CONDITION

Neurodegeneration with brain iron accumulation

A group of inherited neurological conditions that cause iron buildup and progressive problems with movement, thinking, or vision.

WHAT IT IS
Progressive neurological conditions involving abnormal brain iron buildup

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Abnormal movements, muscle stiffness, walking difficulty, vision changes

WHAT CAUSES IT
Mostly inherited gene changes

HOW IT IS DIAGNOSED
Brain MRI and genetic testing

MAIN TREATMENT
Symptom control, rehabilitation, and supportive care

CAN IT BE CURED?
No, no proven cure currently

IS IT AN EMERGENCY?
Sometimes, with choking or breathing difficulty

LONG-TERM OUTLOOK
Progressive course shaped by the specific subtype

Overview

Neurodegeneration with brain iron accumulation, or NBIA, is a group of rare neurological conditions. They cause abnormal iron buildup in deep parts of the brain that help control movement. "Neurodegeneration" means that nerve cells gradually lose function.

NBIA is not one single condition. It includes several genetic subtypes, such as pantothenate kinase-associated neurodegeneration (PKAN), PLA2G6-associated neurodegeneration (PLAN), mitochondrial membrane protein-associated neurodegeneration (MPAN), and beta-propeller protein-associated neurodegeneration (BPAN). Other, less common subtypes are also recognized.

Symptoms and age at onset differ between subtypes. Some begin in infancy or childhood and affect development. Others appear during adolescence or adulthood. Movement problems are

common, but NBIA can also affect vision, speech, swallowing, memory, behavior, and mood.

Iron is normally present in the brain and is needed for healthy cell function. In NBIA, iron collects in particular brain regions, especially the basal ganglia. These structures help coordinate movement. The iron seen on a scan is an important clue, but researchers are still studying how iron buildup relates to nerve cell damage.

Symptoms

NBIA symptoms may develop slowly or become more noticeable over a shorter period. The pattern often gives specialists clues about the subtype.

Movement symptoms can include:

Dystonia may affect the feet, limbs, neck, jaw, tongue, or muscles around the eyes. Jaw and tongue movements can make speaking, eating, or keeping the mouth comfortable more difficult.

Other possible symptoms include reduced or lost speech, swallowing difficulty, and drooling. Some people develop vision loss from damage to the retina or optic nerve. Hearing can be affected in certain subtypes.

Children with early-onset NBIA may have delayed development or lose skills they previously gained. Some subtypes can cause seizures. Changes in learning, memory, attention, behavior, sleep, or mood may occur, especially in forms that begin later.

Not everyone has all of these symptoms. Their severity does not always match the amount of iron visible on a brain scan.

- Dystonia, meaning repeated muscle contractions that cause twisting or abnormal postures
- Spasticity, which is unusual muscle tightness caused by changes in nerve signals
- Parkinsonism, including slowness, stiffness, tremor, or balance problems
- Unsteady walking, frequent falls, or loss of previously learned movement skills
- Chorea, which causes brief, irregular, involuntary movements
- Problems coordinating fine movements, such as writing or using utensils

Causes and risk factors

Most NBIA subtypes are caused by a change in a gene involved in cell metabolism, fat

processing, energy production, or iron handling. The way a condition is inherited depends on the gene.

Many subtypes are autosomal recessive. This means a person usually inherits one altered copy of the gene from each parent. The parents are often healthy carriers. For each pregnancy between two carriers, inheritance follows the same pattern of possible outcomes, regardless of what happened in an earlier pregnancy.

Some forms follow other patterns. BPAN is linked to the X chromosome and often results from a new genetic change that was not inherited from either parent. Neuroferritinopathy is usually autosomal dominant, meaning one altered gene copy can cause the condition.

Having a relative with NBIA may increase the chance of carrying a related gene change. However, a person can be the first in their family to receive the diagnosis. This may happen because relatives are unaffected carriers or because the genetic change occurred for the first time in that person.

Sometimes testing does not find the responsible gene. This does not necessarily rule out NBIA when symptoms and MRI findings strongly support it. Research continues to identify additional genetic causes.

Diagnosis

Diagnosis usually begins with a detailed history and neurological examination. The clinician may assess movement, muscle tone, balance, reflexes, vision, speech, swallowing, development, and thinking skills.

A brain MRI is central to the assessment. MRI uses a strong magnetic field to create detailed images. Special MRI sequences can detect iron in the basal ganglia, particularly the globus pallidus and substantia nigra. The location and appearance of the iron may suggest a particular subtype.

For example, an MRI pattern called the "eye-of-the-tiger sign" is often associated with PKAN. It is not enough by itself to confirm PKAN because similar appearances can occasionally occur in other situations.

Genetic testing may confirm a specific subtype. Testing might begin with a panel covering several NBIA-related genes. Broader tests, such as exome or genome sequencing, may be considered when panel testing does not provide an answer.

Blood tests can help identify or exclude conditions with overlapping features. Tests for iron handling, copper-related proteins, blood cell changes, or metabolic abnormalities may be appropriate, depending on the symptoms and MRI findings. An eye examination, hearing

assessment, nerve tests, or swallowing study may also be used.

Genetic counseling can help you understand what a result means for you and your relatives. A negative or uncertain genetic result may require later review as scientific knowledge improves.

Treatment and management

There is currently no proven cure for most forms of NBIA. Treatment focuses on reducing symptoms, maintaining function, supporting communication and nutrition, and preventing avoidable complications. Care is often coordinated through a neurologist and a team familiar with complex movement conditions.

Medicines may be used for dystonia, spasticity, parkinsonism, seizures, drooling, pain, sleep problems, or mental health symptoms. The choice depends on the subtype and the symptoms causing the greatest difficulty. Benefits and side effects need regular review.

Botulinum toxin injections may help when dystonia or spasticity affects a limited group of muscles. Deep brain stimulation, which uses implanted electrodes to change abnormal movement signals, may reduce severe dystonia in some carefully selected people. It does not stop the underlying condition, and results are not the same for everyone.

Physical therapy can support safe movement, comfort, joint flexibility, strength, and positioning. Occupational therapy may recommend adapted equipment for washing, dressing, writing, school, work, or computer access. Speech and language therapy can support speech, communication devices, and safer swallowing.

Nutrition support may include changes in food texture or methods of eating. If swallowing no longer provides enough nutrition safely, tube feeding may be discussed. This is an individual decision based on nutrition, comfort, safety, and personal goals.

Iron-chelating medicines remove or bind iron. Deferiprone has been studied in NBIA and can reduce brain iron measurements on MRI, but clinical benefit has not been clearly established for everyone. It can also cause serious side effects and requires specialist monitoring. It is not a routine cure or a treatment to start without an experienced medical team.

Researchers are studying treatments aimed at specific genetic and metabolic pathways. Participation in research is optional and does not guarantee personal benefit.

Complications

Movement problems can lead to falls, injuries, reduced mobility, painful muscle spasms, joint

stiffness, and fixed shortening of muscles or tendons. Seating, mobility aids, stretching plans, and treatment of dystonia may reduce some of these effects.

Swallowing problems can cause weight loss, dehydration, choking, or aspiration. Aspiration means food, drink, or saliva enters the airway. This can sometimes lead to a lung infection.

Speech may become difficult to understand, even when the person knows what they want to say. Early access to communication tools can help preserve choice and social connection.

Vision loss, sleep disturbance, constipation, dental problems, and pain can add to daily challenges. Anxiety, depression, impulsive behavior, or other psychiatric symptoms may occur in some subtypes. These symptoms deserve assessment and treatment rather than being assumed to be an unavoidable part of NBIA.

Prevention

Most NBIA subtypes cannot be prevented because they are caused by genetic changes. Diet, exercise, or avoiding iron-rich foods does not prevent inherited NBIA. Restricting dietary iron without medical advice may cause nutritional problems and does not directly remove iron from the brain.

If a specific gene change is known in a family, genetic counseling can explain carrier testing and reproductive options. These may include testing during pregnancy or testing embryos created through in vitro fertilization. The available and acceptable choices are personal and may differ by location.

Some complications can be reduced or identified earlier through regular review of mobility, swallowing, nutrition, breathing, vision, communication, pain, and equipment needs.

Living with it and what to expect

NBIA is usually progressive, meaning symptoms tend to change over months and years. The pace is different across subtypes and between people with the same subtype. Some people have long periods of relative stability. Others experience faster loss of movement or communication skills.

Early-onset forms are more likely to affect development and may become severe during childhood or adolescence. Some adult-onset forms progress more slowly. BPAN often has a childhood phase involving developmental disability, followed by new movement problems such as dystonia and parkinsonism in adolescence or adulthood. These patterns are useful guides, not exact predictions.

Daily life may require increasing support with walking, eating, communication, education, work, or personal care. Many people continue to take part in family life, learning, hobbies, and community activities with suitable adaptations. Communication devices and powered mobility can increase independence even when speech or walking becomes difficult.

Regular follow-up is used to adjust treatment as needs change. It may include neurological review, therapy assessments, nutrition and swallowing checks, vision care, mental health support, and monitoring of medications or implanted devices.

Some severe forms can shorten life, particularly when swallowing or breathing complications develop. Other people live into adulthood or later life. The genetic subtype, age at onset, rate of progression, and complications all help shape the outlook, but they cannot predict an exact course.

When to get medical help

Arrange routine medical review if you notice a gradual change in walking, falls, muscle stiffness, involuntary movements, speech, swallowing, vision, behavior, sleep, or ability to manage daily activities. New pain, weight loss, feeding difficulty, or problems with equipment also deserve timely assessment.

Seek urgent medical help if swallowing suddenly becomes much worse, choking keeps happening, or there are signs of a chest infection after aspiration, such as fever, coughing, breathing discomfort, or unusual sleepiness.

Call emergency services for:

These emergency signs are not unique to NBIA, but they require immediate care.

- Severe difficulty breathing
- Choking with an ongoing blocked airway
- Blue or grey lips or skin
- A seizure lasting longer than expected or repeated seizures without recovery
- Sudden loss of consciousness or inability to wake normally
- A serious injury after a fall

Common questions

Is NBIA caused by having too much iron in my diet or blood?

Usually not. The brain iron buildup in NBIA is linked to altered cell processes caused by a genetic condition. Blood iron may be normal. Cutting iron from your diet does not remove stored brain iron and could lead to deficiency.

Can the iron be removed from the brain?

Iron-chelating treatment can lower some MRI measures of brain iron, but this has not consistently stopped symptoms or reversed existing nerve damage. Such treatment requires specialist oversight because it can have serious side effects.

Is NBIA always inherited from a parent?

No. Many people inherit gene changes from parents who are healthy carriers. Other people have a new genetic change that began with them. The inheritance pattern depends on the subtype.

Does brain iron on an MRI always mean NBIA?

No. Iron normally increases in some brain regions with age, and other neurological conditions can also cause abnormal iron deposits. Specialists interpret the MRI alongside symptoms, examination findings, blood tests, and genetic results.

Will everyone with NBIA lose the ability to walk or talk?

No single outcome applies to everyone. Some forms cause major loss of movement or speech, while others progress more slowly. Therapy, communication technology, mobility equipment, and symptom treatment can support function but do not remove the underlying cause.

Is there a cure for NBIA?

There is no proven cure for most NBIA subtypes. Current care treats symptoms and complications. Research into gene-based, metabolic, and iron-targeting treatments is ongoing.

Sources

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