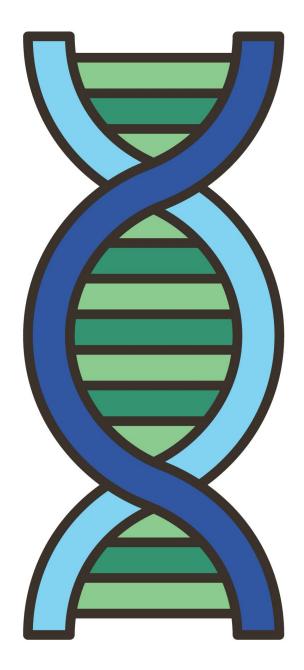


The Genetics of ADHD







Key Points

- DNA is a molecule that carries your genetic code
- Genes are made up of DNA act as a blueprint for making proteins
- Mutations in genes can make them less able to make 'normal' proteins or they can no longer produce a protein at all.
- ADHD is associated with many small mutations in genes
- In almost all cases these mutations are the main cause of ADHD





What is DNA?

Inside each cell of your body, you have a nucleus which contains your genetic material (DNA). This DNA is tightly coiled into structures known as chromosomes (Figure 1), of which you have 23 pairs. Half of your chromosomes you inherited from one parent, and half from the other.

Your DNA is a chemical made up of two long molecules. The molecules are arranged in a spiral, like a twisted ladder (see Figure 1). Inside the spiral shape of DNA, there are building blocks called '**nucleotides'** also known as '**bases'**. The order in which these nucleotides are arranged make up your 'genetic code'. The four nucleotides are called adenine (**A**), guanine (**G**), cytosine (**C**), and thymine (**T**).

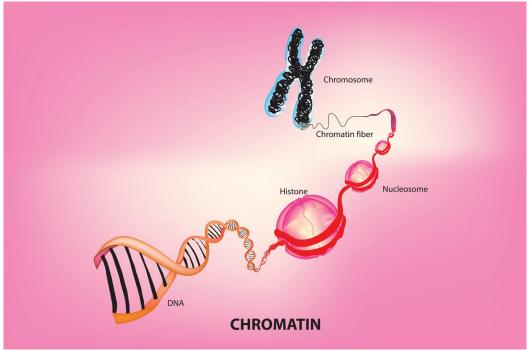


Figure 1: DNA coils into structures known as chromosomes



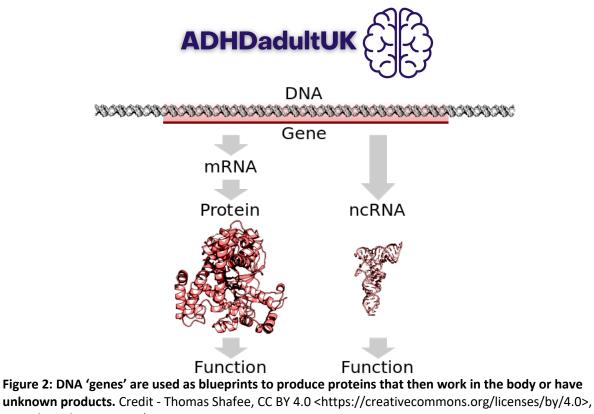


These nucleotides pair up with each other, but only in a very specific way; **A** pairs with with **T** and **C** pairs with **G**, to form '**base pairs**'. In humans, DNA consists of about 3 billion bases, and more than 99% of these are the same in all people. The differences in that last 1% are what make you, you!

What are genes?

Genes are made up of DNA and are therefore inherited from your parents. About 1% of your DNA acts as a blueprint to tell your cells how to make molecules called proteins, and these blueprints are known as genes (see Figure 2). For an example, the gene for insulin is used in the nucleus of cells of the pancreas to allow these cells to make the insulin protein. The first step in this process is often called 'gene expression'. The bases in a gene *must* have the correct DNA code in order to make a protein that looks and works normally.





via Wikimedia Commons)

The other 99% of your DNA, known as 'non-coding DNA', does not act as a blueprint for making proteins. Instead, it can act to 'switch' genes on or off in your DNA or have no known function. In fact, around 8% of human DNA is actually viral, having been inserted into our DNA over millions of years.

Genetic Mutation

A genetic mutation is a change in your DNA sequence, when one or more bases gets deleted. Mutations usually occur when cells are dividing, and your DNA needs to be copied into the new cell. With so many bases, there's a lot of room for error during DNA copying. Mutations are usually substitution (i.e. replacement), deletion (i.e. removal) or insertion (i.e. addition) of the A, T, C and G bases (see Figure 3). If one of these errors occurs, you have a mutation. This means that your DNA blueprint may not be readable by your cells or may have parts of the protein it acts as a blueprint for missing or even have





unnecessary parts added. The result is usually a protein that doesn't function as it normally would.

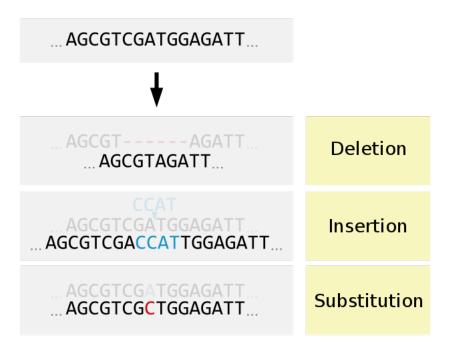


Figure 3: Different ways in which the DNA code can become 'mutated'. Credit - Jonsta247, CC BY-SA 4.0 <https://creativecommons.org/licenses/by-sa/4.0>, via Wikimedia Commons

Mutations that occur or are carried in eggs and sperm can be passed on to children. Another type of mutation, which occurs during our lives is often linked to toxins, like smoking or drinking, and can lead to diseases like cancer but are not passed onto children.





Genetic Mutations and ADHD

A human has around 20,000 genes, and at least 1/3 of these are needed to build a brain and to keep it working. As ADHD tends to run in families, many scientists have looked at the DNA of people with ADHD to try to understand why this is. Studies looking at the DNA in twins, families and adoptions are useful as they help us understand the relative impact of genetics and environment on the risk of a disease or condition arising. For example, if you take two identical twins who have been adopted to different homes, their genetics are almost identical, but their environments are different, which allows insight into the cause of a condition.

What this research has shown, is that <u>genes and their interaction with the</u> <u>environment play a big role in causing ADHD</u>. A large study, looking at over 20,000 people with ADHD found that <u>lots of small mutations in people with</u> <u>ADHD</u>, which on their own wouldn't do much, combine to increase risk for the <u>disorder</u>. These genes together increase the risk for ADHD and are known to predict ADHD symptoms in the general population, and suggests that the genetic causes of ADHD, also influence lower levels of ADHD symptoms in the general population. <u>This means that ADHD is considered a disorder</u>, which is <u>around 80-90% genetic in cause</u>. If a first degree relative of yours has ADHD, you are between 5 and 9 times more likely to also have ADHD than a member of the general population.





In the general population, <u>those with more of these mutations are more likely</u> <u>to have been diagnosed with ADHD</u>. In very rare cases, <u>ADHD can arise from</u> <u>mutations in one single gene</u>, or in <u>an entire chromosome</u>.

Importantly, the twin studies mentioned earlier have shown that <u>shared</u> <u>environments in twins are unimportant</u>, suggesting that it is <u>their genetics</u> <u>which causes them to have ADHD</u>.

The genes which are usually mutated in ADHD, include genes that are <u>involved</u> <u>in how the neurotransmitter dopamine works</u> as well as <u>genes that enable</u> <u>neurons</u>, (the cells in the brain that make the brain work), to develop properly early in life and important genes that regulate how other genes work together.





The Environment

The environment is the world around us, including what we eat, what we are exposed to physically, emotionally and financially (such as deprivation). Environmental factors such as severe deprivation are also likely to play a role in the cause of ADHD. In very rare cases these <u>environmental factors are the</u> <u>main reason for ADHD developing</u>, but in most cases the environment interacts with our genes to alter howe the brain develops.

Environment factors, which have strong science behind them include <u>prenatal</u> <u>risk factors such as exposure to alcohol and drugs, valproic acid, high blood</u> <u>pressure, maternal stress during pregnancy, as well as preterm birth and low</u> <u>birth weight</u>. However, these studies are 'associations', which means they might be related, but one might not cause the other and the genetics of the people in these studies are often not considered.

