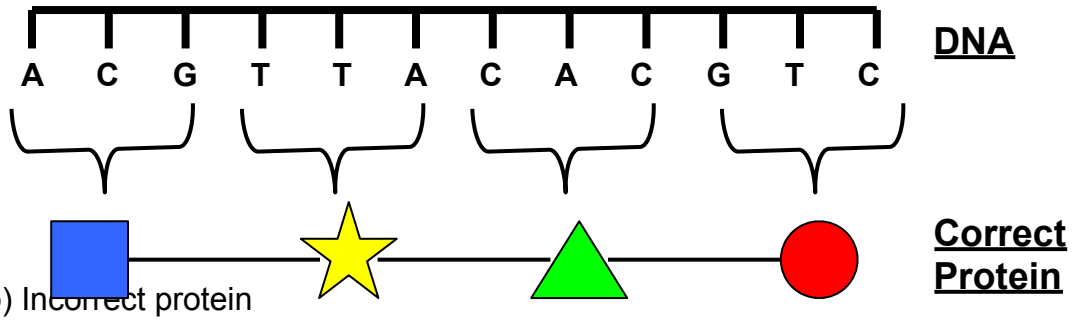
tgheoldmansat → tgh eol dma nsa t

Mutations in genes can cause proteins to be made incorrectly (this is shown in the picture below) or sometimes, the protein will not be made at all. Mutations can happen in genes that make proteins which are important for sending messages between brain cells. These proteins include neurotransmitters as well

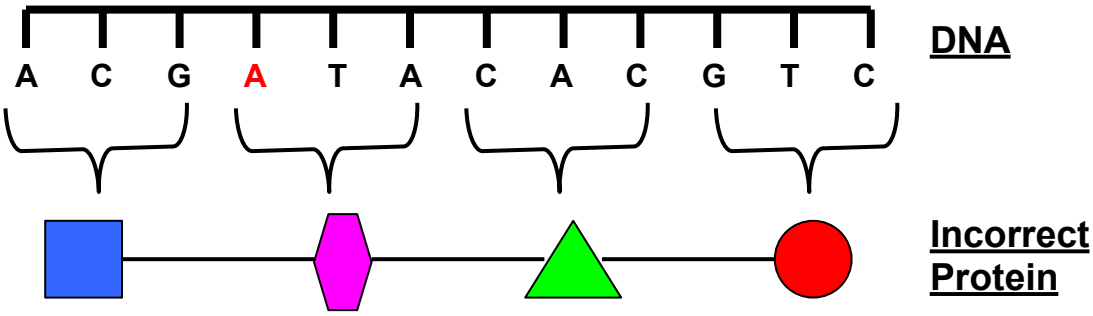
as transporters and receptors for these neurotransmitters. Researchers believe that mutations in these genes might be an important contributing factor to a person developing a psychosis. Mutations in these genes are the genetic vulnerability factors.

**A DNA mutation can cause a protein to be made incorrectly**

a) Correct protein




b) Incorrect protein




You will hear psychiatrists and other health professionals telling you that psychosis is caused by chemical imbalance in the brain. The chemical imbalance in the brain can be caused by mutations in genes that make these chemicals.

> ASIDE – you may have heard on the news recently that if an Individual has a father who is older (over the age of 50 at the time of conception) this can lead to an increased risk of schizophrenia in the child. Researchers think that this is because of the increased chance for mutations (just like those shown above) to happen in the father's sperm as the father gets older. The increased chance of schizophrenia in a child who has an older father is very small.

Researchers think that usually, these genetic vulnerability factors are not enough on their own for a person to develop a psychosis. It is thought that several different mutations in different genes AND some environmental vulnerability factors are needed for a person to develop the illness. To put this another way, it seems that usually having a single mutation is not enough to make a person develop a psychosis.

Because having a mutation in one gene is not enough for a person to develop a psychosis, the genes that are involved in psychosis DO NOT CAUSE psychosis, they only *confer susceptibility* or *increase vulnerability* to psychosis.

***Genes that can increase vulnerability to psychosis***

In the last couple of years, research to find mutations in genes that might increase vulnerability to psychosis has come a long way. Researchers around the world have been trying to find the genes that might increase a person's vulnerability to psychosis.

Genes that make proteins that are involved with sending messages in the brain have been found on many different chromosomes. Recently, mutations in some of these genes (on chromosomes 1, 6, 8, 12, 13, and 22) have been found to increase the chance of a person developing certain types of psychosis like schizophrenia or bipolar disorder. However, each of these genes is thought to increase a person's vulnerability to psychosis by a small proportion.

Although we can be quite confident that some of the genes that have been found are involved with increasing susceptibility to psychosis, we don't yet have a clear understanding of how these genes increase susceptibility. This is because we don't yet fully understand how they work.