Genes and Their Environment

"The primary goal of Behavioral Genetics is to establish correlational relationships between genes and behavior" [1]

Is there a gene for bungee-jumping? Is alcoholism a genetic trait just like blood type? Are there genes for schizophrenia? Is a person's personality a series of chemical reactions in the brain that are determined by their genes?

Scientists who study these kinds of questions are called **behavioral geneticists**. Most of these geneticists would say the data suggest that personality traits are influenced by, but not determined by, genes.

Most human characteristics are not determined by a single gene. Many human characteristics are influenced by several genes working together. In such cases, the simple Punnet Square that can be used to determine blood type won't work easily for determining the frequency of inheritance for such characteristics. And, to make things a bit more complicated, a human characteristic is frequently the result of the interaction of one or more genes and the environment. When we say environment here, we are not talking about just the outside world—where you went to school, what you had for lunch, whether or not you exercise. The environment of a human gene includes 1) the other genes in that cell, 2) hormones and other chemicals to which the cell is exposed, 3) interactions with other cells and tissues, and 4) the environment outside the body. Studies of identical twins can be helpful to study the influence of environment. Since identical twins have identical genes/DNA, scientists can learn a lot by studying how twins that are separated after birth are affected by being raised in two different communities/environments.

Please note: definitions of terms that are in boldface in the text as well as other terms can be found in the Glossary.

Polygenic Inheritance: Inheritance Involving More than One Gene

Hypothetical Example of Multiple Genes Affecting Height

Let's look first at specific traits that are determined by several genes, a phenomenon known as **polygenic inheritance**. A good example is height. Height is a continuously varying characteristic. That is, not all humans are either 5 feet tall or 6 feet tall. Rather,

[1] (Bazzett, Terence J. *An Introduction to Behavior Genetics*. Sunderland, MA: Sinauer Associates, 2008. ISBN 0-87893-049-3)

human heights are distributed through a range. Multiple genes contribute to height. Indeed, geneticists have learned that many genes, scattered widely over multiple chromosomes, appear to contribute additively to the genetic determination of height.[2]

To understand multiple gene involvement in the inheritance of polygenic traits, let's consider a simplified and hypothetical case. Let's assume that only three genes interact with each other to control height and that each gene has two different alleles. For each gene, one allele adds height (additive) while the other allele does not (nonadditive). In addition, the allele that adds height is dominant over the one that does not. Because every child inherits one allele of each gene from each parent, you can look at all three genes and even prepare a Punnett Square for each gene. A couple who each have three dominant alleles and three recessive alleles among the three genes could end up with children who were the same height as they are, but could also be significantly shorter or taller. While more than three genes are normally involved in height determination, this hypothetical example gives the general idea. In fact, with more genes involved, one can see greater extremes in height in offspring than if only a few genes were involved, even when the parents are of fairly average height.

You may be thinking, doesn't environment affect height? Yes, but negligibly. The vast majority of the characteristic of height is genetically determined. If your parents had fed you protein shakes as a child and sent you to a Montessori school, you still would not likely be 7 feet tall. Environment will result in relatively minor adjustments to the genetic underpinnings that determine a person's height.

Other Polygenic Traits and Risks of Illness Influenced by Environmental Interactions

Many characteristics are determined polygenically, including skin colour, weight, blood pressure, and blood cholesterol levels. Of course, these characteristics also have an environmental component. Determining whether a trait is determined by genes or an interaction between genes and the environment can be difficult, but not impossible. In some cases, it is actually quite simple, as when only one or two genes interact with the environment.

For example, the risk of stroke by a blood clot can be related to certain alleles for two genes that control the production of proteins involved in the clotting process (one is called prothrombin while the other is called factor V). Each gene has some alleles that are associated with changes in the nature or production of these proteins. Some of these protein changes may considerably increase the risk of blood clots, particularly if

[2] (Visscher, PM, et al. Am J Hum Genet. 2007 Nov; 81(5):1104-10).

the person with those proteins is exposed to certain environmental factors. Some kinds of oral contraceptives are a good example. They may act as environmental factors by interacting with such proteins after being swallowed and absorbed into the body.

Taking contraceptive pills can have a much greater effect on clotting in women carrying genes that produce the more risky proteins. For example, among women who have *not* inherited the risky proteins, there is a *three times greater risk of stroke* from a blood clot when taking oral contraceptives compared to women who don't take oral contraceptives. However, among women who inherit the risky proteins, taking oral contraceptives increases the risk of a stroke *150 times higher* than similar women with the risky protein who do not take oral contraceptives. Clearly, oral contraceptives can have a substantial environmental effect when interacting with certain genetically inherited proteins

Interactions between Genetic Variation and the Environment: The Case of Behavioural Genetics

Most of the time, however, the interaction between genes and the environment is more complicated, often because of unknown factors. Such unknowns can include the number of genes involved, the percentage of genetic variation in a trait, and the percentage of variation in a trait due to environmental influence. Nowhere is this truer than with behavioural genetics.

Behavioural traits include abilities, feelings, moods, personality, intelligence, and how a person communicates, copes with anger, and handles stress. Disorders with behavioural symptoms are wide-ranging and include phobias, anxiety, dementia, psychosis, addiction and mood alteration. While most illnesses associated with abnormal behavioural traits involve multiple genes, a few such conditions can be traced to a single gene. Huntington disease is a rare example of such a condition.

Huntington Disease: Behavioural Disorder Due to a Single Genetic Mutation

Huntington disease (HD) is a fatal, progressive, neurodegenerative disease caused by a dominant mutated allele. Individuals who are heterozygous for HD usually develop symptoms in their late 30's or 40's. Some early symptoms of HD are mood swings, depression, and irritability or trouble driving, learning new things, remembering a fact, or making a decision. As the disease progresses, concentration on thinking and speaking becomes increasingly difficult and the affected person may have difficulty feeding himself or herself and swallowing. Angry outbursts are the hallmark characteristic of this disease.

Since a mutation in a gene can result in behavioural traits, it is clear that genes can be linked to human behaviours. Unlike HD, however, most behavioural disorders are not the result of a single mutated gene.

Challenges of Identifying Genetic Associations with Variations in Behaviour

Investigating the genetics of behavior is more difficult than understanding a disorder such as sickle cell disease or HD in which an abnormal protein clearly disrupts physiology in a particular way. One of the reasons that such investigations are difficult is that many behavioral disorders share symptoms, which can complicate diagnosis. For example, poor concentration may be a symptom of attention deficit disorder (ADD), major depressive disorders, or post-traumatic stress disorder, to name a few. Further to this, many symptoms, including poor concentration, can be considered variations of normal behaviour – surely everyone from time to time has a hard time concentrating or experiences mood swings when under some degree for stress for a time.

Another challenge to understanding the relationship between genes and behaviours is the highly subjective nature of studies that rely on self-reporting of symptoms by study subjects. A person can also, unintentionally, copy someone's unusual behavior, because he or she does not realize it's unusual. Such sources of confusion do not occur with diseases such as cystic fibrosis, where strictly physical symptoms such as shortness of breath and cough are characteristic manifestations of the disorder.

Although it is necessary to be cautious when assigning a genetic cause to a behaviour, it is still possible to examine genes that contribute to a particular behaviour. Typically, scientists attempt to identify behaviours that appear to be inherited, then focus on identifying and describing candidate genes. (More information on these behavioural disorders can be found in the section Inherited Disease and Genetic Testing.)

Example of Research Exploring the Association between Genetic Control of Nerve Transmission and Behaviour

How are the experiments performed to determine whether a candidate gene is actually involved in a behavioural trait? Let's look at the gene for the serotonin transporter.

Serotonin is a molecule that transmits signals from one nerve cell to another. One cell (the sending cell) produces and releases the serotonin. A nearby nerve cell (the receiving cell) then binds the serotonin and this cell responds to the serotonin signal in a certain way. The longer it takes the serotonin to move from the sending to the receiving cell, the more signaling occurs to the receiving cell.

A particular gene controls the production of a certain protein (called a serotonin

transporter) that can bind to serotonin when it is between the two cells, acting like a ferry that can return it back to the releasing cell. This process of returning the serotonin back to the releasing cell shuts off the initial signal and thus prevents the signal from becoming continuous. Normally, just enough serotonin reaches the receiving nerve cell to cause the appropriate amount of signaling for normal nerve functioning. However, if too much signaling occurs, there can be problems in nerve conduction that result in behavioural disorders such as depression, anxiety, and other mood disorders.

Now certain drugs can slow down the rate at which the serotonin is returned to the releasing cell. These are called selective serotonin reuptake inhibitors (SSRIs) and the antidepressive medications Prozac and Paxil are examples of such drugs. Such drugs can give relief to patients with depression by slowing the transport of serotonin back to the sending cells in certain parts of the brain. This slows the signaling frequency by allowing for a slightly longer time for signaling between nerve cells. Therefore, studying the serotonin transporter gene may give us a better understanding of the mechanism behind these behavioural disorders and lead to better therapies for such disorders.

Clinical Studies Can Find Associations between Different Alleles and Types of Behaviour

It turns out that there are two alleles for the gene associated with the serotonin transporter, called the long and short alleles. The long form is more active and more quickly mops up serotonin from the space between neurons. That is, people with the long form of the gene have a shorter signaling time than people with the short form of the gene. The question then is: can scientists detect a behavioural difference between people with these two forms of the gene?

Researchers at the National Institutes of Health conducted a study in which people's transporter genes were examined. The participants also took a standardized test that measures neuroticism, a term for emotional instability that includes obsessive-compulsive disorder, anxiety neurosis, and a variety of phobias. Each individual was then given a neuroticism score. Not surprisingly, when the scores of all the people were plotted, the scores formed a generally bell-shaped curve. Some people were extremely neurotic, some were extremely tranquil, but the majority of people were somewhere in between. When the neuroticism scores of people with the short allelic form of the serotonin transporter were plotted separately from those with the long form, we see that both sets of people formed a somewhat normal distribution. A careful examination of the graph, however, showed that the average neuroticism score of individuals with the long form of the allele was slightly higher than the average neuroticism score of individuals with the short form of the allele.

Statistical analysis of the results suggested that approximately 1% of the variation in neuroticism scores among humans was due to a variation in the gene for the serotonin transporter. This difference is small, but appears to be real. This result suggests that other genes are also involved as well as the environment. Such careful and methodical study is necessary in order to learn how many genes may be involved and how they interact to result in abnormal variations in human behaviour.