# Structural Differences of the Brain

Severe brain malformations are rare among individuals with 22q differences, but some of these conditions are associated with seizures and developmental delays. This sheet provides general information on the most common brain malformations in children with 22q11.2 deletion syndrome (22q11.2DS).

## Cortical Dysplasia (Focal Cortical Dysplasia, FCD)

- **Some brain cells are abnormal** in their structure, appearance, location, or size. The brain developed differently while the baby was in the womb.
- The area affected is the **cerebral cortex** (outermost layer of the brain which controls movements, thoughts, emotions, problem solving etc.)
- The causes may include genetic changes.
- Symptoms include **seizures and epilepsy**, difficulty learning, muscle weakness on one side of the body
- The goal of treatment for cortical dysplasia is **controlling the seizures**.
  - Medication may not eliminate the seizures completely.
  - Surgery that remove affected tissues may help, but surgeons may need to remove some healthy tissues, which lead to other problems.

## Heterotopia

- **Some brain cells are in the wrong place.** They did not migrate to the correct area of the brain while the baby was developing in the womb.
- One example is **Periventricular Nodular Heterotopia** (**PVNH**)
  - Abnormal clumping of brain cells around the fluid chambers in the brain
  - The causes may include genetic changes
  - Common symptoms include seizures, intellectual disability (variable), difficulty with reading and spelling, and movement problems
- Treatment involves **controlling the seizures** using medications. If that does not work, surgeries, special diets, or nerve simulation may help.

### Brain malformations and 22q differences

- Brain malformations are rare in people with 22q11.2DS but occur at a higher rate than in the general population.
- There are many types of brain malformations. This info sheet covers the less rare ones people with 22q11.2DS.
- Chiari malformation, craniosynostosis, microcephaly, and macrocephaly have been reported in people with 22q11.2DupS.

### Meaning of the terms

**Cortical Dysplasia**

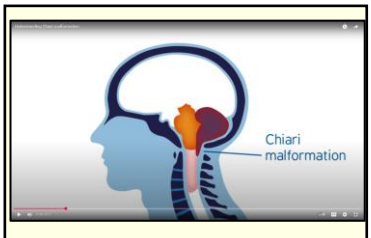
- **cortical** = relating to the outer layer
- **dysplasia** = abnormal

**Periventricular Nodular Heterotopia**

- **periventricular** = around the ventricles
- **nodular** = clumps
- **heterotropia** = out of place

## Chiari Malformation

- **The lower parts of the brain do not fit in the skull, but push down at the bottom opening of the skull towards the spine.**
- The **cerebellum** and adjacent spinal cord segment, which control movement, posture, balance, speech, and coordination, are affected.
- Normally, the brain is surrounded by cerebrospinal fluid (CSF) that protects it, provides it with nutrients, and removes its wastes. This fluid flows from the top to bottom. In Chiari malformation, the brain presses on the base of the skull, blocking the flow of the fluid, causing the fluid to build up in the brain and **increasing the pressure within the skull**.
- Chiari malformation can range from mild to life-threatening .
- Cause: The skull is too small, or something is pushing on the brain.
- Common symptoms: painful headaches, loss of balance, dizziness, movement problems, muscle weakness, vision and hearing problems etc., but some people may not have symptoms.
- Symptom relief for mild cases involve the use of pain medications, physical therapy, hearing aid, eyeglasses, and limiting physical activities.
- In severe cases, healthcare providers may recommend **surgery to remove a small part of the skull** to reduce the pressure on the brain.




Click on the image to watch the Understanding Chiari Malformation video from the Brain and Spine Foundation (UK)

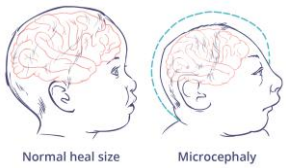
# Structural Differences of the Brain (continued)

## Polymicrogyria (PMG)

- **The brain has too many folds, and the folds are too small**. The affected area and other areas of the brain do not function properly.
- PMG can affect part or all of the brain with different levels of severity.
- The causes include genetic changes (including 22q11.2DS) and virus infections by Cytomegalovirus (CMV) or Zika virus before birth.
- Seizures affect >90% people with PMG. Other symptoms include swallowing and speech difficulties, developmental delays, etc.
- PMG may not be diagnosed unless the patient has a significant event that needs imaging, and that the MRI is read by a specialized radiologist.
- PMG cannot be cured, but doctors can help the patient **manage the seizures using medications**. The patient may also find **medical devices, communicative devices, and physical therapies** helpful.

## Microcephaly

- **The head and brain are smaller than normal.**
- The brain stopped growing before or after birth.
- Microcephaly can be a part of other disorders.
- Possible causes include:
  - Genetic conditions
  - Infections during pregnancy, e.g. toxoplasmosis, cytomegalovirus, German measles (rubella), chicken pox (varicella), and Zika virus
  - Problems during pregnancy/birth
  - **Craniosynostosis** – the bones of the skull fused before the brain finished growing.




- Children with microcephaly may have seizures, developmental delays, intellectual disabilities, and other problems related to brain and nerves.
- If craniosynostosis is the cause of microcephaly, surgery (or multiple surgeries) may be able to correct the problem. Otherwise there is no treatment to enlarge a child's head. Instead, the goal is to use speech, physical, and occupational therapies to maximize the child's abilities.

## Checking the brain and the bones

MRI lets healthcare providers see the inside of the brain, while EEG lets them check brain activities. CT scan and X-ray allows them to check the bones (skull, spinal column). These techniques help with the diagnosis of structural differences of the brain.

Fetal ultrasound during the 2nd (or early 3rd) trimester in pregnancy lets healthcare providers check the head size. After the baby is born, the healthcare provider can use a tape measure.

## Macrocephaly

- **The head is larger** than that of people of the same age
- A large head size may be normal (a family trait) or may point to serious problems (large brain; developmental delay; bleeding, fluid, or tumor in the brain)
- Seek medical help if the person with macrocephaly also has:
  - A bulging area on the head
  - Loss of interest in eating
  - Vomiting
  - Unusual eye movements
  - Unusual sleepiness
  - Extra irritability
- The treatment depends on the cause.

## Resources

- Cortical Dysplasia – Cleveland Clinic
- Cortical Dysplasia in Children – Cincinnati Children's Hospital
- Periventricular Nodular Heterotopia (PVNH) – Epilepsy Foundation
- Periventricular heterotopia – MedlinePlus
- Chiari malformation – Cleveland Clinic
- Chiari malformation – National Health Services, UK
- Cerebral cortex and cerebellum – Cleveland Clinic
- Understanding Chiari Malformation (video) – Brain and Spine Foundation (UK)
- MRI | EEG | CT | X-ray – Cleveland Clinic
- What is Polymicrogyria – PMGawareness.org
- Polymicrogyria (PMG) – Epilepsy Foundation
- Macrocephaly – Cleveland Clinic
- Microcephaly – Mayo Clinic
- Microcephaly – Johns Hopkins Medicine
- Fetal ultrasound – Johns Hopkins Medicine
- Craniosynostosis – Johns Hopkins Medicine
- Updated clinical practice recommendations for managing [**children**][**adults**] with 22q11.2 deletion syndrome – 2023
- Neurologic challenges in 22q11.2 deletion syndrome – 2018
- Hemizygous mutations in SNAP29 unmask autosomal recessive conditions and contribute to atypical findings in patients with 22q11.2DS – 2013
- Cross-sectional and longitudinal findings in patients with proximal 22q11.2 duplication: A retrospective chart study – 2022
- Atypical nested 22q11.2 duplications between LCR22B and LCR22D are associated with neurodevelopmental phenotypes including autism spectrum disorder with incomplete penetrance – 2019
- ❖ Microcephaly image – Dept of Health and Aged Care, Australia

International 22q11.2 Foundation

The mission of the International 22q11.2 Foundation is to improve the quality of life for individuals affected by chromosome 22q11.2 differences through family and professional partnerships.
This information is brought to you by the Foundation for educational purposes only. It is not intended to be taken as medical advice. If you have concerns, please talk to your healthcare provider.

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