Disorders of cortical formation: Magnetic Resonance Imaging (MRI)

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Authors: P. M. Hernandez Guilabert¹, M. P. Vallejo Desviat¹, M. I. Garcia Hidalgo², R. Moreno de la Presa², R. Morcillo Carratalá²; ¹Madrid/ES, ²Toledo/ES
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Learning objectives

The aim of this exhibit is to review the embryologic stages of the cerebral cortex and factors that may disturb his right development.

We also illustrate the classification of disorders of cortical formation resulting of that factors, describing their magnetic resonance imaging (MRI) findings.
Background

Some of the neurons that form the cerebral cortex are generated in the walls of the developing lateral ventricles, while others are generated in the walls of the developing third ventricle.

During the 7th week of gestation a proliferation of young neurons occurs in the subependymal layers of the walls of the lateral ventricles. This area of proliferation, known as the germinal matrix, is the region in which the stem cells undergo mitosis to produce the neurons and glia that will form the mature brain. After mitosis and during the 8th week of gestation, some of the newly generated cells will remain in the germinal zone while others will migrate from the germinal zone toward their eventual destinations to form the cerebral cortex. After their arrival in the cortex, neurons become arranged in discrete lamina and establish synaptic contacts with local and distant neurons in a process known as cortical organization.

These 3 major stages of cortical development are not temporally separate: proliferation (2nd - 4th months of gestation) continues after migration begins and migration (3rd - 5th months of gestation) continues as organization (22th weeks of gestation - 2 years of age) commences.

Germinal matrix usually regresses and disappears at 32-34 week of gestation.

Accordingly, cortical formation is divided into 3 stages (proliferation, migration, and organization) and any abnormality that disturbs one or more of these stages can result in a cortical malformation.
Findings and procedure details

Disorders of cortical formation are a heterogeneous group characterized by an abnormal structure of the cerebral cortex caused by interruption of his normal development sequence.

These abnormalities may include chromosomal mutations, destructive events, such as infections or ischemia that damage the germinal matrix, or the presence of exogenous toxins (such as drugs or alcohol from ingestion of toxic substances) or endogenous toxics from metabolic disorders.

The clinical manifestations of disorders of cortical formation vary considerably and they depend on the stage of arrest, but they mostly cause treatment-resistant epilepsy and development delay.

Magnetic resonance imaging (MRI) is currently the better imaging technique for the diagnosis of these processes, and it is even possible to perform prenatal diagnosis.

Barkovich et al in 1996 proposed a classification scheme based on the first step at which the development process was disturbed:

- **Proliferation**: decreased (microlissencephaly), increased (hemimegalencephaly), abnormal (focal cortical dysplasia)

- **Migration**: undermigration (complete lissencephaly), overmigration (congenital muscular dystrophy) or ectopic migration (heterotopia).

- **Organization**: derranged organization (polymicrogyria or squizencephaly).

**MICROLISSENCEPHALY**

This disorder results from decreased cell production or increased apoptosis in the germinal zone of the cerebral cortex.

It is characterized by congenital microcephaly (head circumference <3SD below normal for that age) and it is classified into microlissencephaly (severe form) and microcephaly with a simplified gyral pattern (mild form):

- Microlissencephaly is characterized by abnormal sulcation, with smooth cortical surface and with a thickened cortex (>3mm). It is usually associated with other congenital anomalies.
- Microcephaly with a simplified gyral pattern patients present too few sulci and normal cortical thickness (3mm).

HEMIMEGALENCEPHALY

Enlarged and dysplastic hamartomatous overgrowth of part or all of the cerebral hemisphere, with cerebral cortex normal or dysplastic (heterotopia, PMG or lissencephaly). Lateral ventricles are enlarged and frontal horns present a characteristic shape: straights and pointed anteriorly and superiorly.

It may be associated with syndromes such as epidermal nevuis syndrome, NFM type I, Klippel-Trenau-nay syndrome and tuberous sclerosis.

FCD (Focal Cortical Dysplasia)

Heterogeneous group of lesions characterized by the presence of abnormal neurons and glial cells within a localized region of the cerebral cortex; it includes a spectrum of malformations ranging from mild to very severe forms.

It appears as a localized area of cortical thickening with any indistinct gray-white matter junction. There is also macrogryria and abnormally deep sulci. In FCD with balloon cells or Taylor type we can also found a subcortical linear or curvilinear focus of abnormal signal (low signal intensity on T1-weighted images and high on T2), which extends from the gray-white matter junction to the superolateral margin of the lateral ventricle.

COMPLETE or CLASSIC LISSENCEPHALY (Type 1)

Complete form is characterized by smooth brain surface with complete agyria, while patients with incomplete lissencephaly present parieto-occipital agyria with frontotemporal pachygyria. They are also several subtypes based on the underlying genetic abnormality.

It results from arrest of the migration process so the cortex is thick because it encompasses radial columns of the arrested cells. The subcortical white matter is thin, with a lack of the normal gray-white matter interdigitation and there is a circumferential band of high signal intensity on T2-weighted images, most prominent in the parieto-occipital cortex, corresponding to a sparse cell zone with increased water content.

COBBLESTONE LISSENCEPHALY (Type II) or CONGENITAL MUSCLE DISTROPHY

It results from overmigration of the neuroblasts and glial cells beyond the external glial limitations into the subarachnoid space. It is characterized by nodular brain surface, ocular anomalies and congenital muscular disorders.
It includes a spectrum of anomalies: Walker-Warburg syndrome, Muscle-eye-brain disease and Fukuyama congenital muscular distrophy, being this last one the mildest form and the most common.

**HETEROTOPIA**

Collections of normal neurons located in abnormal locations, anywhere from the subependymal region to the cerebral cortex, due to arrest of neuroblast migration.

- **Periventricular or subependymal heterotopias**: they are located in close proximity to the ventricular wall, mostly in the trigone and occipital horns of the lateral ventricles. They appear as round or oval nodules isointense to the normal gray matter on all sequences and do not enhance after contrast injection. Mild ventricular dilatation may be seen.

- **Subcortical heterotopias**: located within the subcortical or deep white matter, always contiguous to the overlying cortex or the underlying ventricular system. They can be nodular, curvilinear (may contain blood vessels and cerebrospinal fluid (CSF)) and mixed. Affected hemisphere may decrease in size and the overlying cortex is thin with shallow sulci.

- **Band or laminar heterotopia**: It is a rare anomaly seen predominantly in females and may be familiar, with X-linked dominant inheritance. These patients present a smooth layer of the gray matter that often follows the curvature of the overlying cortex (“3-layer-cake” sign). The cortex may be normal or pachygyric.

Heterotopias may be associated with pachygyria, agenesis of corpus callosum, Chiari II malformation, arachnoid cyst, schizencephaly and cephalocele.

**POLYMICROGYRIA (PMG)**

It is characterized by small prominent convolutions separated by shallow sulci with an irregular appearance of the cortical surface and cortical white matter, commonly located in regions adjacent to the Sylvian fissures. Cortex is also slightly thickened (5 - 7mm) with an abnormal increased T2 signal intensity of the underlying white matter. Anomalous vein is commonly seen in the region of PMG.

**SQUIZENCEPHALY**

It is characterized by gray-matter lined clefts that extend through the entire hemisphere, from the ependymal lining of the lateral ventricles to the subarachnoid space. The wall of the cleft is lined with dysmorphic gray-matter and they are filled with CSF.
The anomaly may be closed-lip type (type I) in which the walls of the cleft appose one another directly, obliterating the CSF space; and the open-lip type (type II) in which the lips are separated and CSF fill all the way of the cleft.

It may be associated with septo-optic dysplasia, optic nerve hypoplasia, absence of septum pellucidum or other types of cortical malformations.
Fig. 1: Disorders of cortical formation according to stages

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Fig. 2: Coronal FLAIR weighted images of right hemispheric hemimegalencephaly

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Fig. 3: Left temporo-occipital focal cortical dysplasia (FCD) with cortical thickened, subcortical hyperdense band on T2 SE weighted images and indistinct gray-white matter junction. Enlarged occipital horn of lateral ventricle associated.

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**Fig. 4:** Walker-Warburg syndrome (WWS), the most severe form of lissencephaly type II. T2 SE and FLAIR weighted images show cortical thickened with agyria and circunferencial subcortical band of high signal on T2. Cerebellar atrophy associated.

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**Fig. 5:** Periventricular heterotopia located in the occipital horn of left lateral ventricle.

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Fig. 6: Left frontal nodular heterotopia.

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Fig. 7: Coronal IR weighted images of band heterotopia.

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**Fig. 8:** Polymicrogyria associated with left temporal and subcortical heterotopia. Axial FLAIR and coronal T1 weighted images.

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Fig. 9: Left unilateral lissencephaly open-lipe type (type II) with cortical dysplasia associated.

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Fig. 10: Sagital T1 weighted images show frontal lissencephaly close-lip type (type I).

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Fig. 11: Incidental founding in 90 years-old asymptomatic woman. Axial CT shows lissencephaly close-lip type.

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Conclusion

MR imaging is essential for the right diagnosis of these unusual disorders of cortical formation, demonstrating the extent and suggesting the cause of the anomaly for an optimal treatment of our patient.
References


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