

# JOURNAL

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ADDICTIVE DISORDERS

## The Role of Genetics in an Individual's Response to Mind Altering Substances: Is behavior and, more specifically, the way individuals respond to certain stimuli determined by their genetics? <sup>1</sup>

### ARTICLE

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The topic of how or if genetics play a significant role in how humans behave has been the subject of controversy for many decades. Yet most scientists have had no difficulty accepting that much of the behavior of other animals is influenced by what is innate. Furthermore when the discussion moves towards the possibility that addiction or rather addictive behavior might be an inheritable trait the discussion can become rancorous. There are some who still believe that addiction is as a result of a character flaw or moral turpitude.

In the not to distant past and even today many people even some well educated people believe that humans in general behave the way they do as a result of the environment in which they were raised as children. However, there are many in today's world who accepts the idea that it is not the environment alone that holds sway over the individual's personality and/or behavior.

In an order to answer the question posed by the sub-title of this paper, an attempt will be made to briefly discuss the early days of genetics.

Then proceed to exam in a very elementary way some basic biology involving DNA, RNA, protein and cell structure. Next the behavior of animals will be examined and an attempt made to link behavior with genes. Finally a connection will be made to show that addictive behavior is no different than many other inherited traits that surface when triggered by the environment including volitional acts of the individual.

### The Beginning

It is generally accepted that classical genetics began with the painstaking work done by Gregor Mendel. Mendel began experimenting with cross-breeding the garden pea sometime in 1856.

(1) He was admitted to the Augustinian order to become a monk in Brno, Moravia. As a result

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of certain political changes which required religious institutions at that time to serve the State as well as the church many of the monks took up teaching. Probably all of the monasteries of the time had a tradition of encouraging study and to some extent fostered a rich intellectual life. The study of science was encouraged as long as it did not raise questions that challenged the power of the church.

From a young age Mendel exhibited an interest in agriculture which had been recently established as a scientific discipline. (2) He had the good fortune to enroll at the University of Vienna and there he studied plant physiology and experimental physics as well as other subjects. (3) Sometime in 1843 he joined the Augustinian Abbey of St. Thomas as a novice, which is a person who is in the first stage of studying for the catholic priesthood. It appears that he was a steady student and had the support of the then abbot of the monastery.

The Abbey of St. Thomas where Mendel lived and worked had numerous scientific instruments and a significant botanical collection as well as a large library with a good selection of various texts. He spent much time studying and learning the use of these instruments. Along these lines he was encouraged. That may have been the case because the abbey may have been in the business of growing apples and making wine. Whatever the reason he was permitted to spend a great deal of time studying and experimenting with garden peas. The idea being that knowledge about cross fertilization of one species may well be applicable to other species.

As a result of his studies and experiments in hybridizing Mendel broke new ground in a field that very few at the time understood. He wrote about hereditary particles (4) which are known as genes today. In his papers he writes that from one parent comes one particle which will determine the round shape of the seed, and from the other parent the wrinkled shape. (5)

Mendel's experimentation with peas resulted in his observation that "characters or traits pass as unmodified units from parents to successive generations according to set ratios" (6) He suggested that each parent has pairs of particles (genes) but only one from each parent went to the offspring. Mendel also wrote that particles may come in different forms. Today these are known as alleles.

He observed that when he interbred different types of peas, such as a round one with a wrinkled one he noted that all the offspring were round. He concluded that one of the genes was dominant.

Although he is considered the father of genetics. This recognition did not come until some time after the publication of his writings. His work had achieved a breakthrough that was not recognized until much later.

### **Genetics and behavior**

In order to consider the influence that genetics may have on behavior it is probably a good idea to examine the basics of genetics and even the molecular structure of cells and genes.

All organisms are made up of cells and molecules. Even so it is relatively easy to see that no two organisms are exactly alike even if they are made up of similar molecules and cells. For example huge trees and small babies are made up of molecules and cells, yet it is easily seen that they are not alike in appearance. The reason for this can be attributed to the way that the

proteins within cells have been instructed to work. In order to obtain a better understanding of this we need to take a look at genetics.

In the past several years the level of awareness of the field of genetics has risen tremendously. Especially when it became generally known that the human genome study was being undertaken. The study or project as it is more commonly known began sometime in 1990. It was named the U.S. Human Genome Project coordinated by the Department of Energy and National Institutes of Health and expected to last 15 years. (7)

The goals of the project were as follows: (8)

- identify all the approximately 30,000 genes in human DNA.
- determine the sequences of the 3 billion chemical base pairs that make up human DNA.
- store this information in databases.
- improve tools for data analysis.
- transfer related technologies to the private sector.
- address the ethical, legal, and social issues that may arise from the project.

The first draft of the sequences was completed ahead of schedule in 2003 (9). However, the so-called first draft was missing approximately 10% of the “euchromatin” which are the gene rich portions of the genome and about 30% of the genome itself. (10) Since then more work has been done on the genome and on October 21, 2004, the New York Times reported that the latest results indicated a reduction of the number of human genes from what was first reported which was in the area of 30,000. The new number is about 20,000 with another 5,000 awaiting discovery. (11) Furthermore that this number would probably not change since the study was largely completed.

The completion of the Human Genome Project is really the beginning of a new frontier which in some respects holds more mysteries than any that humans have previously experienced. Consider, that most if not all natural science prior to and including the Genome project can be described as descriptive as opposed to experiential. Now as a variety of new projects begin during this Post-Genome period, scientists have the ability to arrange and re-arrange genes; play with proteins by changing the codes. And who knows what else? The results promises mixed possibilities that range along a spectrum of grand optimism regarding the successful managing of diseases and/or a horror of mistakes resulting in gross monsters (lips that grow where ears should be etc.), and the triggering of newer and more deadly illnesses.

So the sequencing of the DNA is by and large completed. However understanding the “hows and whys” of the coding and the resulting proteins and their functions will take longer. Nevertheless over time and as a result of ongoing research more and more scientists will begin to see and understand the links that exist between genes and their products including behavior.

### **Cells, Genes, DNA and other ingredients**

In order to have a basic understanding of the genome let us start with the fundamental unit of all organs of the body and that is a cell. Cells are composed of proteins and fat molecules. These proteins and molecules make up many different parts of the cell such as:

membrane, vacuole, nucleus, centriole, ribosomes, chloroplast, mitochondrion and several others. Each of these parts carries out specific processes within the cell.

The nucleus which is best described as the controlling unit in the cell is made up of a nuclear envelope, nucleolus, chromatin, and nucleoplasm. It is important to examine the basic make up of the nucleus of the cell, because it is there that the DNA is housed.

The nuclear envelope is the outer covering of the nucleus and is made up of two membranes. The function of these membranes is to control movement in and out of the nucleus itself. It is permeable and acts as both a barrier and a gateway.

The chromatin is made up of long thin strands of DNA. It contains instructions that control cell metabolism and heredity.

The nucleolus is a non-membranous matrix of RNA and protein. Its function is to copy instructions from the DNA. RNA is a nucleic acid named ribonucleic acid and is primarily involved in the synthesis of protein.

DNA (deoxyribonucleic acid) itself is made up of what is called nucleotide units, which are types of molecules. The DNA itself is described as a nucleic acid made up of four main nitrogenous bases named adenine, cytosine, guanine and thymine. These bases are sequenced in side by side arrangements along a DNA strand and are part of a chromosome. The order in which these side by side arrangements occur spells out exact instructions to a particular organism or a part of one. (12) Each DNA strand is made up of these nitrogenous bases in which each group of three letters make up a word. Several of these "words" make up a sentence. Each sentence or group of words is actually a gene. Genes tell the cells to make proteins which enable the cell to perform specific actions. Genes seem to function as an instruction manual. These instructions come in the form of "letters" which are actually nitrogenous bases mentioned earlier. The letters appear like rungs on a ladder and may read, "ATC; CTC; GAA; TAA." This combination is a series of words which may make up a sentence. The sentence is actually a gene as previously stated.

Chromosomes are made up of long thin strands of DNA. Genes which are considered the units of heredity are located on chromosomes in the nucleus of cells. There are many genes on each chromosome.

Each organism has its own set of DNA including humans. An organism's complete set of DNA is called its genome. (13) They vary in size from organism to organism. Human genomes have approximately three billion DNA base pairs and all human cells contain a complete genome except for red blood cells. (14). The inside of cells and the parts inside cells are very adept at copying DNA. DNA itself seems to have an eagerness to copy and be copied. This is probably one of the reasons that certain viruses depend on cells in order to spread inside the body. These viruses use the cells as a means to grow and multiply within the body. Both beneficial and non-beneficial viruses work the same.

Genes are part of DNA and the DNA comes in strands of considerable length. One strand of DNA usually contains many genes. It appears that humans have somewhere between 20,000 and 25,000 genes. Much less than originally thought. (15)

When the DNA strands are examined under a microscope what is revealed is an uneven distribution of the genes along the strands. In some areas there is a dense area of genes and in other areas relatively few genes. The areas that are heavily populated seem to contain primarily the nucleotides “guanine and cytosine.” In the sparsely populated sections the nucleotides there are “adenine and thymine.” (16) Incidentally these nucleotides are usually identified by the first letter of their name i.e. A, T, C, and G.

DNA controls the manufacture of proteins within cells through a process called protein synthesis. (17) In fact all human features and functions are more than likely the result of proteins. These proteins are the product of the coding contained in the nucleotides on the strands of DNA. The DNA is literally wrapped tightly into cells which are then packed into chromosomes. What is astonishing about all of this, is that to say that DNA is wrapped into a cell fails to capture a true picture of the DNA which is contained in a cell. The length of a strand of DNA that is unraveled is approximately two meters. Yet it fits into a cell which is about 10 micrometers wide. (18) And this is not an isolated case. Within each of the millions and millions of cells in a human this phenomenon exists.

So far we have the genome which is the entire DNA contained in an organism; also the chromosomes which contain the genes; the genes which are made up of chemical nucleotide bases identified as adenine (A), cytosine (C), thymine (T), and guanine (G). Genes do not do the good or bad work in the body; it is the proteins that do most of the work. (19)

Genes are essentially the blue print or step by step guide for the way our bodies are made. They contain all of the directions for building the proteins that our bodies require to function. One strand of DNA contains thousands of genes. All of these genes are necessary in order that our bodies can work efficiently.

The DNA is packaged into compact units called chromosomes, with a total of 46 chromosomes in each cell. What is interesting is that of these 46 chromosomes, 23 come from one parent and 23 the other. There is one exception and that is a “gamete”, which is either a mature male or female germ cell. These cells have a total of 23 chromosomes and so when they come together and form a union, it will have 46.

A protein's chemical make-up and its function are dependent on the coding of a particular gene, i.e. the sequence of the nucleotides that prompted its creation. However, proteins generally do not replicate, which means that they do not pass along any imperfections they may have sustained during the course of their existence. It is the DNA which makes the proteins that are replicated each time there is cell division. Therefore damage done to DNA could very well be passed on, depending of course on the type of damage sustained and where it occurs in the cell.

So scientists have begun to explore and understand the fundamental way that genes work. For example, all cells have most of the original genetic information that was exchanged when conception took place. It is the protein made up of amino acids that are the work-horses, and it is the nucleotides that trigger enzymatic actions which make things grow and change and come into being. Yet oddly enough with millions and millions of DNA strings only 10% of this DNA codes for proteins. The rest appears to be long strings of DNA that scientists have not been able to identify their purpose. (20) Although the literature suggests that these strings may act like switches that affect in some way to turn the genes on or off.

The connection between genes and behavior begins at the most fundamental level and that is at the level of movement. The use of sunlight or even electric light as a source of energy for movement by plants is well known. It can be seen when a plant grows or turns to face the sun. A type of microbe named "Archaeobacteria" or arachea has been identified by scientists as able to utilize energy from light via a light sensitive molecule called "rhodopisn." This molecule is actually made up of two smaller molecules called retinol and opsin. Opsin is a protein. This is important because we see again that proteins are the primary catalysts in the work of organisms. As a result of the chemical make up of the rhodopisn molecule the archea bacterium is able to absorb light and use the energy obtained to move towards a light source. (21)

DNA by itself is not capable of triggering the protein synthesis activity. The trigger is RNA. RNA is a single stranded nucleic acid made up of nucleotides. Its full name is Ribonucleic Acid and it is involved in the transcription of genetic information stored in the DNA i.e. it transcribes the information located in the DNA into proteins. There are three types of RNA molecules and they are, messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). All are involved in the process of synthesizing proteins.

RNA is very similar to DNA except that it has a single strand as opposed to DNA's double strand. Another important distinction that RNA is able to travel outside the nucleus of the cell. There is some speculation known as the "RNA hypothesis" which states that RNA is the precursor to all life on the planet. This hypothesis is based on the fact that retroviruses, which are a type of virus, use RNA as their only genetic material. (22) This is very different from the norm in that most organisms including viruses have "genomes" made up of DNA sequences not RNA. However, a retrovirus genome is made up of RNA and therefore has a reverse transcription procedure going from RNA into DNA. Probably because of this difference retroviruses tend to mutate very often and makes for a high degree of resistance to antiviral treatment.

Another important player in the process of protein manufacture is Ribosome. Ribosomes are structures which are made in the nucleus of the cell. The main function of ribosomes is to assemble the amino acids into a gradually lengthening protein chain. There are two types of ribosomes, one called "free," and the other "bound." Free ribosomes can be found in the cytosol of each cell and are more common than "bound" ribosomes. Free ribosome is responsible for proteins that form structure or motile elements. Bound ribosomes are responsible for assembling the protein that becomes part of membranes.

Each step in the process of the development of an organism is crucial to its survival, and any misstep could be either fatal or leave the organism at a possible disadvantage in the struggle of living. Proteins play a vital role in this struggle. In fact they are the machines that make living things function. Whether these organisms are flowers or humans they depend on the smooth functioning of their parts which are made up of proteins. Every cell contains thousands of different proteins which work together like parts in the engine of an automobile to run the cell. Each part does a separate job in order that things go smoothly. To accomplish this requires a variety of proteins. There are receptor proteins that are on the endings of nerve cells, structural type proteins that serve in muscles, and literally millions of others that enable the human or animal body to function. All of these proteins are made in the nucleus of cells. The process starts with the transcription of the DNA by RNA which then delivers and translates the instructions to the Ribosomes where the protein is produced exactly according to the instructions that came from the gene.

**BEHAVIOR Continued**

Genes impact many aspects of all animals' lives including humans. Two very obvious ones are the physical traits that include things like hair color, eye color, a person's height and so on. Behavior is another trait that is associated with inherited genes. This may be more readily seen in dogs. For example, sheep dogs that are bred for herding seem to pass that behavior or instinct along to their offspring. Various dogs that are selected by hunters to retrieve, known as retrievers are another example.

Behavior could be described as the movements' animals make or respond to some stimuli. These involve the obvious locomotion ones such as walking, running, and swimming. But there are also other movements such as digestion, eating or feeding, mating or even breathing. Then the kind of movement that an animal makes when it pricks its ears up to listen or even when birds whistle. Standing still may be considered a behavior. The list is endless.

With all these numerous behaviors, the question naturally follows, why do animals including humans engage in behaviors. Or rather why do they engage in specific types of behaviors? Are these behaviors totally random or do they arise out of some need. Some of the answers are relatively straight forward. An animal eats in order to live. It runs away from a predator in order to live. So clearly some of these behaviors are connected to survival.

It is even possible to argue that not only is behavior related to survivability but certain body organs which currently seem to play no critical role in sustaining life, may at one time been crucial in doing so. For example the appendix in the human animal does not seem to serve any purpose, but it may have at some past time.

There is no doubt that genes play a very important role in all of life. Also although much is known about what they do, there is a great deal more to be learned. Currently scientists have been able to deduce that genes create the physical features of all beings and contribute to certain traits and behaviors. Nevertheless there is uncertainty as to what extent genes impact all of behavior. For example in the field of Ethology which deals with the study of animal behavior, one of the first aspects of animal behavior that has been identified by the scientists involved in this field is "fixed action patterns." (23) Fixed action patterns are considered to be a repertoire of stereotyped behaviors that most if not all animals exhibit. Since an ethologist is really more like a zoologist he/she tends to study the *natural* behavior of animals i.e. innate types of behavior as opposed to *learned* behavior. A "fixed action pattern" where there is no evidence that the behavior has been learned.

This paper focuses on the idea that some behavior has as its base a genetic footing. Obviously many behaviors are learned including some that may have resulted from the specific environment in which the individual lives. However even in those cases, it is conceivable that the genetics of the individual plays a significant role. This can be seen when "behavioral traits" are considered. Behavioral traits are characteristics of the way certain animals act. For example sheep dogs possess some kind of herding instinct that makes it easier for them to herd other animals. Or retrievers are very good at fetching game that their owners have shot.

In the case of a hospital nursery that houses newborn babies, the differences in the behavior of each of the babies are remarkable. Humans are willing to accept the notion that the behavior of animals, even primates is driven by "instincts." But they are less willing to go along with that

concept when it is applied to the human primate. However man's behavior may not be as unique as he likes to think. All primates walk upright, humans walk more upright, all primates have flexible hands, humans have greater flexibility, primates appear to communicate by grunting and other sounds, humans have speech. Non-human primates search for food, shelter, and mates, humans do the same and in addition they search for far more. In this last regard the behavior of humans seem impossible to logically explain. Humans search endlessly for other than food, or shelter, but rather they climb mountains, go to the depths of the oceans, run across deserts, reach out to the stars, and travel to the moon. They seek to attach reasons to explain this behavior because it appears obsessive. However this seemingly endless striving may have a genetic link.

The behaviors that both humans and animals engage in seem to have an element of "seeking" or "searching." And in many respects these behaviors are very similar. Both humans and non-humans search for food, shelter, at times a mate. However, humans also engage in behaviors that are more subtle, at least that is what humans presently think. For example humans seek sensations, new discoveries, new places and so on. They are willing to go to extremes and risk their well being or even life in order to obtain or achieve some of these goals.

When non-humans manifest similar traits the behavior is attributed to the instinct of the animal. Instinct is another way of saying that the animal is genetically wired to do what it is doing or what it did.

Consider how potent the innate drive to behave in certain ways is in some situations. Some animals will sometimes or always move as a large group for food or water for what appears to be weather related reasons. For example in both the Northern and Southern hemispheres the migration of ducks and other animals are triggered by either the cold weather or the position of the sun. The grey whale swims approximately 12,000 miles from the Arctic waters of Alaska to the warm waters of the Gulf of Mexico in order to breed and back again. They do not give birth until the following year when they again return to the Gulf. (24) The monarch butterfly is another example of what seems to be behavior immutably linked to genetics. This specie of butterfly lives in Canada during the summer, and as the weather begins to change in the autumn, the monarch begins a long trek to Mexico, which is over 3,000 miles away. This is extreme behavior to say the least. But that's not all. In addition to traveling this tremendous distance, the monarch looks for a specific type of plant on its return journey to Canada in the spring. They seek out the "milkweed" plant on which to lay their eggs. No other plant will suffice. Apparently the eggs are laid on the branches of the milkweed and once the eggs hatch the plant becomes a food source for caterpillars. Once the caterpillars metamorphose into butterflies they begin their journey to Canada and the cycle begins again.

This kind of behavior does not seem to have any logical explanation in the ordinary sense that is in terms of seeking food or sex rather it appears to be the result of something innate. It is certainly seems a clear example of genetically based behavior.

"Curiosity" is another very noticeable behavior that is prevalent among humans. It is so widespread and appears at such an early age that it appears to be something that is innate rather than learned. It has manifested itself throughout the history of mankind in many ways such as climbing Mt. Everest, crossing oceans in small sailboats prior to knowing what is on the other side, and nowadays the exploration of space. None of these exploits have to do with the need for food. Yet many resources, including the loss of lives have been spent in these and

other similar endeavors. This tendency can be observed in many young children who are constantly looking, and seeking and asking the never ending “why” question.

Scientists have been searching for answers regarding the so-called nature versus nurture controversy for a long time now. The question of why a person behaves in a certain way has provoked many different responses. Basically the question has to do with the origins of the behavior. Whether the behavior is rooted in the genes of the person or is the result of the environment in which the person lived? The argument has gone back and forth for some time. But recently it appears that more and more scientists have come to the conclusion that genetics play a more significant role than originally thought.

Scientists have more or less come to the conclusion that many traits are inherited but at the same time they explain that it is not an all or nothing phenomenon. They are constantly working on ways to test theories when feasible. Traditionally there have been a variety of methods used in research. However there are three that have been used most frequently to determine whether a trait in a given population is the result of genetics or the environment. And if possible to what extent each of these factors plays in impacting the trait.

In these research studies the behavioral characteristic being studied is measured or described on a continuum rather than a “have it or don’t have it” manner. So that a particular phenotype such “addiction” which may be characteristic of an addictive personality is not an all or nothing phenomenon. Not only can certain phenotypes manifest themselves on a continuum, but they may do so in different behaviors. For example an addict may be a substance abuser of alcohol, tobacco, cocaine and other substances. The phenotype of addiction can range further than the abuse of substances and into gambling, food bingeing or starving, shoplifting, risky sexual behavior and so on.

The methods most frequently used are family, twin and adoption studies. These methods are not new and have been in use for quite some time. One example of their early use is in the field of agriculture, in order to increase the yield per acre of any particular crop.

Generally when research is carried out the researchers are looking at a certain behavioral trait present among a group of individuals and attempting to observe any differences. It is on these differences that the researchers would focus, in order to determine their cause. That is whether the difference is the result of genetics, environment or a combination. If the cause is genetics then further study is done to determine if it is the result of one gene or several. Generally this is done by observing the amount of variance in the population sample for a particular phenotype.

The three traditional methods previously mentioned, i.e. family, twin and adoption studies all utilize what is called quantitative genetics.( 25 ) This method enables the researchers to measure the observed behavior on a continuous scale. Usually a threshold along the scale is identified based on both genetic and environmental factors. Measurements belonging to those individuals that fall above the threshold are identified as possessing that particular genetic trait; those with measures that fall below the threshold are considered not to possess the trait for purposes of the study.

Scientists who study specific traits as they pertain to identical twins will compare the amount of agreement or similarity that these traits have among the identical twins as compared to fraternal twins. The results are used as a measure of genetic relevance.

Some studies utilize adoptees in order to study behavioral characteristics. these adoptees may be fraternal or identical twins that reside away from their biological parents. In addition they lived away from these parents from early childhood. These children's behaviors are studied to determine if there are aspects of the behaviors that could be attributed to genetics. Conversely environmental influences are studied when genetically unrelated children who live together are compared.

Other studies which measure emotional stability or lack thereof have been carried out with twins. The results from these studies suggest "a moderate role of genetic influences in explaining individual differences in emotional stability."(26)

Studies involving twins, adoptees and schizophrenics indicate substantial evidence of a genetic basis which influences the development of schizophrenia. (27) In fact in 1995 there were several studies that reported findings for a genetic region linked to one or more genes thought to be involved in the development of schizophrenia. (28) However, there is a great deal of uncertainty about these results because replication of these findings has not been achieved.

Research that examines emotional stability/neuroticism has also been done with separated fraternal and identical twins as the subjects. The results showed that identical twins had a high degree of similarity in emotional stability compared to control groups. Fraternal twins had about half the similarities compared to the identical twins. (29) In other studies involving twins that looked at the incidence of schizophrenia, the studies revealed that the concordance rates for identical twins were four more times greater than for fraternal twins. It did not matter with whom or where the children lived. (30)

What these studies seem to show is that there is something other than the environment that contributes to certain emotional states. The result that shows greater concordance also leads to the conclusion that heredity or gene inheritance must play a significant role i.e. the identical twins study. In another example of a study which showed high concordance was the inherited disorder known as Down's syndrome which has an aspect of mental retardation that almost always accompanies it. In fact scientists have been successful in associating this disorder with a specific anomaly i.e. an extra chromosome 21.

Generally even when a physical trait or behavior is linked with a gene, scientists are careful to acknowledge that most if not all behaviors and physical traits are the result of a variety of genetic and environmental factors. The reason is that as more information is discovered regarding the science of genealogy what becomes very clear is how many nuances must be taken into consideration before concluding with some degree of certainty that a gene or several genes is/are responsible for this or that behavior.

Genes are turned off or on by various means and when a protein is encoded it can be affected by any number of factors all of which can interfere with its ability to do what its normal cellular function is meant to do. So although genes maybe a critical determinant in what an organism becomes and how it behaves, they are not the only determining factor.

So the mere fact that genes have been coded in a certain order does not mean that some particular outcome is automatic. Consider that the current estimate of between 20,000 and 30,000 genes make up the human genome and that somewhere between 95% and 97% of that DNA is similar to that of chimpanzees. (32) This may not seem like a big difference, and

perhaps it isn't. However, remember that a gene is comprised of "letters" which are really different kinds of nucleotides and that there are some 3 billion of these letters that make up the human genome and it is the order in which these letters are arranged that is critical for the outcome. A mere 3 to 5% difference is a major difference. The innumerable possibilities that could occur as a result of slight changes in the order of these letters are just the tip of the iceberg in terms of the end results.

For example in addition to the order of the "letters" mentioned above, there is another phenomenon discovered by geneticists sometime in the 1980s that play a role in these outcomes. What was discovered was a small group of genes that the scientists gave the name "hox genes." (33) These geneticists were working with fly genes when they noticed that certain of the genes acted like architects of the fly's body. In other words these genes determined where the head would be placed and the wings and so on. These particular genes apparently are present in all animals including humans and do basically the same task.

The "hox genes" work with proteins that are named "transcription factors." These proteins when triggered by the hox genes attach themselves to parts of the DNA called "promoters." Promoters act like switches or a switch that turn genes off or on. In addition most genes will only be turned on or activated if several of their promoters have attracted or caught transcription factors. (34) Clearly this is a complicated business and for the time being the researchers involved in these studies are or seem to be at the relatively early stages of understanding this system. Any change no matter how slight seems to be able to affect the outcome in a way that might be different from what might have happened if each step preceded as expected. Then again it is possible that the "system" may not be as sensitive as first appears. There are many unanswered questions.

### **Behavior/Instincts**

The idea that innate behavior, what is sometimes referred to as "instincts" is something that humans and other animals are born with is not new. But for some scientists and others it is easier to accept that idea as it relates to non-human animals. Nevertheless, there have been those who interpreted what they observed as instinctive behavior such as William James who wrote about newborn babies engaging in behaviors such as sucking, claspings, crying and identifying these behaviors as examples of instinctive as opposed to learned behaviors. (35)

Another example of instinctual behavior as it pertains to wasps was revealed by Niko Tinbergen who while conducting a variety of experiments observed that the digger wasp would dig a burrow, go catch a caterpillar, paralyze it with a sting and bring it back to the burrow. Then the wasp would lay an egg on top of the caterpillar in order that the new born wasps would have food once they were born. (36) Tinbergen found no evidence that the digger wasp learned this behavior from its parents.

For centuries dogs have been known to manifest behaviors specific to their breed, and some may have been bred to perform particular tasks. For example retrievers are used by hunters, other dogs by sheep farmers for herding, and the famous or infamous hound dogs sniffing the scent of some escaped convict and relentlessly tracking the culprit until caught.

The thoroughbred race horse bred for fast racing is another example. These horses are unique in their ability in run fast. As opposed to the sturdy farm horse that is capable of long hours of pulling heavy loads.

Then there is behavior that is associated with a particular gender. Apparently as a result of hormonal activity in the body of babies while still in the womb, masculinization occurs. This process is triggered by the expression of a gene on the Y chromosome. (37) Behavioral differences between boys and girls are largely the result of when their brains were formed. Infants are not blank slates as was believed several years ago, they are born either as males or females to a large extent. And they are born this way for many reasons, but mainly because of a genetic and hormonal influence. It is probably true that after birth both sexes will learn many cultural nuances about the environment in which they live but they will have been born with behaviors that are typically male and typically female. An example of what is meant by typical male and female behaviors is baby girls spending more time making eye-contact with someone than boys; whereas boys seem to be more active than the girls.

Other research that focuses on brain chemistry has looked at disorders which seem to be gene influenced. One example associated primarily with males is Asperger's syndrome which in some ways is similar to autism. The theory goes that both asperger's syndrome and autism is the result of a brain that is unable to empathize with others in the same way as people who do not have these conditions. A scientist by the name of Simon Baron-Cohen has done some interesting research in this area. (38) In one particular test called a false-photo test a child takes a Polaroid photograph of a scene, then while the picture is developing sees the experimenter move one of the objects in the scene. The child is then asked which position the object will occupy in the photograph. Autistics at a relatively earlier age than non-autistics have no difficulty with this test. The reason is that autistics have a better grasp of the concrete and less of a grasp of how other persons might see something. In other words autistics do not empathize with others to a high degree. (39)

Let's take a look at even more complex phenomenon and that is "personality." First of all let's look at the definition that psychologists currently use to describe the word. Personality according to the psychologists is defined using five factors. They are openness, conscientiousness, extraversion, agreeableness and neuroticism. (40) Scientists generally agree that based on the results of several twin studies that a little over 40% of the variation in personality is due to genetic factors, less than 10% is due to shared environmental influences, and about 25% is due to unique environmental influences experienced by the individual i.e. things like illness, friends, place of residence. The remaining 25% or so is measurement error. (41) These results highlight the role genes play in an area that few scientists a few years ago would have given any credence.

But there is more to come. Researchers began to ask the question, is it possible that a gene or genes could have an effect on a person's personality? The answer seems to be a "yes." There is a gene that triggers a protein that is associated with a person's personality. This protein is called a brain-derived neurotrophic factor and it is located on chromosome 11. Apparently the gene that triggers this protein is relatively short, in that it is comprised of about 1335 letters. (42) These letters spell out the recipe for the protein that will effect the growth of neurons in the brain. Among that string of letters in the 192<sup>nd</sup> place in the gene is a G for most people, but for some people it is an A. In the string of 1335 letters this is sometimes the only change. However this difference results in a different protein made based on whether there is a G or an A. One kind of protein made will have an essential amino acid called methionine instead of

valine in the 66<sup>th</sup> position of the protein. Valine is also an essential amino acid. Most if not all humans have two copies of each gene. This means that there are three possible combinations. The possible combinations are two methionines, or two valines, and those with one methionine and one valine.

In tests carried out with appropriate samples of people a questionnaire concerning personality was handed out which might reveal the kind of brain-derived neurotrophic factor with which they were born. The results were as follows: those people with two methionines were noticeable less neurotic than the people with one Valine and one methionines, who were less neurotic than those with two valines. (43) The study as reported is fascinating for many reasons including that it reveals a possible connection between a person's personality and genetics. However, the researcher uses the word "noticeably" as in noticeably less neurotic. What does that mean? Three people observing the same behavior may very well have different interpretations. What might seem like behavior that is "noticeably" odd to one observer may appear a little different but not noticeably odd to another observer. Nevertheless it does appear that some connection has been made between the brain-derived neurotrophic factor protein and types of behavior.

The study goes on to report that those humans with two valines are the most depressed, self conscious, anxious and vulnerable. Those with the two methionines are the least of all the above. Of twelve other facets of personality that were measured only one showed any association with this gene and that was "openness of feelings." (44)

This study is interesting, although some question could be raised regarding the use of the word "noticeably." How does a researcher measure "noticeably?" Is it the kind of study in which the results could be replicated? Nevertheless it is interesting from the point of view that it makes a connection between a gene and particular states of mind. Because the study goes on to report that those humans with two valines are the most depressed, self conscious, anxious and vulnerable, and those people with two methionines are the least depressed. This particular study also examined twelve other facets of personality but only one of the twelve showed any association with a gene and that was "openness of feelings." (45)

Another study involving twins done by Thomas Bouchard showed some other types of interesting results. Bouchard's study examined both identical and fraternal twins who were separated from each other a few weeks after birth. He looked at their attitudes towards religion and politics. What he found was that the way identical twins thought about these two areas showed a high correlation of 62% versus a correlation of only 2% for fraternal twins.(46) Indicating that the way they thought was very similar, perhaps as a result of the similarity of the construction of their brains.

This leads us into another area filled with controversy about whether IQ is a matter of nature or nurture. This is a subject that has been a point of contention for what seems like eons. However it appears that both genes and the environment play a role in the IQ of people. For example the results of some studies show that for people younger than 20 years the contribution of "shared environment" to variation in IQ plays a significant role. However, "shared environment" to variation in IQ falls to zero as the group gets older. (47) Another way of saying the same thing is that in young people the environment plays a greater role in IQ measure than innate ability. But as the group gets older the environment becomes less and less of a factor until it has little or no influence at all. Much like personality, intelligence appears to be largely inherited but affected to some degree by the particular experience of the individual. In fact the

so-called Flynn effect notes that IQ scores are steadily rising at the rate of at least five points per decade. (48) This is comparable to “height” where it seems that people who are exposed to better nutrition and living conditions are taller.

### **Ancient History or The continuing Battle (nature vs. nurture)**

For a long time now both in terms of scientific endeavor and in everyday non-scientific life there have been attempts, and statements made to the effect that a particular behavior is the result of inheritance (nature) or the environment (nurture). No where is that struggle as intense as in the field of mental health disorders, and schizophrenia in particular. This disease has been studied for a long time and very intensely, but so far there has been no definitive finding of its cause. Much progress has been made in the treatment of the disease to the extent that some patients function reasonably well with the help of medication.

The cause of the illness has been attributed to just about everything including viral infection, parenting, brain development, diet, genes, yet no one thing has been pinned down as the cause. Since only some people get the disease and under different circumstances it seems it would have been very easy to pin point the cause. Yet the only common thread so far noted is that the disease runs in families. However, not all members of the family get the disease and both males and females are subject to its onslaught. It appears that genes play a role, but they are clearly not the only actors. Richard Dawkins writing in one of his essays (49) uses an interesting metaphor of a blueprint versus a recipe. He likens the effect of genes to that of a recipe in most circumstances as opposed to a blue print. A blue print is a detailed point for point specification of a particular end product. For example a house or a bike. An important feature of a blue print is that given the end product, someone with some knowledge of the subject matter could recreate the blueprint working in reverse. However the end result of a recipe is a product that is qualitatively different and although an expert maybe able to identify some of the ingredients used in the recipe, the recipe could not be precisely recreated through a reverse process. It could be argued that genes in many cases work in a very similar way to recipes. They are part of a recipe but many other ingredients contribute to the end product. Things like the environment, nutrition, and other ingredients all contribute and affect the end product. The overall message seems to be that genes play an important role, but not in a vacuum. Everything happens in some sort of environment and the things that make up the environment impact the outcome. The genes themselves are in more cases than not what scientists call “determinists,” but because of the so-called switches i.e. promoters and transcriptors that switch the genes off and on in response to external stimuli they are not as deterministic as they might otherwise be. At any given moment in the brain or body of an animal including the human animal genes are being affected by what is happening in the environment they are living in and in conjunction with the coding of any particular gene the response is unpredictable. The idea that we are solely the result of our genetic inheritance seems unlikely and so does the notion that we are totally the sum total of our life experiences. Yet these two extreme positions are exactly the positions that some of the brightest minds in academia have spent vast resources to prove.

Genes appear to be basically a kind of foundation or beginning which enables the organism to grow, develop and procreate. However because of what scientists have defined as promoters and transcriptors which act like switches, in that they switch genes on and off as a result of external instruction or stimuli, these same genes may or may not create the RNA and thus the protein to do some predetermined action. Make no mistake about it genes make specific things happen. There are myriad examples of this such as the oxytocin receptor genes which allow

pair bonding among prairie voles a type of mice, or the CREB genes which facilitates memory, without these genes there would be no learning, or BDNF which enables binocular vision to happen through experience, thus the world can be seen three dimensionally, or FOXP2 which enables human beings to acquire the language of those with whom they live.(50) There are many other fascinating examples and they all appear to lead to one outcome, and that is the survivability of the individual.

A study was done in the South Island of New Zealand by a Terri Moffitt and Avshalom Caspi. The study involved men born in 1972 – 1973 in the city of Dunedin. From a group of over 1000 boys 442 were selected and controlled for at least two generations of white grandparents, similar economic and social class. Eight (8) % of the boys were severely maltreated between the ages of 3 and 11 and 28% were probably maltreated in some way. The two investigators were interested in testing these children for differences in one particular gene called “monoamine oxidase A” or MAOA, in order to see if this gene made a difference in the behavior of these children. A bit of explanation regarding this gene at this point will be helpful in understanding the outcome of their study. The MAOA gene is associated with a promoter with a 30 letter phrase which is repeated either 3, 3 and 1/2, 4 or 5 times. The monoamine oxidase A gene with the 3-repetition and 5-repetition versions are much less active than the genes with either 3 and 1/2 or 4. So Moffitt and Caspi divided the young men into those with high activity MAOA genes and those with low activity genes. The men with high activity MAOA genes were virtually immune to the effect of mal-treatment. They did not get into trouble much even if they had been mal-treated as youngsters. However, those with the low-active genes were much more anti-social if mal-treated and got into trouble, but if not mal-treated as a youngster these men were even less anti-social than the other group. In other words possession of the gene by itself or mal-treatment alone did not result in anti-social behavior. The recipe required that both ingredients, that is the low active genes and the maltreatment have to be there for the negative result. (51)

## Conclusion

So far the progress that scientists have made in the field of genetics is phenomenal. Not only has the sequencing of the DNA been completed, but the composition of every protein is now known. (52) These are the first critical steps in understanding how humans are put together. These steps are like understanding how the foundation of a building is constructed and the materials used. However the researcher has not stopped. More research is being done to understand how best to cure or treat those ailments that are known to have a genetic link. The initial approach is to work with those ailments that have been identified as having a single gene link. For example illnesses like cystic fibrosis and hypercholesterolemia and others have been identified as caused by a single faulty gene. Techniques that enable the replacement of the faulty with a good gene would eliminate the ailment. Work is progressing in this area. However many or perhaps most illnesses are caused by more than one gene and other approaches are being studied.

The study of genes involves much more than the genes themselves. The research shows that genes and their impact on behavior are connected to myriad of other phenomena within the body as well as what is outside of the body. It seems that this field of study is in its infancy and much more will be learned in time. The evidence strongly suggests that there is very little that we as humans do that is not connected in some way to our genetics. However, having said that it is also very clear that the environment is part of everything that happens.

Addiction or substance abuse has to do with the brain. It is frequently described as a brain disease. The research data has clearly established numerous links between genes and behavior in humans and other animals. Even though substance use initially involves voluntary acts, that does not preclude the possibility that there exists innate factors that contribute to the behavior associated with addiction. It seems more than likely that there would be some connection between genes and addiction. After all given the many examples of genes influencing a myriad of behaviors both in humans and other animals it would be most unlikely that there would be an exception in this case. In fact because there are those who engage in substance abuse behavior but do not become addicted could mean that a genetic predisposition exists in those who do develop the problem. Further the evidence in general seems to support the theory that human behavior is affected by genes to some extent. It as if our bodies are repositories for the genes to have a temporary place to stay until they are passed on and so the susceptibility of some children can frequently be traced to that of the biological parent. We see this in all kinds of disease and illnesses. And if there are no new genes unless it is a mutated one, then genes will reappear time and again with possibly the same result if switched on. After all every gene comes from an ancestor. Perhaps that is why some researchers are pushing forward with work in gene therapy. All of the sequencing of the genome was done by computers via the use of software. Once the translation of the entire genome is in the computer memory and the biomedical scientists determine that a particular string of DNA is the norm, any other sequence may be compared to the original which is stored in memory and the difference noted. For example if a non addict has a sequence of a particular protein in the limbic system that reads "ATACTCGAA" or whatever and the sequence of a protein taken from the limbic system of an addict reads "ATACTGCAA", then that difference and many others could be fairly quickly be identified by computer programs. Where gene therapy comes in would be the ability to successfully alter the sequence. These kinds of changes would not only be applicable to one field of endeavor such as addiction, but rather could conceivably be applied across a wide spectrum of areas of health.

In the face of resistance in some quarters some scientists are working in this arena in the hope that they will achieve a breakthrough as have occurred in other fields. Consider cloning which involves taking a cell from the tissue of an adult animal and letting it grow in a Petri dish, then removing the nucleus of that cell and injecting it into an egg from a female. Then at a certain point implanting the fertilized egg into a suitable female recipient for further development. The result of this procedure is a clone. This along with the ability to grow a variety of human body parts using similar techniques make for interesting times ahead. Because if addiction or more appropriately addictive behavior begins in the brain and scientists are able to identify which specific gene or genes are contributing to the behavior, then in the future replacement of this gene or these genes may be possible. This by itself along with other kinds of treatment may very well be in the not to distant future.

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