Diagnosing dyslexia

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Abstract

Understanding mental diseases and disorders stems from research on polygenic traits. Traits in an organism are coded from genes. Traits may be coded for by a single gene (monogenic traits) or by multiple genes (polygenic traits). Many developmental disorders are polygenic and the extent to which the environment will influence the expression of the trait will always vary. Development disorders in the brain such as dyslexia usually affect an individual's ability to think properly in different situations. The diagnosis of dyslexia has been an onset problem. Dyslexia untreated at a younger age can result in a child being held back in their education. Most children feel discouraged and confused when they are held back. Genetic testing offers a different approach to diagnosing children with dyslexia. The specific proteins that exhibit the most activity in the brain associated with dyslexia are KIAA039, DCDC2, ACOT13, DYX2, DYX3 and FAM65B. If any of these proteins are mutated by the genetic code, it will lead to a protein being constructed improperly. Understanding the proteins as a whole will serve a better diagnostic tool for diagnosing dyslexia.

Keywords: dyslexia, genetics, Y chromosome

Introduction

Behavioral genetics focuses on why people differ. For about a century psychologists would say that the environment plays a very important role in disorders and diseases. However, there is a new approach in understanding mental diseases and disorders. Understanding mental diseases and disorders stems from research on polygenic traits. Traits in an organism are coded from genes. Usually when referencing a trait there is only a single gene that codes for that trait. Sometimes however, you may have multiple genes coding for one trait (Polygenic trait). Many developmental disorders are polygenic. Every trait in every organism is heritable; the extent of how much the environment will influence the trait will always vary.

Background and literature review

Development disorders in the brain such as dyslexia usually affect an individual's ability to think properly in different situations. This puts people with development disorders at a disadvantage among their peers. There is a broad array of mental disorders that are currently known. In the Journal of Biological Psychiatry. the article *Genetics and Mental Disorders* states that one in five Americans over their lifetimes, irrespective of age, gender, or race, will have issues associated with developmental disabilities (1). Another study by the University of Michigan illustrated that, "About 70-80% of all of reading, writing, and spelling difficulties is due to dyslexia. In America it is thought that up to 17% of the population has some type of dyslexic disorder" (2). This disorder has a serious effect on a young student's learning capabilities; if a student cannot process what he or she is writing or reading it will be hard for them to conceptualize a concept.

The diagnosis of dyslexia has been an onset problem. In a recent study published by Science News, the article *Brain Training Aids Kids with Dyslexia* proclaimed that while "kids cannot be diagnosed with dyslexia until they reach the age of 9, they can be classified as "at risk for dyslexia" (3). This is because the current screening for dyslexia is observational; it is based on a child's ability to read and write. This leaves early diagnosis out of the scope since a physician must wait until a child is of age to read and write. If a physician attempts to diagnose at an earlier age it may not be a sound diagnosis since the child may actually be developing at a slower rate than others (5).

Dyslexia untreated at a younger age can result in a child being held back in their education. Most children feel discouraged and confused when they are held back. Genetic testing offers a different approach to diagnosing children with dyslexia. Genetic testing would be more effective than diagnosing the disorder later the child's life (age of 9). The genetic testing would provide a family with information that is necessary to know if a child has a predisposition to develop dyslexia embedded in their genetic code. When children are diagnosed at a

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younger age and the proper interventions are utilized, this can have a significant effect on their overall reading and language skills development (6). Instead of waiting for symptoms to appear, genetic testing will allow families to prepare the child's life in matters that will allow the child to thrive.

Diagnosing individuals using their genetic information and comparing it to a majority of the population has been both successful and inconsistent. Finding a link between a disorder and a gene has a few protocols to it. One, you must find a genetic marker (10). Every gene in the body is made up of two alleles (an allele is a variation of a trait) (10). There are two types of alleles, dominant and recessive. These alleles can code for a variety of different expressions. For example, a person with blue eyes has recessive alleles and a person with brown eyes has dominant alleles. These alleles make up genes that make up the phenotypes seen in organisms. Sometimes, an allele can serve as a genetic marker, or a link to a disease. A genetic marker is like a microscopic beacon that gives a rough estimate of where a disease may be located. In other words a genetic marker can be any DNA variation with a known location on a chromosome that can be observed and followed from generation to generation (4). Common genetic markers include genes that are easily coded for by their characteristics. Blood type is an example of a genetic marker (10). There are many different blood types, and if one person has a disease associated with a specific blood type then that would make a good genetic marker. For example the inheritance of blood types in families may also show a link to a family disorder/disease. If one allele of a blood type is associated with a disease and others are not, then you have a genetic marker (blood). It may be such that only people with blood types O are afflicted with the disease. Finding the marker is a challenge, and finding the specific allele involved with the marker is an even bigger challenge. There are more reliable makers or "beacons" across the body that can be used. These new markers are also known as single nucleotide polymorphisms that are found across the genome (10). Single nucleotide polymorphisms (SNP) are changes in the DNA that alternate the nucleotide sequence; they do not affect the individual (6). Figure 1 shows how an SNP is just one nucleotide difference between individuals. To be considered a polymorphism rather than a mutation, the rare allele of the polymorphism must be seen in 1% or more of the population.

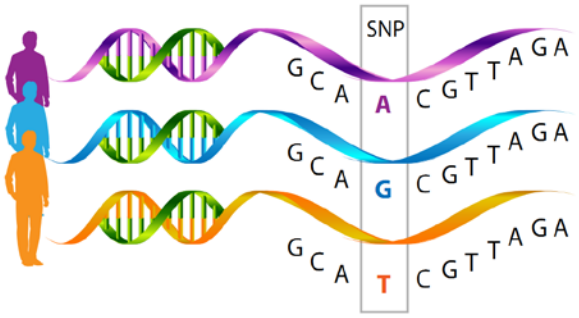

Figure 1

One of the greatest challenges of the biomedical enterprise is linking human genetic variation to very common disorders such as dyslexia. The struggle of associating the variation in SNPs with dyslexia is first finding the genes that are affecting the trait. A common method to link SNPs to diseases/disorders is genome wide association study (GWAS) and comparing it to electronic health records. This entails looking at all of the common SNP's that are affecting the phenotype of an individual (3). However, this approach was determined to be too broad and showed a lot of inconsistency because you were looking at millions of SNPs throughout the entire genome. A new approach that has showed some success has been a whole-exome sequencing study (WES). Instead of analyzing the entire genome of an individual, we can narrow down the sequencing into only the coding DNA. Instead of looking at millions of SNPs, now only thousands can be analyzed. Whole-exome sequencing can narrow down the sample even more, by analyzing only the SNPs that are associated with the brain. Rather than sequencing 100% of the genome, we could sequence 2%; this saves time, effort, and money. The study that showed success in this specific type of sequencing was one that homed in on familial hypercholesterolemia, which is a genetic condition that results in high low-density lipoprotein cholesterol and an increased risk of earlier-onset cardiovascular disorder (7). This disease is very similar to dyslexia in the sense that it is a polygenic disorder. There are multiple genes that affect the trait. The study for hypercholesterolemia showed that most people who had the disorder had mutations in that are associated specifically in proteins that code for the heart. Whole-exome sequencing allows us to know who is predisposed to the familial hypercholesterolemia disease. WES can be done in the same way for dyslexia. Looking for common mutations in the genes that code for the brain has good potential in diagnosing dyslexia. Knowing whether or not an individual will be prone to a disease allows them or others to control and manipulate their environment. In the case of hypercholesterolemia an individual can control their diet a lot better to prevent a heart attack. Diagnosing dyslexia in children could have a significant effect on their capacity for learning.

There is a common misconception that people with learning disabilities are incapable of learning. But in reality, those with learning disabilities just need the proper tools and guidance to allow them to learn at their optimal level, which hinges on early diagnosis and informed interventions. Most people may be held back or even drop out of school because of their learning

disability, and majority often don't know they have a disability. Dyslexia is a common disorder, and knowing the predisposition to the disease can calm the symptoms dramatically. The environment plays a significant role and in the severity of the disability, and if it is not manipulated in a favorable way its effects can be detrimental to the individual. So understanding how to diagnose the disorder in an efficient way at an earlier age will actually be more beneficial than waiting until the individual is at least 9 years old. There are many prospective students and bright thinkers who can benefit from having such a useful tool early in their life.

Methods:

The research that I will be conducting will be to analyze literature that focuses on dyslexia as a genetic disorder. I will be looking for research that examines mutated proteins in the brain that are now thought to be associated with the disorder.

Findings:

The brain is very complex. There are hundreds of genes in the genome that code for the proteins in the brain. The genes that code for proteins in the brain and may play a significant role in the emergence of dyslexia are found on chromosome 5. When the chromosome is mutated there has been observed a difficulty with working memory when trying to comprehend symbols, language and concepts. Working memory functions with our senses. First someone will stimulate their stimulus (seeing a symbol) then their mind will create a phonologic loop and visuospatial sketchpad to integrate the stimulus into their memory. When this is done enough it will actually allow someone to create a concept in their mind that will be integrated into their long-term understanding of the world, or other concepts associated with learning. When there are mutations on this chromosome there has been a lot of association dyslexia, however the chromosome is not a great diagnostic tool because of the variation within it. Sometimes there can be mutations in the chromosome in people who don't manifest the same behavior issues (or the triggers have not kicked in yet). This speaks to a limited diagnostic tool.

When diagnosing dyslexia it becomes more accurate for researchers to actually look for specific proteins specifically related to the disorder. Looking at the disorder by observing an entire chromosome can lead to a lot of variation. The presence of variation does not make the chromosome a good diagnostic tool. The specific proteins that exhibit the most activity with the brain associated with dyslexia are KIAA039, DCDC2, ACOT13, DYX2, DYX3 and FAM65B. If any of these proteins are mutated by the genetic code, it will lead to a protein being constructed improperly. Usually if there is a problem with the biological structure, there will also be a problem with the resulting function (though in rare situations this may not always hold true). These proteins are associated with IQ language and reading. Although findings want to show that one protein is highly associated with dyslexia, it is actually more of a mosaic of all proteins being misfolded than just one being the diagnostic mechanism. Although many of these proteins are associated with dyslexia, none of them are certainly the diagnostic tool.

Finding the actual diagnostic mechanism responsible for dyslexia has been a challenge for scientists for many years. Understanding the proteins as a whole will serve a better diagnostic tool for diagnosing dyslexia.

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