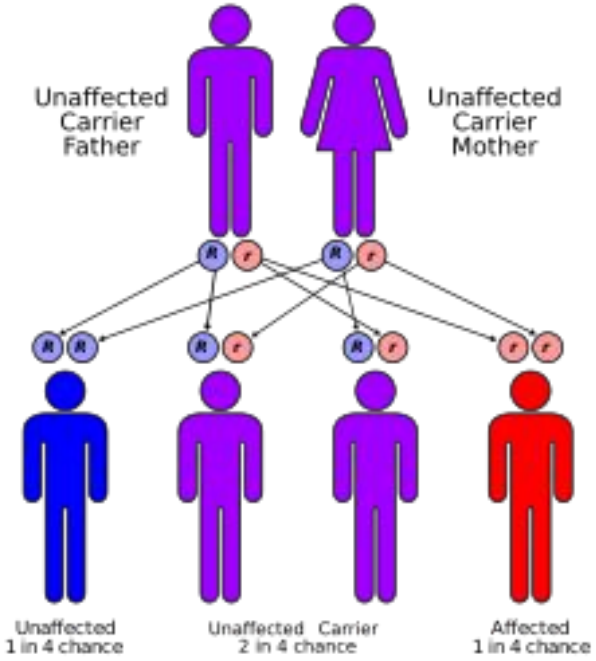
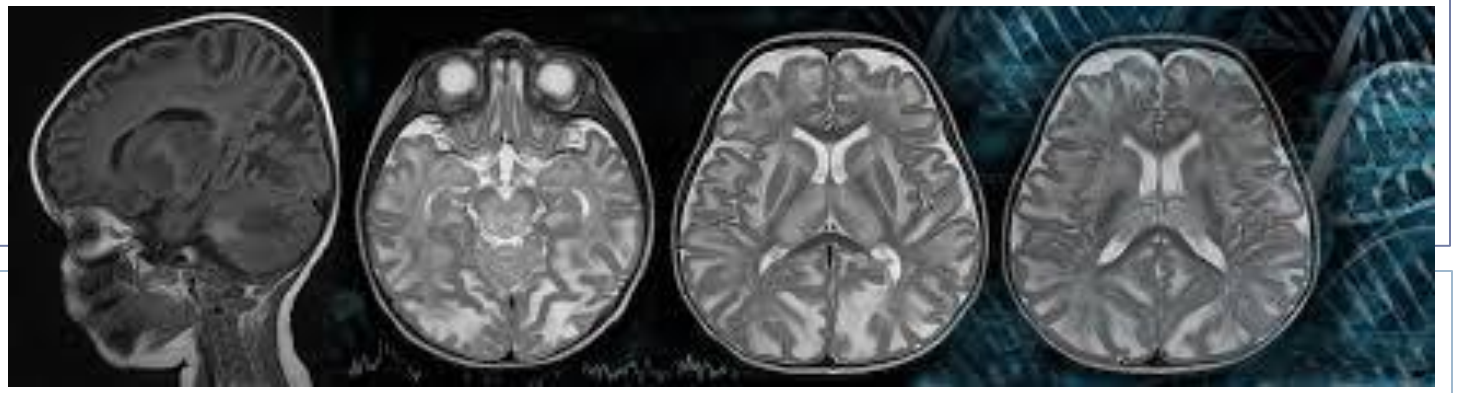
Canavan disease





What is **Canavan disease**

It is an autosomal recessive degenerative disorder that causes progressive damage to nerve cells in the brain, and is one of the most common degenerative cerebral diseases of infancy. It is caused by a deficiency of the enzyme **aminoacylase 2.**

It is characterized by degeneration of myelin in the phospholipid layer insulating the axon of a neuron and is associated with a gene located on human chromosome 17.

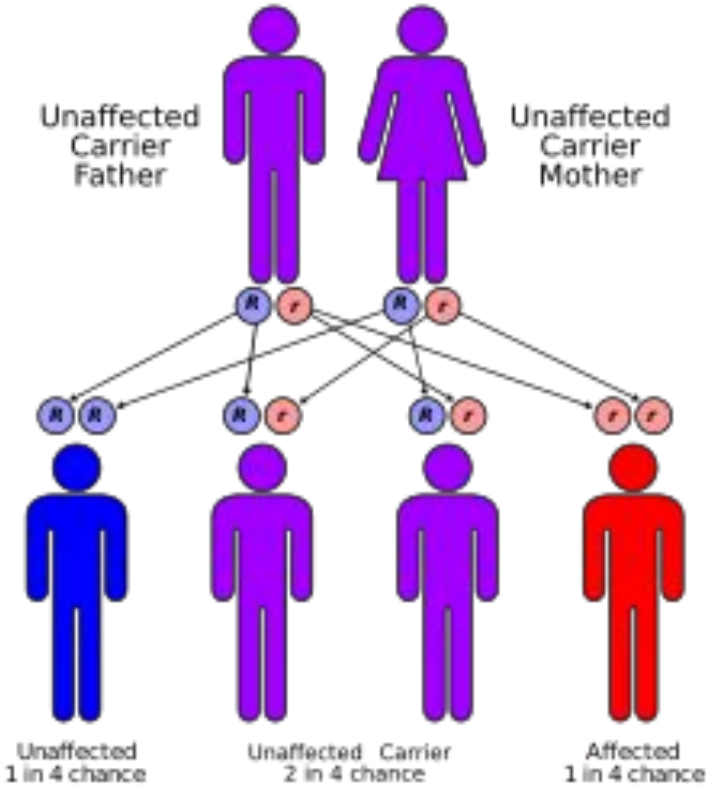
Other names for Canavan disease ;
-ACY2 Deficiency
-ASPA Deficiency

Symptoms

- Symptoms of the most common form of Canavan disease typically appear in early infancy usually between the first three to six months of age.
- Canavan disease then progresses rapidly from that stage, with typical cases involving intellectual disability, loss of previously acquired motor skills, feeding difficulties, abnormal muscle tone and poor head control.
- Paralysis, blindness, or seizures may also occur.

Inheritance

- Canavan disease is inherited in an autosomal recessive fashion. When both parents are carriers, the chance of having an affected child is 25%.



Diagnosis

- The diagnosis of neonatal/infantile Canavan disease relies on demonstration of very high concentration of N-acetylaspartic acid (NAA) in the urine. In mild/juvenile Canavan disease, NAA may only be slightly elevated; thus, the diagnosis relies on molecular genetic testing of *ASPA*, the gene encoding the enzyme aspartoacylase.

Causation of the disease

- Canavan disease is caused by a defective *ASPA* gene which is responsible for the production of the enzyme aspartoacylase.
- Decreased aspartoacylase activity prevents the normal breakdown of *N*-acetyl aspartate, wherein the accumulation of *N*-acetylaspartate, or lack of its further metabolism interferes with growth of the myelin sheath of the nerve fibers of the brain.
- The myelin sheath is the fatty covering that surrounds nerve cells and acts as an insulator, allowing for efficient transmission of nerve impulses

Treatment

- No cure for Canavan disease is known, nor is there a standard course of treatment. Treatment is symptomatic and supportive. Physical therapy may help improve motor skills, and educational programs may help improve communication skills.
- Seizures are treated with antiepileptic drugs and gastrostomy is used to help maintain adequate food intake and hydration when swallowing difficulties exist.

Treatment

- Also, an experimental treatment uses lithium citrate. When a person has Canavan disease, his or her levels of *N*-acetyl aspartate are chronically elevated. The lithium citrate has proven in a rat genetic model of Canavan disease to be able to significantly decrease levels of *N-acetyl aspartate*.

Prognosis

- The more common and serious version of Canavan disease typically results in death or development of life-threatening conditions by the age of ten, though life expectancy is variable, and is highly dependent on specific circumstances. On the other hand, the milder variants of the disorder seem not to have any effect on lifespan.

Prevalence

- Although Canavan disease may occur in any ethnic group, it mostly affects people of Eastern European Jewish ancestry with about one in 40 (2.5%) individuals of Eastern European Jewish ancestry being a carrier.

History

- Canavan disease was first described in 1931 by Myrtelle Canavan. In 1931, she co-wrote a paper discussing the case of a child who had died at 16 months old and whose brain had a spongy white section.
- Canavan was the first to identify this degenerative disorder of the central nervous system, which was later named "Canavan disease"

Research

- Research involving triacetin supplementation has shown promise in a rat model. Triacetin, which can be enzymatically cleaved to form acetate, enters the brain more readily than the negatively charged acetate.
- The defective enzyme in Canavan disease, aspartoacylase, converts *N*-acetylaspartate into aspartate and acetate. Mutations in the gene for aspartoacylase prevent the breakdown of *N*-acetylaspartate, and reduce brain acetate availability during brain development.

Research

- Acetate supplementation using triacetin is meant to provide the missing acetate so brain development can continue normally.
- A team of researchers headed by Paola Leone at the University of Medicine and Dentistry of New Jersey, has tried a procedure involving the insertion of six catheters into the brain that deliver a solution containing 600 to 900 billion engineered virus particles.

Research

- The virus, a modified version of adeno-associated virus, is designed to replace the aspartoacylase enzyme. Children treated with this procedure to date have shown marked improvements, including the growth of myelin, with decreased levels of the *N*-acetyl-aspartate toxin.
- Researchers at the University of Toledo and Atomwise discovered the first drug-like inhibitors of *N*-acetyltransferase.

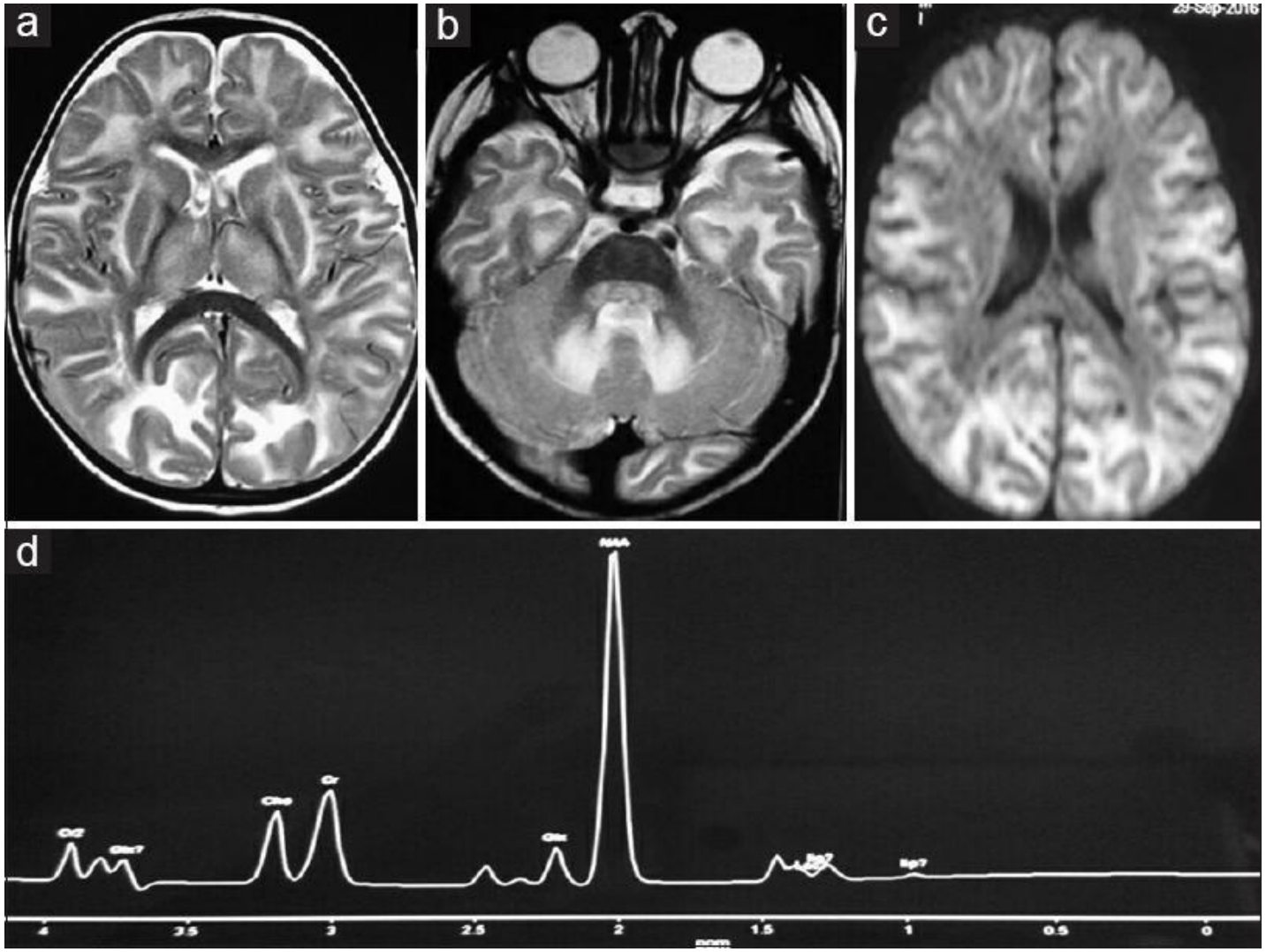
Case Study

- A 15-month old boy, the second child born out of a non-consanguineous marriage, presented with a history of delayed attainment of milestones. At 15 months of age, the child had no head control. There was only social smile, and the child could only speak monosyllables.

Case Study – MRI - MRS

- (MRI) of the brain T2 axial image revealed marked symmetrical hyperintensity of cerebral white matter involving the subcortical arcuate fibres.
- (MRS) from the left parietal white matter showed N-acetyl-aspartate (NAA) peak with normal creatine and choline peaks, consistent with the diagnosis of Canavan disease.

Case Study – MRI - MRS



Images of Kids with canavan disease

Questions

- 1. canavan disease is an autosomal _____ degenerative disorder.
- 2. Canavan disease relies on demonstration of very high concentration of what in the urine ?
- 3. what is the cure for this disease?