

Canavan Disease

Canavan disease is a genetic disorder that occurs most frequently in people of Ashkenazi Jewish descent (1 in every 6400), although it can occur in any ethnic group. Canavan disease mainly affects the central nervous system. Specifically, it causes a demyelination of nerve cells within the white matter of the brain (the area of the brain in which signals are sent to the other parts of brain and spinal cord). Myelin protects nerve cells, and without it, the proper messages are not able to be sent from the brain to the body. Babies with Canavan disease are missing an essential enzyme called aspartocyclase. This enzyme is necessary to break down a chemical known as NAA. Without this enzyme, NAA accumulates in the white matter of the brain, and problems relating to myelination will occur soon after the baby is born. Infants with Canavan disease appear normal until a few months of age. However, they then begin to show signs of regression because they lack aspartocyclase. This results in a deterioration of the central nervous system which ultimately causes the baby to lose motor and developmental skills (loss of head control is one of the early signs of the disorder), its capacity to swallow, have an enlarged head circumference, and develop increased muscle tone and stiffness. Seizures and blindness are also clinical signs of the disease. The disease can be variable among affected individuals, however, it is progressive in all cases. Canavan disease is ultimately fatal with death usually occurring before the age of five.

How does a person get Canavan disease?

Canavan disease is a genetic disorder that is inherited from one's parents. As a result, a child must be born with Canavan to have it. It cannot be caught like a virus.

Genes, the units of inheritance

Canavan disease is passed down from parents to children by genes. Genes are the units of inheritance that carry the information to make you what you are. For example, you have genes for hair color. Genes come in pairs: half of our genes come from the mother and the other half come from the father. Our genes determine our physical development, they determine what we will look like, how our organs will form, and also how all the chemicals in our body are produced. Collectively, we have several thousands of genes, and each one is involved in our physical development. A baby who has Canavan disease has a pair of genes that are not functioning properly. A gene cannot work if it has a mutation. A mutation is a change in the gene which prevents it from functioning. In the case of Canavan, an important chemical, aspartocyclase, cannot be made. Aspartocyclase is needed in the brain to control the amount of NAA, and without it there will be an excess of NAA that will eventually cause the central nervous system to deteriorate.

How is Canavan disease inherited?

One in 40 people of Ashkenazi Jewish descent carry one mutation for Canavan disease. The mutation prevents the gene from working. These individuals are known as carriers and show no symptoms of the disease. They are perfectly healthy because they have another functional gene that can make aspartocyclase. Therefore, they are normal. In order for a child to have Canavan disease, both parents must be carriers of a Canavan mutation and pass the mutation on to their child. Therefore, a person with Canavan disease has two Canavan mutations, unlike their carrier parents who have only one. This pattern of inheritance is called autosomal recessive inheritance.

Autosomal recessive inheritance

For a couple in which both partners are Canavan disease carriers, in every pregnancy there is a 25% chance (1 in 4) of having a child with Canavan disease (the chance that each parent will pass on their Canavan gene is 1 in 2, or 1/2, so the chance that the child will receive both genes is $1/2 \times 1/2$, which is 1 in 4). There is also a 50% chance (1 in 2) of having a child who will be a healthy carrier like his/her parents. And there is a 25% chance of having a child who does not carry the Canavan gene at all.

Present treatment

Currently there is no way to treat a person with Canavan disease. Even though the enzyme which is deficient is known, there is no way presently to get it into the brain cells to control the amount of NAA. Currently, the symptoms of Canavan disease can sometimes be managed with the use of certain medications and feeding tubes. To reduce the incidence of Canavan disease, an emphasis has been placed on public education, and more recently, carrier detection and prenatal diagnosis.

Carrier detection

Many people can find out if they carry a mutation for Canavan disease through DNA testing. A DNA test can look directly at a person's aspartocyclase genes and can determine if that person has one of two common mutations in the Canavan gene. This test can detect approximately 98% of the individuals who are carriers of Canavan disease. If a person tests negative, this means that the chance that he/she is a carrier is not zero, but it has been reduced from 1 in 40 to 1 in 1950. Only a blood sample is needed for DNA testing.

Prenatal diagnosis

For couples who find out they are both carriers and are at a 1 in 4 risk to have a child with Canavan disease, it is possible to find out if a baby will have Canavan disease before birth through prenatal diagnosis. Fetal cells for analysis can be obtained either through amniocentesis or chorionic villus sampling (CVS). The fetal DNA can then be analyzed to determine if the fetus has inherited both parents' mutations. You should speak with your obstetrician and genetic counselor regarding these procedures. Prenatal diagnosis, under these circumstances, is greater than 99% accurate.