CONDITION

Lissencephaly

Lissencephaly is a brain development condition in which the brain has fewer folds than expected.

WHAT IT IS
Congenital brain condition with reduced or absent brain folds

BODY SYSTEM
Brain and nervous system

MAIN SYMPTOMS
Seizures, developmental delay, feeding problems, unusual muscle tone

WHAT CAUSES IT
Genetic changes, rarely prenatal infection or reduced blood flow

HOW IT IS DIAGNOSED
Brain MRI, often followed by genetic testing

MAIN TREATMENT
Seizure control, nutrition support, therapies, and coordinated care

CAN IT BE CURED?
No - brain structure cannot be reversed

IS IT AN EMERGENCY?
Sometimes - prolonged seizures or serious breathing difficulty

LONG-TERM OUTLOOK
Lifelong disability, ranging from moderate to profound

Overview

Lissencephaly is a condition that develops before birth. The name means "smooth brain." A typical brain surface has many ridges and grooves. In lissencephaly, some or all of these folds are missing or less developed than expected.

The folds do not form normally because nerve cells do not reach their intended places while the fetal brain is developing. This is called a neuronal migration disorder . The brain's outer layer may also be unusually thick and less organised.

Lissencephaly describes a group of related brain malformations rather than one single pattern. Some brains are almost completely smooth. Others have broad, simplified folds or affected areas alongside more typical brain tissue. Doctors may use terms such as agyria for absent folds and pachygyria for unusually broad folds.

The brain difference itself is present from birth and does not keep spreading. However, its effects may become clearer as a child grows. Lissencephaly often affects development, movement, feeding, and seizure control. The level of support needed can differ greatly depending on the brain areas involved and the underlying cause.

Symptoms

Symptoms often appear during infancy, although a milder form may be recognised later. A baby may have difficulty feeding, poor head control, or delays in reaching early milestones.

Seizures are very common. They may begin in the first months of life and can take several forms. Some children develop infantile spasms , which are brief, repeated movements such as sudden bending, stiffening, or head drops. These often happen in clusters, especially after waking.

Other possible features include:

Some children have facial features, eye problems, muscle disease, or other organ differences linked to a particular genetic syndrome. These are not present in every form of lissencephaly.

Symptoms do not show exactly how much of the brain is affected. MRI findings, development, seizure pattern, and genetic results all help build a fuller picture.

- Moderate to profound developmental and learning disability
- Low muscle tone, stiffness, or a mixture of both
- Difficulty swallowing, coughing during feeds, or slow weight gain
- Limited control of the head, trunk, arms, or legs
- A smaller-than-expected head as the child grows
- Vision or hearing difficulties
- Breathing problems, especially when saliva or food enters the airway

Causes and risk factors

Most lissencephaly is caused by a genetic change that disrupts early brain development. Important genes include PAFAH1B1 , DCX , and TUBA1A , although many others can be involved.

Some genetic changes are inherited from a parent. Others happen for the first time in the egg, sperm, or developing embryo. A new change is called de novo . It is not caused by anything a

parent did during pregnancy.

A deletion of part of chromosome 17, including the PAFAH1B1 gene, causes Miller-Dieker syndrome. This syndrome usually produces severe lissencephaly alongside characteristic facial and other medical features.

Changes in DCX cause an X-linked form. The effect can differ according to a person's sex chromosomes. Some people have classic lissencephaly, while others have bands of misplaced nerve cells beneath the brain's surface, called subcortical band heterotopia .

Another pattern, called cobblestone lissencephaly , happens when nerve cells move beyond the brain's intended outer boundary. It may occur with certain congenital muscular dystrophies and eye abnormalities.

Less commonly, a major interruption of fetal brain development may produce a lissencephaly-like appearance. Possible causes include particular infections during pregnancy or reduced blood flow to the developing brain.

There are usually no lifestyle-related risk factors. A family history of lissencephaly, unexplained developmental disability, recurrent pregnancy loss, or a known related genetic change may affect the chance of recurrence.

Diagnosis

Brain magnetic resonance imaging, or MRI , is the main test used to confirm lissencephaly. MRI creates detailed pictures without using radiation. It shows the number and shape of the brain folds, the thickness of the outer brain layer, and whether other structures are affected.

A doctor may also arrange:

Genetic testing may begin with a chromosome test, a panel of genes, or broader testing such as exome or genome sequencing. Not every person receives a specific genetic diagnosis, even after detailed testing.

Lissencephaly can sometimes be suspected before birth through ultrasound. Fetal MRI may give more detail, but brain folding develops over time, so earlier imaging may not show the full pattern. Results need interpretation by specialists in fetal imaging and brain development.

- An electroencephalogram, or EEG , to record electrical activity during suspected seizures
- Genetic testing to look for a chromosome change or a change in one or more genes
- Swallowing, vision, hearing, movement, and developmental assessments
- Blood or other tests when infection or a metabolic condition is suspected

Treatment and management

There is no treatment that can create the missing brain folds. Care focuses on reducing symptoms, supporting development, and making daily life safer and more comfortable.

Seizure treatment is often a major part of care. The choice of anti-seizure medicine is based on the seizure type, EEG findings, age, and side effects. Infantile spasms need prompt specialist assessment because early treatment can matter. Some difficult-to-control epilepsy may be managed with a medically supervised ketogenic diet or other specialist approaches.

Feeding support may include positioning, modified food textures, or high-calorie nutrition. A swallowing assessment can identify whether food or liquid is entering the airway. If eating by mouth is unsafe or does not provide enough nutrition, tube feeding may be discussed. A gastrostomy tube delivers food directly into the stomach through the abdomen.

Physical therapy can help with posture, movement, flexibility, and safe handling. Occupational therapy supports daily activities and equipment needs. Speech and language therapy may address swallowing and communication, including gestures, picture systems, switches, or eye-gaze devices.

Management may also include:

Care is usually coordinated across neurology, rehabilitation, nutrition, genetics, primary care, and community services. Families may also need respite care, home nursing, school support, and help obtaining suitable equipment.

- Medicines, stretching, splints, or equipment for muscle stiffness
- Wheelchairs, supportive seating, standing frames, and sleep positioning
- Respiratory care for weak cough, mucus, or repeated chest infections
- Treatment of reflux, constipation, sleep problems, pain, and dental needs
- Vision and hearing support
- Palliative care to improve comfort and quality of life at any stage

Complications

Epilepsy can be difficult to control, and some people have several seizure types. Long or repeated seizures can require emergency treatment.

Swallowing problems can allow saliva, food, or liquid into the lungs. This is called aspiration . It can lead to chest infections or pneumonia. Poor feeding may also cause dehydration, slow

growth, or nutritional deficiencies.

Limited movement and abnormal muscle tone can contribute to stiff joints, hip displacement, spinal curvature, fragile bones, and discomfort. Regular positioning and movement plans can help reduce these problems, although they cannot always prevent them.

Other possible complications include reflux, constipation, sleep disturbance, reduced ability to clear mucus, and breathing pauses. A person who cannot communicate pain through speech may show it through sleep changes, increased muscle tightness, crying, withdrawal, or altered behaviour.

Prevention

Genetic forms of lissencephaly usually cannot be prevented. They arise during very early brain development, often because of a new genetic change that could not have been predicted.

If a causative genetic change is found, genetic counselling can explain how it occurred and the chance of it happening in another pregnancy. That chance may be low after some new changes, but it is not always zero because a parent can occasionally carry the change in only some egg or sperm cells.

For families with a known inherited change, options may include testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices rather than required steps.

Routine measures to reduce infection during pregnancy can lower the risk of some fetal infections, but they cannot prevent most cases of lissencephaly.

Living with it and what to expect

Lissencephaly is lifelong. The underlying brain structure does not return to normal, but it also does not progressively disappear. Developmental skills may grow slowly over months and years, remain limited, or sometimes be lost after severe seizures or illness.

Many children need lifelong help with mobility, communication, feeding, and personal care. Some learn to sit, move with assistance, recognise familiar people, communicate preferences, or use adapted devices. People with milder brain changes may gain a wider range of skills. MRI findings alone cannot predict every ability.

Seizures may change with age. They can become easier or harder to control, and new seizure types may appear. Keeping an up-to-date seizure plan helps family members, schools, and

support workers respond consistently.

Health needs often change as the body grows. Equipment, feeding plans, medication, seating, and communication systems need periodic review. Routine follow-up commonly focuses on seizures, nutrition, breathing, sleep, comfort, joints, spine, vision, hearing, and caregiver support.

Life expectancy is difficult to predict. People with milder forms may live into adulthood. Severe epilepsy, aspiration, repeated respiratory infections, and profound movement impairment can shorten life. The healthcare team may be able to discuss outlook more meaningfully after considering the individual MRI pattern, genetic cause, feeding safety, breathing, and seizure control.

When to get medical help

Arrange routine follow-up if seizures, feeding, sleep, movement, constipation, equipment needs, or comfort have gradually changed. A review is also appropriate if a child has stopped making expected progress or appears to have lost a skill.

Seek prompt medical advice for:

Call emergency services if a seizure lasts five minutes or longer, unless the person's emergency plan gives a different threshold. Emergency help is also needed for repeated seizures without recovery, serious breathing difficulty, blue or grey lips, severe choking, or unusual unresponsiveness after a seizure.

If rescue seizure medicine has been prescribed, follow the person's written seizure plan. Do not place anything in their mouth or try to hold them down during a seizure.

- New repeated jerks, head drops, stiffening, or bending spells
- More frequent seizures or a clear change in seizure pattern
- Regular coughing, choking, or wet-sounding breathing during meals
- Poor fluid intake, fewer wet diapers, or unexplained weight loss
- Increasing stiffness, pain, hip asymmetry, or skin pressure areas
- Fever or cough in someone at risk of aspiration

Common questions

Is lissencephaly fatal?

Lissencephaly is not always fatal, but severe forms can shorten life. The greatest risks often come from hard-to-control epilepsy, aspiration, and respiratory infections. Some people, particularly those with milder forms, live into adulthood.

Can a child with lissencephaly walk or talk?

Some children develop supported movement, a few spoken words, or another reliable way to communicate. Others do not walk or use speech and need full physical assistance. Communication can still happen through facial expression, sounds, gestures, pictures, switches, or eye-gaze technology.

Is lissencephaly inherited?

It can be. Some genetic changes pass through families, while many occur for the first time in the affected child. Genetic testing and counselling can provide more specific information about recurrence in a family.

Does "smooth brain" mean the brain has no folds at all?

Not always. Complete absence of folds is called agyria, but many people have a mixture of absent and unusually broad folds. The location and severity of these changes differ among forms of lissencephaly.

Can lissencephaly be diagnosed before birth?

Sometimes. Later pregnancy ultrasound or fetal MRI may show reduced brain folding. Earlier scans may not detect it because folds are still developing. Prenatal imaging may suggest the condition, with confirmation through specialist imaging and sometimes genetic testing.

Does lissencephaly get worse over time?

The brain malformation itself is not progressive. Its effects can change as a person grows, however. Seizures, muscle stiffness, feeding safety, breathing, and joint problems may improve, remain stable, or become more difficult.

Sources

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