CURSO NACIONAL DE NEURORRADIOLOGÍA

S.E.N.R Sociedad Española de Neurorradiología

Radiología en la Patología Neurodegenerativa, Desmielinizante e Infecciosa del SNC

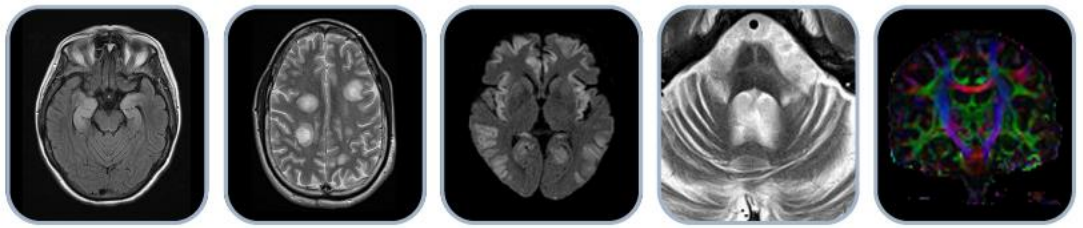
15 y 16 de febrero de 2024 | MADRID

Sede: CINESA. C/ Fuencarral 136

MALFORMACIONES DEL DESARROLLO CORTICAL (RADIOLOGÍA)

Sofía Glez. Ortiz

Hospital Clinic. Barcelona



MALFORMACIONES DEL DESARROLLO CORTICAL:

1. INTRODUCCIÓN

2. DIAGNÓSTICO POR IMAGEN: TÉCNICAS/PROTOCOLOS

3. HALLAZGOS DE NEUROIMAGEN

4. PERSPECTIVAS DE FUTURO

INTRODUCCIÓN

Extenso y heterogéneo grupo patológico > por alteración en el desarrollo normal SNC > consecuencia de alteraciones genéticas, infecciosas, vasculares o metabólicas

Amplia gama de fenotipos anatómicos y funcionales

Acuden a NRX:

Edad infantil :

- **Retraso del desarrollo**
- **Déficit motor/paresias**
- **Epilepsia**

Edad adulta:

- **Epilepsia**

INTRODUCCIÓN

Barkovich et al. 1996

> Introducción del término

> Clasificación inicial: basada en la fases del desarrollo cortical:

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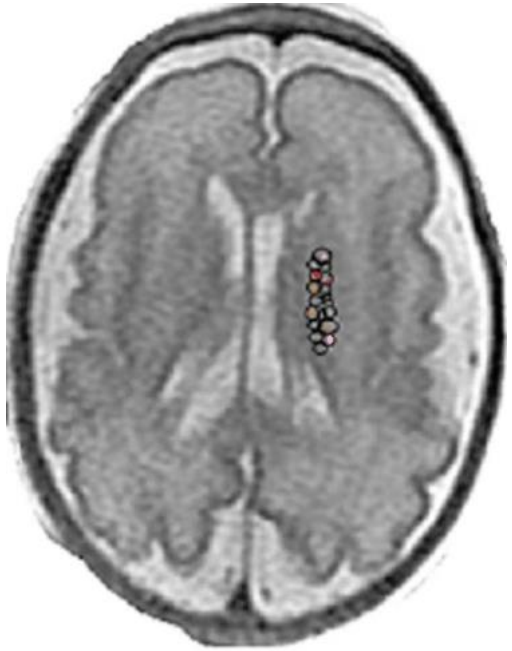

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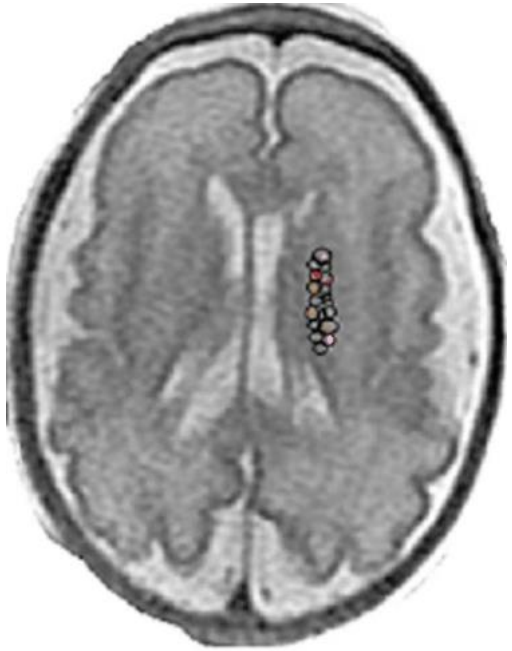

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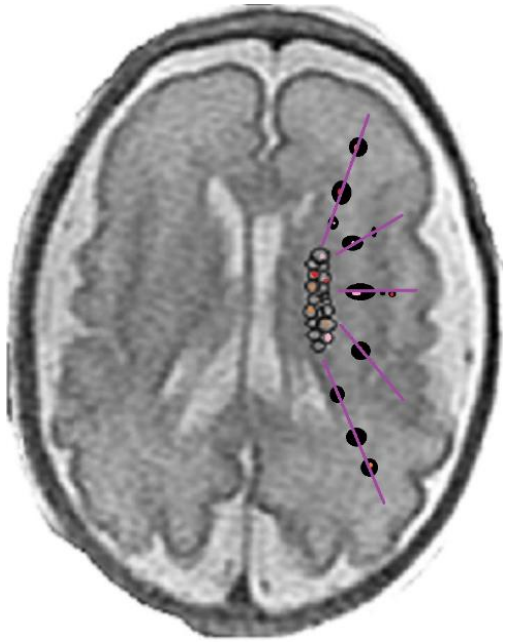

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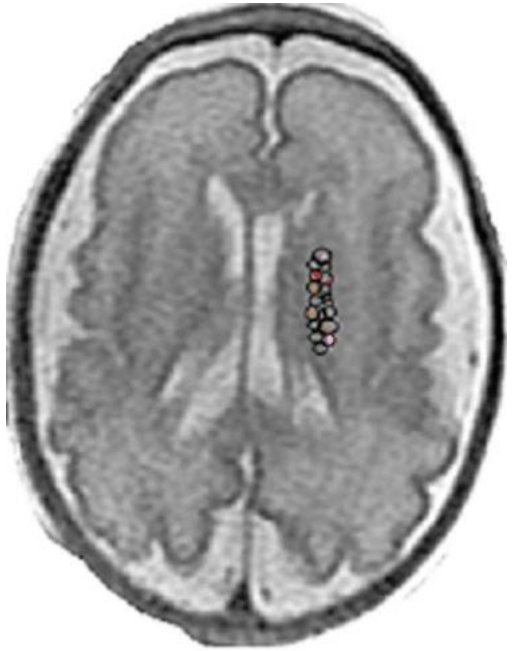

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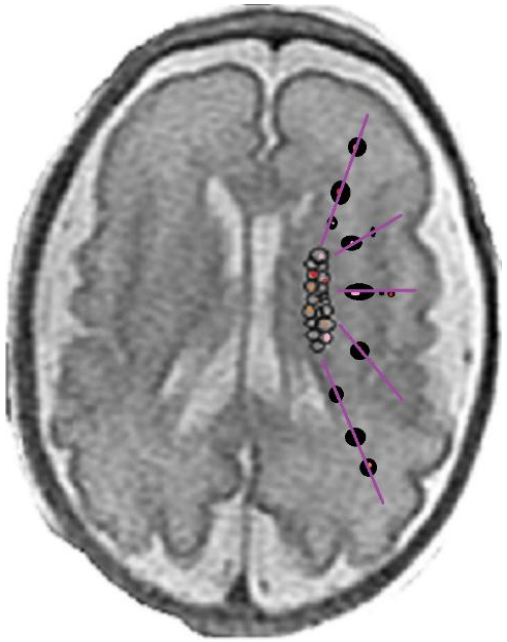
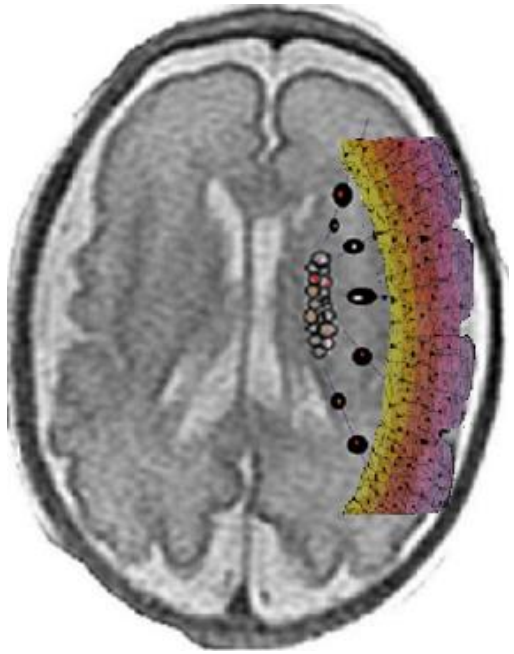
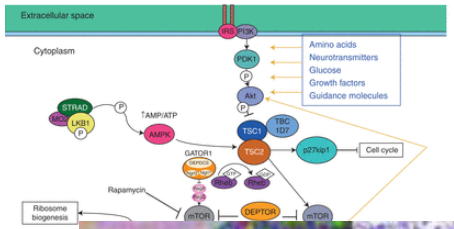


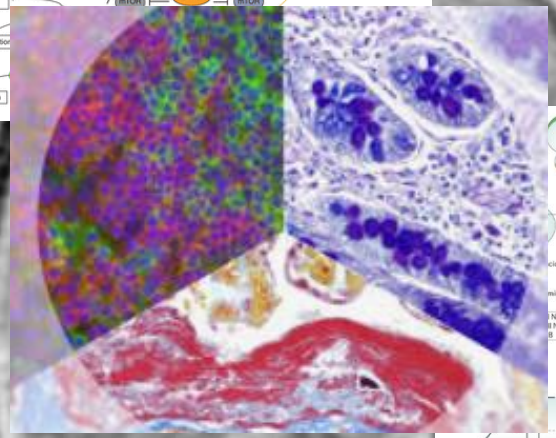
ORGANIZACIÓN

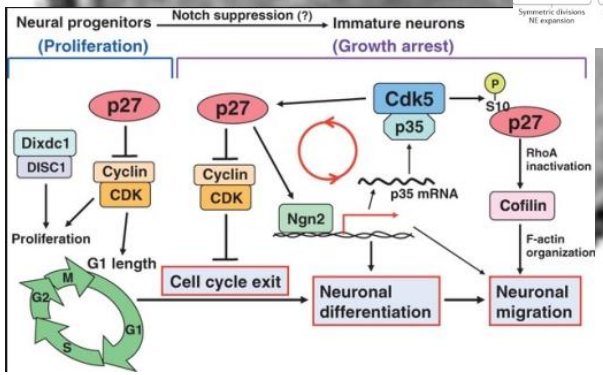


INTRODUCCIÓN

GRUPO I







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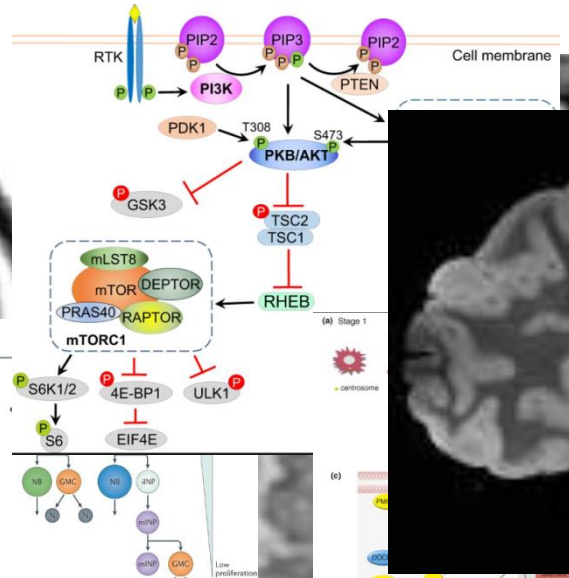
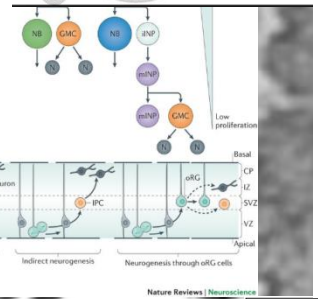
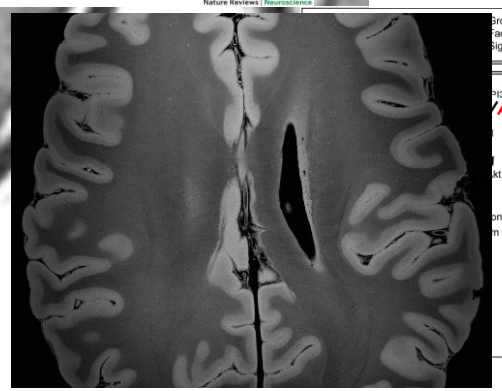
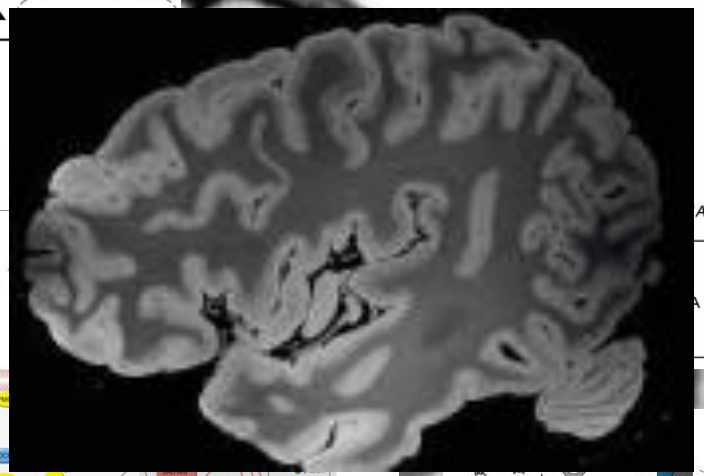
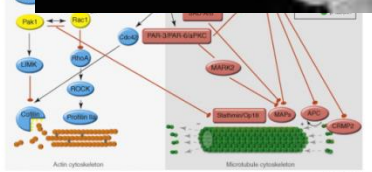
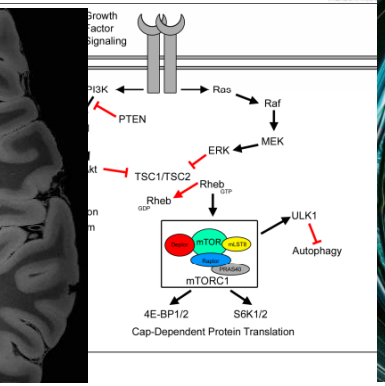




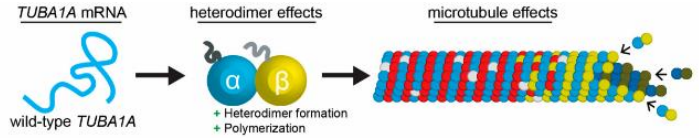


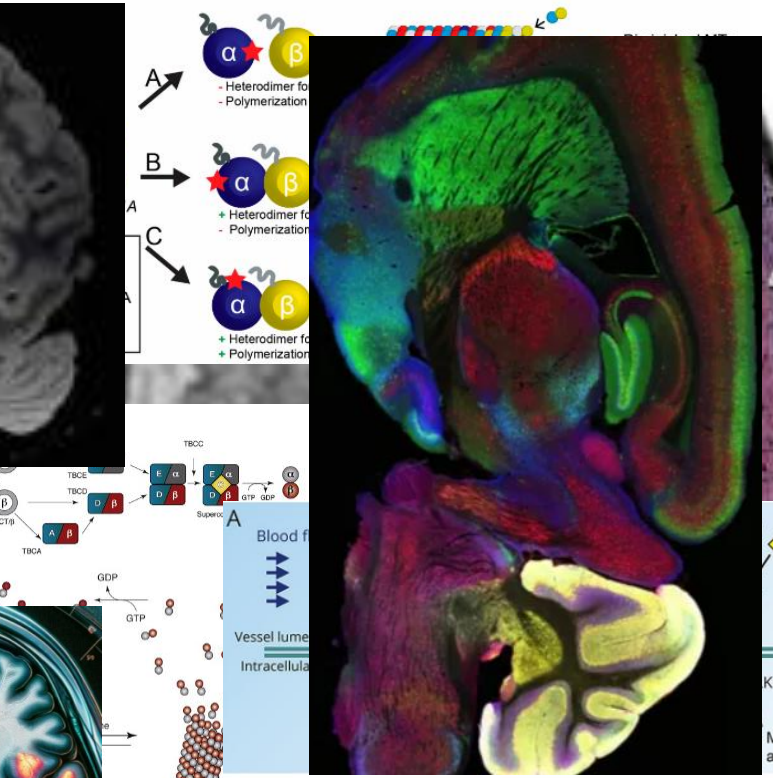


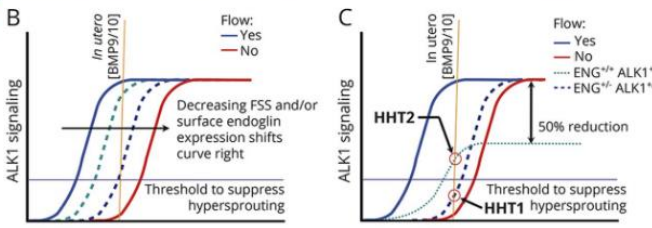




GRUPO III







INTRODUCCIÓN

1996

Review article

A Classification Scheme for Malformations of Cortical Development

By A. J. Barkovich[1], R. I. Kuzniecky[2], W. B. Dobyns[3], G. D. Jackson[4], L. E. Becker[5] and P. Evrard[6]

[1]Department of Radiology, University of California San Francisco, San Francisco, CA, USA, [2]Department of Neurology, UAB, UAB Epilepsy Center, Birmingham, Alabama, USA, [3]Department of Child Neurology, University of Minnesota, Medical Center, Minneapolis, Minnesota, USA, [4]Institute of Child Health, University of London, London, UK, [5]Department of Pathology, The Hospital for Sick Children, Toronto, Ontario, USA, [6]Pediatric Neurology Service, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

Abstract

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Received October 31, 1995; revised, accepted January 8, 1996

Neuropediatrics 27 (1996) 59–63

Introduction

Malformations of the cerebral cortex are a class of brain anomalies that are being recognized more and more frequently as a cause of epilepsy and neurodevelopmental disorders (2, 3, 4, 5, 6, 7, 8, 11, 19, 20, 23, 34, 37, 42, 43, 44, 51). However, the nomenclature for these disorders is not uniform, and no standard system for their classification has been established. As a result, confusion exists regarding proper nomenclature and different names are sometimes used for malformations that appear identical on clinical, radiologic,

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Theoretical basis for the classification

The classification (Table 1) is based on three
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assumptions are justified by the importance of the concept of the framework. We have limited our major categories to proliferation, migration, and organization although we recognize that other processes, such as apoptosis, may become important in the future as our knowledge of brain development progresses. We have also made relatively major assumptions about the pathogeneses of specific disorders in order to place them within the framework that we have created. We wish to make it clear that the framework is, in effect, separate from the disorders. Our philosophy is that the specific placement of the disorders is a flexible entity; it will evolve as our knowledge of genetics and embryology evolves. We envision our classification framework as a challenge to more specifically define developmental events in order to classify specific malformations more rigorously and definitively.

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2001

Neurology®

Classification system for malformations of cortical development: Update 2001

A. J. Barkovich, R. I. Kuzniecky, G. D. Jackson, et al.
Neurology 2001;57;2168-2178
DOI 10.1212/WNL.57.12.2168

This information is current as of December 26, 2001

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://www.neurology.org/content/57/12/2168.full.html

Views & Reviews

Classification system for malformations of cortical development

Update 2001

A.J. Barkovich, MD; R.I. Kuzniecky, MD; G.D. Jackson, MD; R. Guerrini, MD; and W.B. Dobyns, MD

AMERICAN ACADEMY OF NEUROLOGY®

INTRODUCCIÓN

2005

Review article

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Neurolog

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Neurology 2001;57;2168-217
DOI 10.1212/WNL.57.12.216

Views & Reviews

Classification system for malfor
cortical development
Update 2001

A.J. Barkovich, MD; R.I. Kuzniecky, MD; G.D. Jackson, MD; R. Guerrini, MD

Article abstract—The many recent discoveries concerning the molecular biologic bas
development and the discovery of new such malformations have rendered previous classi
classification of malformations of cortical development is proposed, based on the stage of
neuronal migration, cortical organization) at which cortical development was first affec
created based on known developmental steps, known pathologic features, known genet
necessary, neuroimaging features. In many cases, the precise developmental and gen
classification was made based on known relationships among the genetics, pathologic fe
tures. A major change since the prior classification has been the elimination of the s
focal/multifocal malformations, based on the recognition that the processes involved in the
tally different; the difference may merely reflect mosaicism, X inactivation, the influence
mal imaging. Another change is the listing of fewer specific disorders to reduce the need for
in other smaller tables that list specific malformations and malformation syndromes. Thi
practicing physician in that its framework allows a better conceptual understanding of the
of neuroimaging characteristics allows it to be applied to all patients without necessitating
based classifications.

NEUROLOGY 2001;57:2168–2178

Views & Reviews

HIGH YIELD CME

A developmental and genetic classification for malformations of cortical development

A.J. Barkovich, MD; R.I. Kuzniecky, MD; G.D. Jackson, MD; R. Guerrini, MD; and W.B. Dobyns, MD

Abstract—Increasing recognition of malformations of cortical development and continuing improvements in imaging techniques, molecular biologic techniques, and knowledge of mechanisms of brain development have resulted in continual improvement of the understanding of these disorders. The authors propose a revised classification based on the stage of development (cell proliferation, neuronal migration, cortical organization) at which cortical development was first affected. The categories are based on known developmental steps, known pathologic features, known genetics (when possible), and, when necessary, neuroimaging features. In those cases in which the precise developmental and genetic features are uncertain, classification is based on known relationships among the genetics, pathologic features, and neuroimaging features. The major change since the prior classification has been a shift to using genotype, rather than phenotype, as the basis for classifying disorders wherever the genotype–phenotype relationship is adequately understood. Other substantial changes include more detailed classification of congenital microcephalies, particularly those in which the genes have been mapped or identified, and revised classification of congenital muscular dystrophies and polymicrogyrias. Information on genetic testing is also included. This classification allows a better conceptual understanding of the disorders, and the use of neuroimaging characteristics allows it to be applied to all patients without necessitating brain biopsy, as in pathology-based classifications.

NEUROLOGY 2005;65:1873–1887

Malformations of cortical development are more common than was recognized in the era before MRI and the recent increase in the treatment of neocortical epilepsy by surgery.[1-3] They are common causes of epilepsy and developmental delay.[4] They are important in the study of developmental neuroscience, as an understanding of the causative genes and their protein products gives insights into the processes of cerebral cortical development.

In 1996, a classification scheme for malformations of cortical development, based on the first developmental step (cell proliferation, neuronal migration, cortical organization) at which the developmental process was disturbed, was proposed;[5] this classification was updated in 2001.[6] At that time, the authors noted that the classification was not final, but that it provided a framework for classification of both known and as yet undescribed malformations and that it would continue to be modified as our knowledge advanced. This classification system has proved useful in helping those physicians who diagnose and treat patients with malformations of cortical development and has been adopted by many individuals in the field. At the time of the 2001 revision, it was noted that substantial new information had accumulated concerning both normal and abnormal cortical development, particularly regarding the genetic basis and imaging features of many malformations of cortical development and that such advances were likely to continue. Since that revision, several new genes and new mutations of known genes for disorders with microcephaly,[7-13] lissencephaly,[14-15] cobblestone cortex,[16-19] heterotopia,[12-20] and polymicrogyria[21-24] have been mapped or cloned (table 1). These genetic studies have revealed that the type of mutation is often as important as which gene has been mutated in determining the clinical and imaging phenotypes of the affected patients.[14-19,25,26] In addition, new malformations

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From the Departments of Radiology (Neuroradiology) (Dr. Barkovich), University of California, San Francisco; NYU Comprehensive Epilepsy Center (Dr. Kuzniecky), Department of Neurology, New York University, New York; Brain Research Institute and Austin and Repatriation Medical Centre (Dr. Jackson), University of Melbourne, Australia; Developmental Neuroscience Department (Dr. Guerrini), University of Pisa, and IRCCS Stella Maris Institute (Dr. Guerrini), Pisa, Italy; and Departments of Human Genetics, Neurology, and Pediatrics (Dr. Dobyns), University of Chicago, IL.

Disclosure: The authors report no conflicts of interest.
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NEUROLOGY 2005;65:1873–1887

INTRODUCCIÓN

2012

Review article

59

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By A. J. Barkovich[1], R. I. Kuzniecky[2], W. B. Dobyns[3], G. D. Jackson[4], L. E. Becker[5] and P. Evrard[6]
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Introduction

Malformations of the cerebral cortex are a class of brain anomalies that are being recognized more and more frequently as a cause of epilepsy and neurodevelopmental disorders (2, 3, 4, 5, 6, 7, 8, 11, 19, 20, 23, 34, 37, 42, 43, 44, 51). However, the nomenclature for these disorders is not uniform, and no standard system for their classification has been established. As a result, confusion exists regarding proper nomenclature and different names are sometimes used for malformations that appear identical on clinical, radiologic, and pathologic examination. In this manuscript, we propose a rational classification system for these malformations, based on fundamental embryologic and genetic principles and a combination of neuroimaging, gross pathologic, and histologic criteria. Through the use of this classification system, we believe most presently known malformations of cortical development can be uniquely classified; moreover, this classification provides a framework for the classification of disorders that are not yet described. Finally, this classification provides the practicing clinician with a logical framework for thinking about these disorders and classifying his or her patients.

Theoretical basis for the classification

The classification (Table 1) is based on three fundamental embryologic events of cortical formation: (I) cellular proliferation in the germinal zones; (II) migration of cells

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Neurology®

Classification system for malformations of cortical development: Update 2001

A. J. Barkovich, R. I. Kuzniecky, G. D. Jackson, et al.
Neurology 2001;57;2168-2178
DOI 10.1212/WNL.57.12.2168

This information is current as of December 26, 2001

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://www.neurology.org/content/57/12/2168.full.html

Views & Reviews

Classification system for malformations of cortical development

Update 2001

A.J. Barkovich, MD; R.I. Kuzniecky, MD; G.D. Jackson, MD; R. Guerrini, MD; and W.B. Dobyns, MD

Article abstract—The many recent discoveries concerning the molecular biologic bases of malformations of cortical development and the discovery of new such malformations have rendered previous classifications out of date. A revised classification of malformations of cortical development is proposed, based on the stage of development (cell proliferation, neuronal migration, cortical organization) at which cortical development was first affected. The categories have been created based on known developmental steps, known pathologic features, known genetics (when possible), and, when necessary, neuroimaging features. In many cases, the precise developmental and genetic features are uncertain, so classification was made based on known relationships among the genetics, pathologic features, and neuroimaging features. A major change since the prior classification has been the elimination of the separation between diffuse and focal/multifocal malformations, based on the recognition that the processes involved in these processes are not fundamentally different; the difference may merely reflect mosaicism, X inactivation, the influence of modifying genes, or suboptimal imaging. Another change is the listing of fewer specific disorders to reduce the need for revisions; more detail is added in other smaller tables that list specific malformations and malformation syndromes. This classification is useful to the practicing physician in that its framework allows a better conceptual understanding of the disorders, while the component of neuroimaging characteristics allows it to be applied to all patients without necessitating brain biopsy, as in pathology-based classifications.

NEUROLOGY 2001;57:2168–2178

HIGH YIELD CME

A developme classification fo cortical

A.J. Barkovich, MD; R.I. Kuzniecky, MD; G.D

Abstract—Increasing recognition of malformations of techniques, molecular biologic techniques, and knowled improvement of the understanding of these disorders. development (cell proliferation, neuronal migration, cor The categories are based on known developmental steps when necessary, neuroimaging features. In those cas uncertain, classification is based on known relationsl features. The major change since the prior classificatior basis for classifying disorders wherever the genotype–p changes include more detailed classification of congenit mapped or identified, and revised classification of cong genetic testing is also included. This classification allov of neuroimaging characteristics allows it to be applied based classifications.

NEUROLOGY 2005;65:1873–1887

Malformations of cortical development are more co mon than was recognized in the era before MRI the recent increase in the treatment of neocorti epilepsy by surgery.[1-3] They are common causes epilepsy and developmental delay.[4] They are imp tant in the study of developmental neuroscience, an understanding of the causative genes and th protein products gives insights into the processes cerebral cortical development.

In 1996, a classification scheme for malformati of cortical development, based on the first devel mental step (cell proliferation, neuronal migrati

NEUROLOGY 2005

known and as yet undescribed malformations that it would continue to be modified as our kno

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doi:10.1093/brain/aws019 Brain 2012: 135; 1348–1369 | 1348

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

A developmental and genetic classification for malformations of cortical development: update 2012

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Malformations of cerebral cortical development include a wide range of developmental disorders that are common causes of neurodevelopmental delay and epilepsy. In addition, study of these disorders contributes greatly to the understanding of normal brain development and its perturbations. The rapid recent evolution of molecular biology, genetics and imaging has resulted in an explosive increase in our knowledge of cerebral cortex development and in the number and types of malformations of cortical development that have been reported. These advances continue to modify our perception of these malformations. This review addresses recent changes in our perception of these disorders and proposes a modified classification based upon updates in our knowledge of cerebral cortical development.

Keywords: cerebral cortex; malformation of cortical development; microcephaly; cortical dysplasia; polymicrogyria
Abbreviations: FCD = focal cortical dysplasia

Introduction

Malformations of cortical development have been of interest to clinicians and neuroscientists for many decades (Friede, 1989; Sarnat, 1992; Norman *et al.*, 1995). In 1996, the term malformation of cortical development was introduced to designate a collectively common group of disorders in children with developmental delay and young people with epilepsy; a classification scheme was introduced, based upon the earliest developmental step at which the developmental process was disturbed

Received July 20, 2011. Revised November 14, 2011. Accepted December 5, 2011. Advance Access publication March 16, 2012

INTRODUCCIÓN

VARIAS REVISIONES: 2016 2020

REVIEW

Malformations of Cortical Development

Rahul S. Desikan, MD, PhD and A. James Barkovich, MD

Malformations of cortical development (MCDs) compose a diverse range of disorders that are common causes of neurodevelopmental delay and epilepsy. With improved imaging and genetic methodologies, the underlying molecular and pathobiological characteristics of several MCDs have been recently elucidated. In this review, we discuss genetic and molecular alterations that disrupt normal cortical development, with emphasis on recent discoveries, and provide detailed radiological features of the most common and important MCDs.

ANN NEUROL 2016;00:000–000

The term malformation of cortical development (MCD) was first introduced in 1996 to describe a group of disorders that result from disturbances of the normal developmental processes of the human cerebral cortex and cause a wide range of developmental disorders of the cortex that are common causes of neurodevelopmental delay and epilepsy.[1] As a means of elucidating these disorders, a classification scheme was developed, based on the earliest stage at which the neurodevelopment process is first disrupted, and has been subsequently updated.[2,3]

In this review, we discuss fundamental concepts underlying each component of the classification scheme,[3,4] discuss recently elucidated genetic mutations and disruptions of molecular pathways, and provide detailed imaging features of the most common and important MCDs. The malformations are discussed based upon the developmental process that is affected by the presumed causative mutation, with defects in earliest processes discussed earliest and those proposed to affect the latest processes discussed last.

doi:10.1093/brain/awaa174 BRAIN 2020: 143; 2874–2894 | 2874

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

Definitions and classification of malformations of cortical development: practical guidelines

Mariasavina Severino,[1] Ana Filipa Geraldo,[1,2] Norbert Utz,[3] Domenico Tortora,[1] Ivana Pogledic,[4] Wlodzimierz Klonowski,[5] Fabio Triulzi,[6] Filippo Arrigoni,[7] Kshitij Mankad,[8] Richard J. Leventer,[9] Grazia M.S. Mancini,[10] James A. Barkovich,[11,12]* Maarten H. Lequin,[13]* and Andrea Rossi[1]* on behalf of the European Network on Brain Malformations (Neuro-MIG)

*These authors contributed equally to this work.

Malformations of cortical development are a group of rare disorders commonly manifesting with developmental delay, cerebral palsy or seizures. The neurological outcome is extremely variable depending on the type, extent and severity of the malformation and the involved genetic pathways of brain development. Neuroimaging plays an essential role in the diagnosis of these malformations, but several issues regarding malformations of cortical development definitions and classification remain unclear. The purpose of this consensus statement is to provide standardized malformations of cortical development terminology and classification for neuroradiological pattern interpretation. A committee of international experts in paediatric neuroradiology prepared systematic literature reviews and formulated neuroimaging recommendations in collaboration with geneticists, paediatric neurologists and pathologists during consensus meetings in the context of the European Network Neuro-MIG initiative on Brain Malformations (https://www.neuro-mig.org/). Malformations of cortical development neuroimaging features and practical recommendations are provided to aid both expert and non-expert radiologists and neurologists who may encounter patients with malformations of cortical development in their practice, with the aim of improving malformations of cortical development diagnosis and imaging interpretation worldwide.

Introduction

Malformations of cortical development have been of interest to clinicians and neuroscientists for many decades (Friede, 1989; Sarnat, 1992; Norman *et al.*, 1995). In 1996, the term malformation of cortical development was introduced to designate a collectively common group of disorders in children with developmental delay and young people with epilepsy; a classification scheme was introduced, based upon the earliest developmental step at which the developmental process was disturbed

Received July 20, 2011. Revised November 14, 2011. Accepted December 5, 2011. Advance Access publication March 16, 2012

INTRODUCCIÓN

MCD classification	MDC Type	Definition	Major mechanism/ Genetic pathways/ Genes
Group I Altered proliferation or excess apoptosis	**Primary microcephaly/Micrencephaly** (microcefalia vera)	Decrease of brain parenchymal volume at birth	MPCH: ANKLE2, ASPM, CASC5, CDK5RAP2, CENPJ, CIT, COPB 2, CEP135, CEP152, CDK6, CENPE, KIF14, MAP11, MCPH1…
	Brain overgrowth spectrum (MEG, HMEG total HMEG, partial HMEG, Bi-HMEG, dysplastic MEG)	Increase of brain parenchymal volume	PI3KCA, AKT3, CCND2, PIK3R2, AKT1, PTEN, MTOR, RHEB, STRADA, TSC1, TSC2, PTCH1, KIF7, GLI3 ...
	FCD type IIa **FCD type IIb/Cortical tubers**	Disruption of cortical lamination with presence of dysmorphic neurons (FCD IIa) and balloon cells (FCD IIb/cortical tubers)	AKT3, DEPDC5, MTOR, NPRL2, NPRL3, PI3KCA, RHEB, TSC1, TSC2…
Group II Abnormal neuronal migration	**Heterotopia**	Clusters of normal neurons in abnormal locations: - Periventricular heterotopia - Subcortical (non-band) heterotopia	AKT3, APC2, ARGEF2, C6orf70, CENPJ, COL18A1, CRB2, DCHS1, EML1, FAT4, FLNA, GPSM2, KATNB1, INTS8, MAP1B, MCPH1, MOB2, NEDD4L, OFD1, PLEKHG6, RAI1, TUBB…
	LIS (Agyria-pachygyria spectrum and subcortical band heterotopia; LIS type I)	- Thickened cortex with gyral abnormalities ranging from agyria (absent gyration/complete LIS) to pachygyria (reduced gyration/partial LIS) - Subcortical band heterotopia	Tubulins, Actins and actin-related MAPs, Microtubule MAPs/motor proteins, Reelin signaling, Transcriptional factors, Caspase-mediated apoptosis
	Cobblestone (LIS type II)	Irregular, pebbled external and internal cortical surfaces resembling the morphology of a cobblestone	Dystroglycanopathies: B3GALNT2, B4GAT1, B3GNT2, DAG1, DOLK, DPM1, DPM2, DPM3, FKTN, FKRP, GMPPB...
	PMG	Excessive number of abnormally small cerebral gyri	Genetic defects and In utero infections (teratogens, traumatic and ischemic events), metabolic disorders…
	Schizencephaly	Cleft lined by polymicrogyric grey matter and/or heterotopia extending the full thickness of cerebral hemispheres from ventricular surface (ependyma) to periphery (pial surface)	In utero infections, teratogens, traumatic and ischemic events. Genetic defects
Group III Abnormal postmigrational development	**Dysgyria**	Cortex with regular thickness and inner/outer surfaces but with minor abnormalities of sulcal depth and orientation	ACTA2, FGFR3, FGFR2, Tubulins (e.g. TUBB2B, TUBB3)
	FCD type I and FCD type III	Abnormal lamination (III: adjacent to other principal lesion	post-translational protein modification/glycosylation: SLC35A2
	Secondary Microcephaly/Micrencephaly	Decreased brain parenchymal volume with onset after birth	ANKLE2, CASK, CDKL5, CREBBP, EGP5, EIF2AK3, IER3IP1, EP300, ERCC6, ERCC8, FOXG1, MECP2, PYCR2, RAB3GAP1, RAB3GAP2, RAB18, SLC1A4, SLC9A6, SMPD4, TBC1D20, TCF4, TMX2, UBE3A

Definitions and classification of malformations of cortical development: practical guidelines. Severino M et al. Brain. 2020

INTRODUCCIÓN

- CLASIFICACIONES NO SON RÍGIDAS: descubrimiento de nuevos genes, proteínas y vías/rutas

- Terminología común y una clasificación genotipos-fenotipos actualizada : mejor comunicación interdisciplinar

- **NEUROIMAGEN > INFORMES >** Mejores descripciones, más específicas, patrones de alteración de neuroimagen

a) pueden mejorar la tasa de diagnóstico > mejor orientación clínica y demanda pruebas genéticas dirigidas > tratamiento

b) facilitar el descubrimiento de nuevas correlaciones genotipo-fenotipo

DIAGNÓSTICO POR IMAGEN: TÉCNICAS/PROTOCOLOS

- DEFINITIVO: HISTOLÓGICO

- FENOTIPO, GENOTIPO

-**1º > APROXIMACIÓN > HALLAZGOS DE NEUROIMAGEN**

TÉCNICAS DE NEUROIMAGEN:

ECOGRAFÍA

PERIODO PRENATAL

RETO DIAGNÓSTICO

Alteraciones aberrantes de la sulcación

Microcefalia y Megalencefalia (∅)

~~Asimetrías parciales o Heterotopias~~

SI SOSPECHA: ECO Y RM POSTNATAL

TOMOGRAFÍA COMPUTERIZADA

RADIOPROTECCIÓN

PRUEBA "AUXILIAR":

- calcificaciones (CMV)

- contraindicación de RM

RESONANCIA MAGNÉTICA

PRUEBA DE ELECCIÓN

3 TESLA > 1,5 T

PROTOCOLOS OPTIMIZADOS

(mejor resolución espacial/contraste)

PROTOLOCOS ADAPTADOS POR EDAD

(mielinización)

INFORMACIÓN CLÍNICA

(características sindrómicas, tamaño cabeza, epilepsia)

DIAGNÓSTICO POR IMAGEN: TÉCNICAS/PROTOCOLOS

PROTOCOLO RM

ADULTOS

Harmonized Neuroimaging of Epilepsy Structural Sequences > "HARNESS-MRI protocol" ILAE 2019

(Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: A consensus report from the International League Against Epilepsy Neuroimaging Task Force. Bernasconi A et al. *Epilepsia*. 2019;60(6):1054-1068. doi:10.1111/epi.15612)

3D T1-weighted
Seq. type: gradient echo , isotropic voxel (1x1x1 mm), no gap

3D FLAIR
Seq type: turbo spin echo, isotropic voxel (1x1x1 mm), no gap

2D Coronal T2-weighted
Seq type: turbo spin echo, voxel (0.4x0.4x2 mm
no interslice gap

Alternative 3D FLAIR **2D FLAIR-TSE** Axial/Coronal (2–3 mm)

PEDIATRÍA

CONSIDERACIÓN > PROCESO DE MADURACIÓN Y MIELINIZACIÓN CEREBRAL:

- Contraste entre córtex y s. blanca es máximo antes de comienzo de mielinización
- Durante proceso mielinización > este contraste disminuye y aumenta progresivamente grosor cortical
- Periodo "isointensidad T2" entre 8-12 meses (enmascara algunas MDC)

↓

1. PROTOCOLOS ADAPTADOS POR EDAD

2. PERIODO DE PRESENTACIÓN CLÍNICA DE MDC FRECUENTE DURANTE 1º AÑO

(NECESARIO REPETIR RM TRAS PERIODO DE MIELINIZACIÓN)

RECIÉN NACIDOS e INFANTES:

3D T1-weighted

Seq. type: gradient echo , isotropic voxel (1x1x1 mm), no gap

~~**3D FLAIR**~~

~~Seq type: turbo spin echo, isotropic voxel (1x1x1 mm), no gap~~

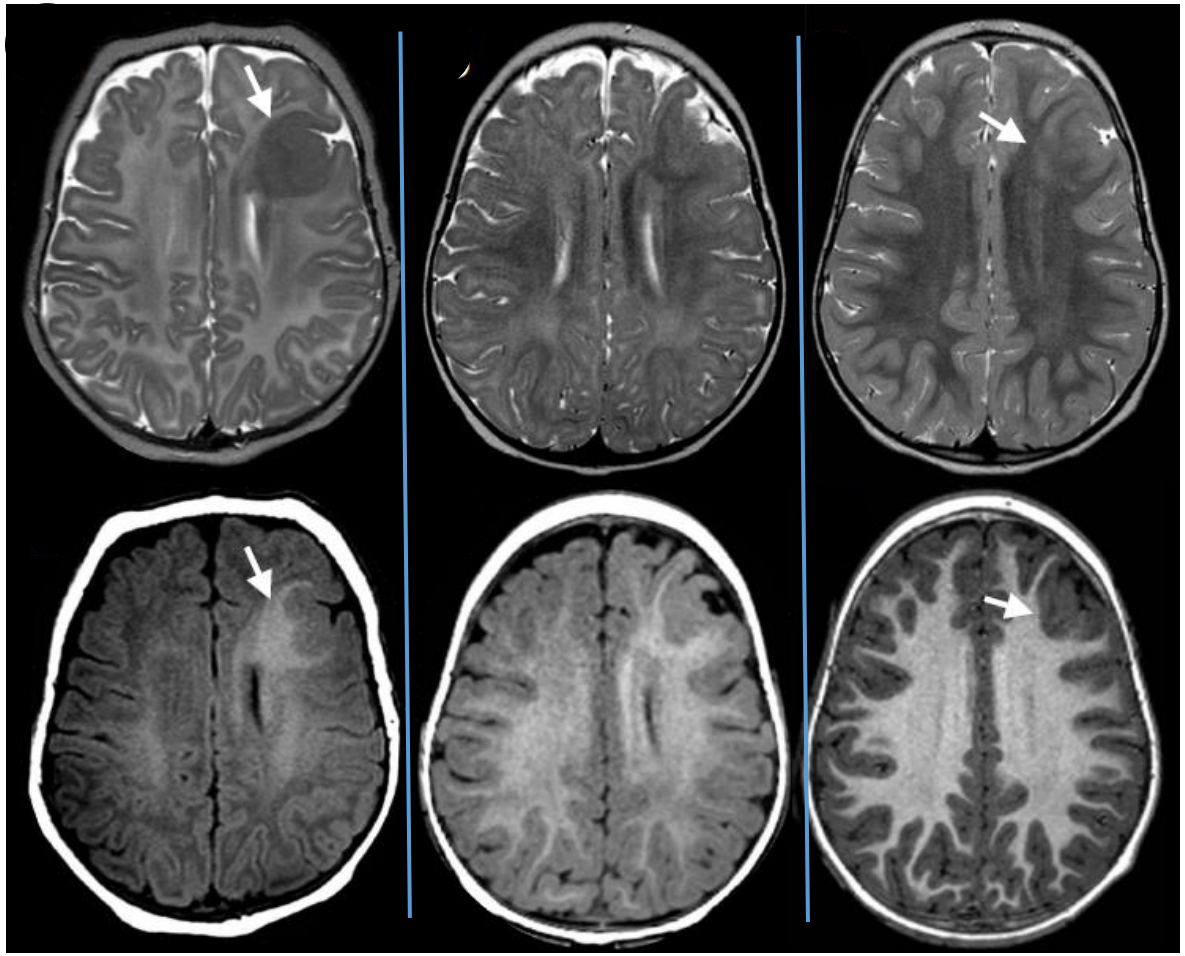
2D T2-weighted 3 PLANES

DIAGNÓSTICO POR IMAGEN: TÉCNICAS/PROTOCOLOS

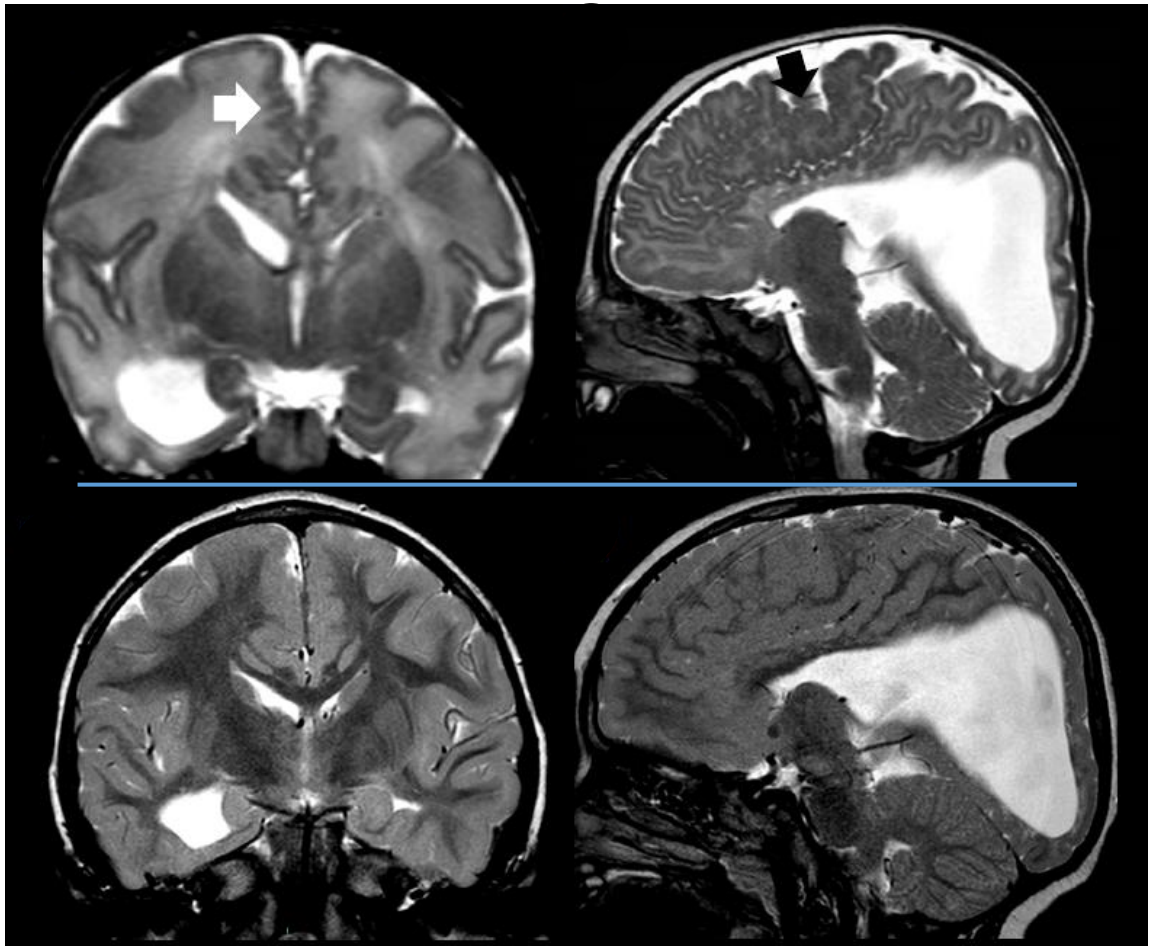
PROTOCOLO RM

APARIENCIA CAMBIANTE DE SG Y SB EN PERIODO DE MIELINIZACIÓN Y MADURÁCIÓN

DCF: neonato 8 meses > 2 años



PMG: neonato y 18 meses



Definitions and classification of malformations of cortical development: practical guidelines. Severino M et al. Brain. 2020

HALLAZGOS DE NEUROIMAGEN DE MDC

MICROCEFALIA

GRUPO I

Clínicamente: al nacimiento circunferencia cefálica < 3SD

M. PRIMARIA/GENÉTICA (~~M.VERA~~)

Congénita (en la neurogénesis: "in útero"/al nacimiento) > mutación gen (conocida solo aprox. 60%: SINDRÓMICAS/NO SINDRÓMICAS)

M. SECUNDARIA/ADQUIRIDA

Adquirida tras "insulto" perinatal (post- neurogénesis) (infección, vascular)

RM:

Disminución vol. cerebro (ventriculomegalia por ↓ sustancia blanca)

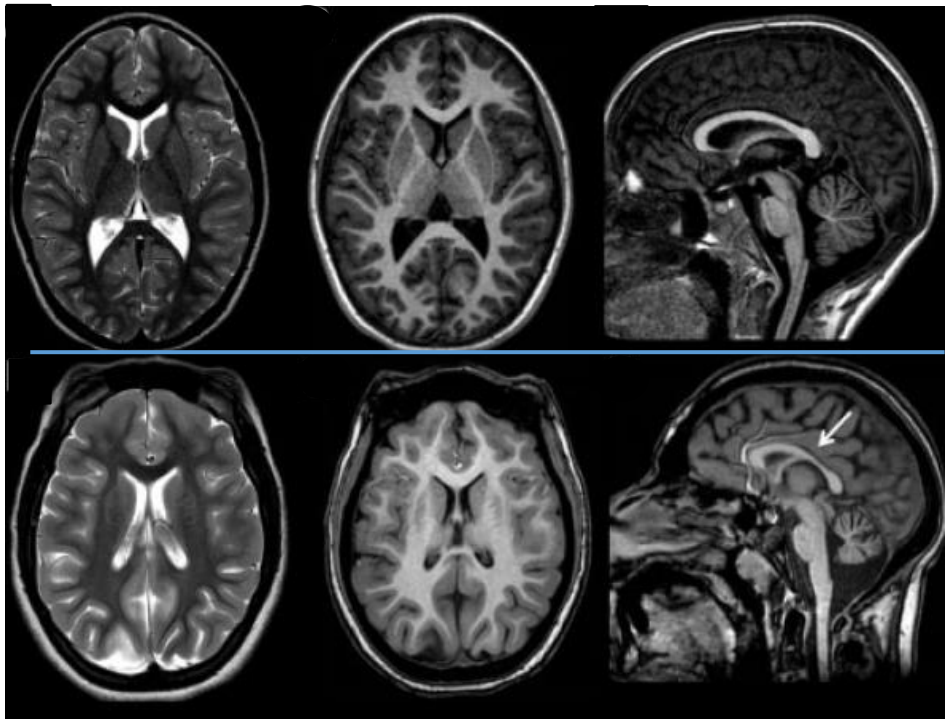
Patrón giral simplificado grosor córtex normal

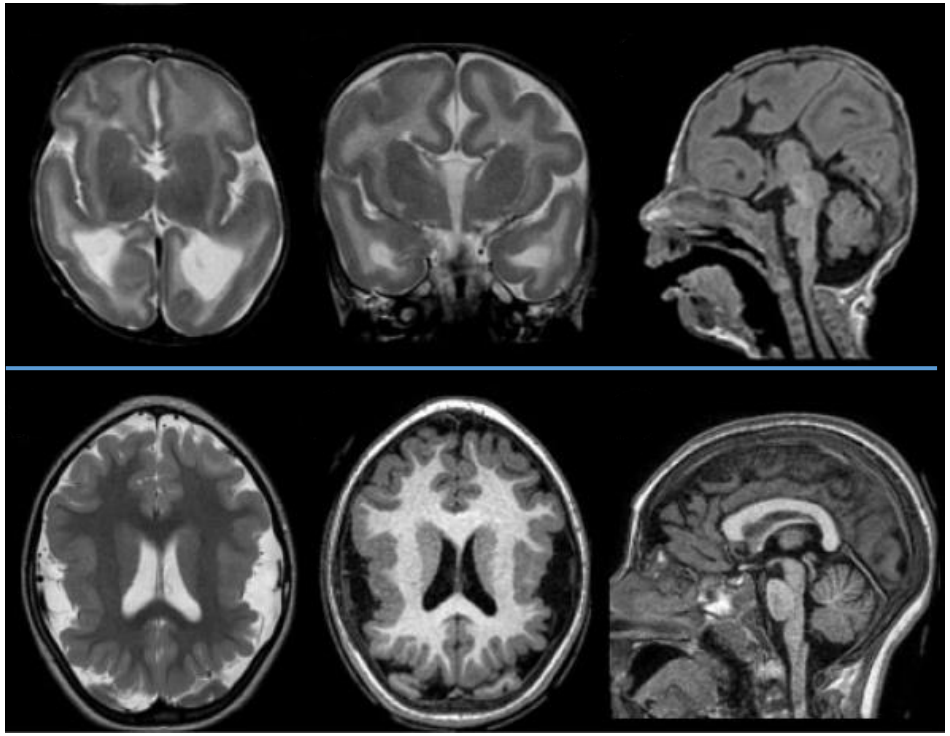
M. asociado a Lisencefalia

M. asociada a PMG o Heterotopia

Asociación otras alteraciones*: otras MDC, calcificaciones, alteración SB

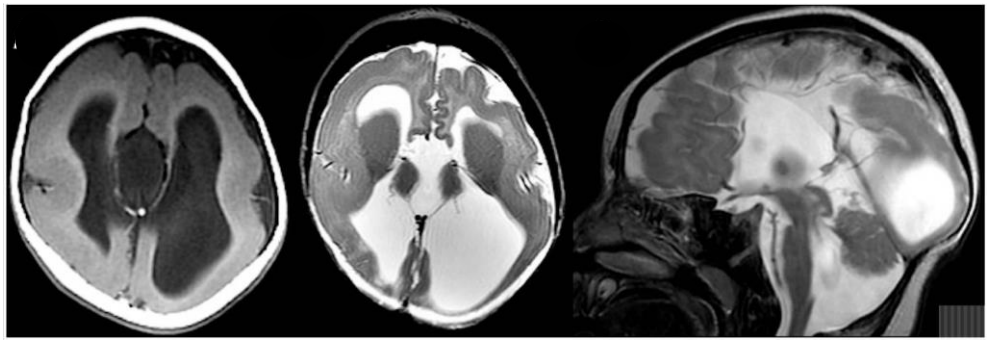
MICROCEFALIA





Microcefalias asociadas a distintos patrones girales/corticales

Severino M et al. Definitions and classification of malformations of cortical development: practical guidelines. Brain. 2020;143(10):2874-2894



Microcefalia asociada a mutación *TUBA1A*

Malformations of Cortical Development. Ann Neurol. 2016. Rahul S. Desikan and A. James Barkovich

MEGALENCEFALIA/espectro sobrecrecimiento cerebral

GRUPO I

MEGALENCEFALIA ≠ MACROCEFALIA (Clínicamente > no necesariamente macrocefalia)

Espectro de diferentes desórdenes que producen aumento tamaño encefálico: distintos genes y mutaciones de la vía mTOR

Megalencefalia displástica (DMEG)
SD. Megalencefalia-polimicrogiria-polidactilia-hidrocefalia
Megalencefalia-malformación capilar

RM:

Focal/lobar/hemisférico aumento del volumen cerebral (MOSAICISMOS)

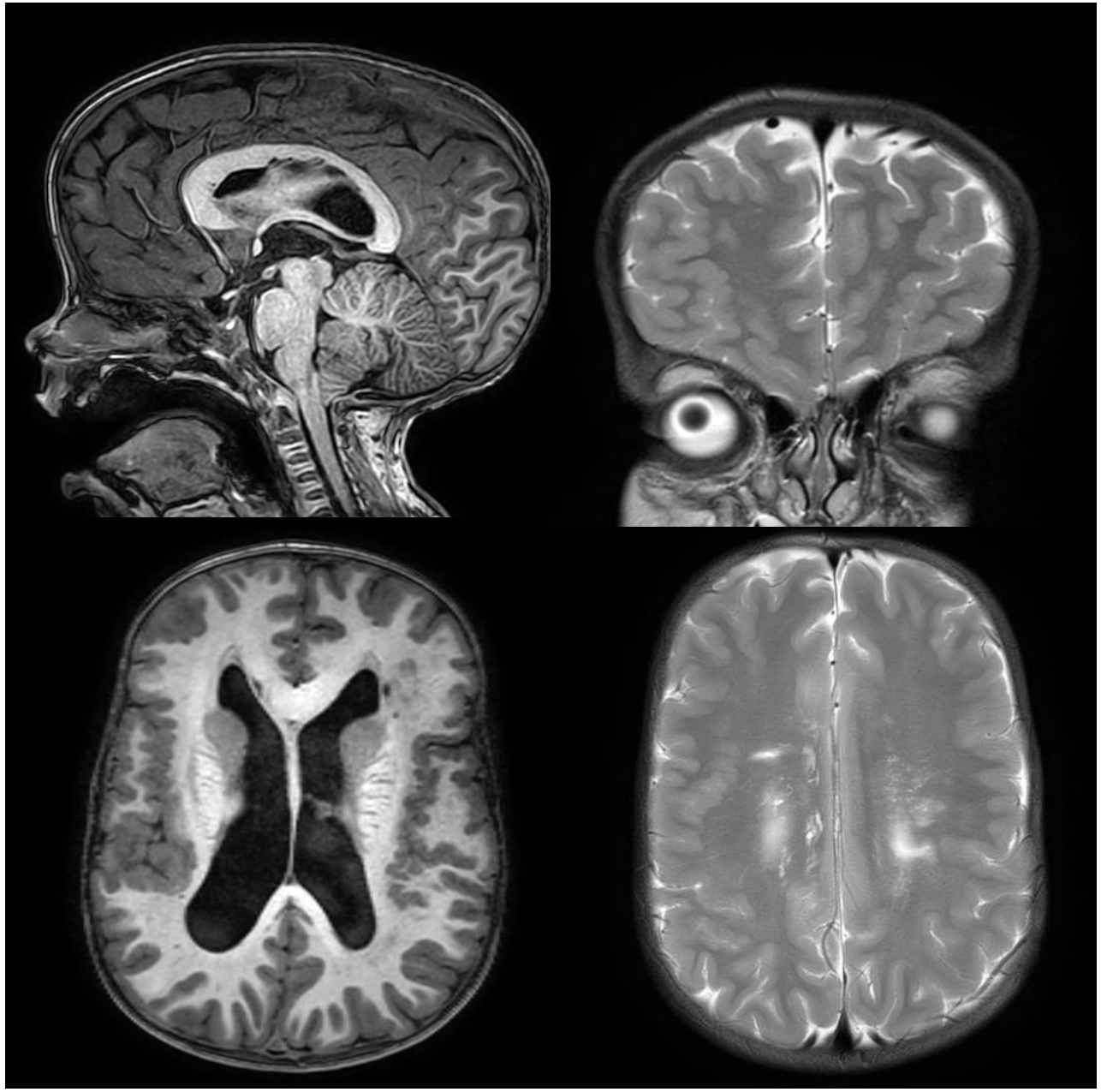
Raramente tronco del encéfalo y cerebelo

Alteración del patrón giral: variable (polimicrogiria, paquigiria, lisencefalia)

Otros hallazgos: pérdida diferenciación cortico-subcortical, aumento de tamaño ganglios de la base…

* *Ventriculomegalia asimétrica** (en hemisferio más afectado)

MEGALENCEFALIA



Megalencefalia-malformación capilar

Niña 5 años. Macrocefalia +7 desviaciones estándar.
Hemihipertrofia hemicara y EE Derechas.
Malformación vascular cutánea difusa

Cortesía Dr. Muchart

HETEROTOPIA

GRUPO II

Conglomerados de SG en localizaciones heterotópicas (ISOSEÑAL con SG)

Según **Localización** y **Morfología** > subtipos y alteración genética subyacente

HETEROTOPIA NODULAR PERIVENTRICULAR

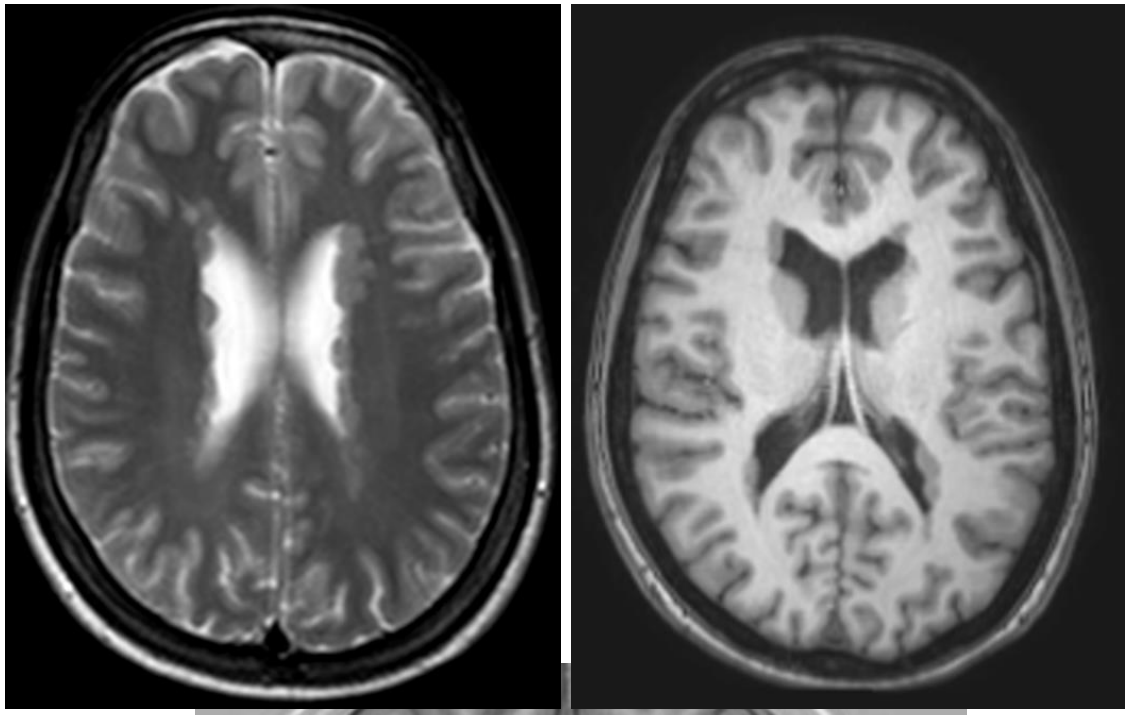
GRUPO II

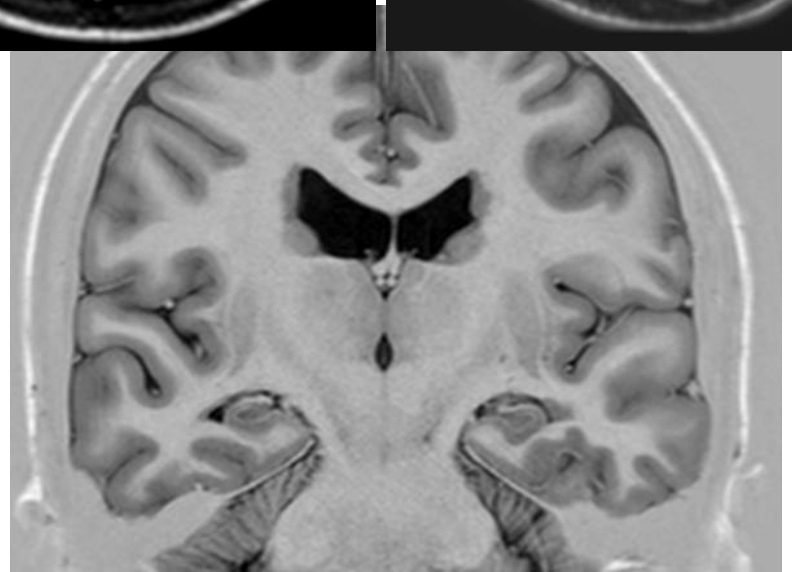
- Nódulos de SG recubriendo superficie ventricular: variable en **Número** y **Localización**

- La + FRECUENTE.

- Puede asociarse a otras alteraciones

- Dco. Dif: nódulos subependimarios de Esclerosis Tuberosa (hiperintensos, Ca, captación cte.)





Mujer 32 a. con ERT

HETEROTOPIA SUBCORTICAL

GRUPO II

- Conglomerados irregulares SG > extensión puramente subcortical o desde superficie ventricular al córtex (córtex adyacente alterado: adelgazado, surcos poco profundos)

- AMPLIO ESPECTRO IMÁGENES: no totalmente establecida su terminología/subclasificación:

* H. "transmantle": de ZV a Córtex

* "Curvilínea": conglomerados subcorticales "arremolinados"

* "Lóbulo dentro de un lóbulo": todo un lóbulo

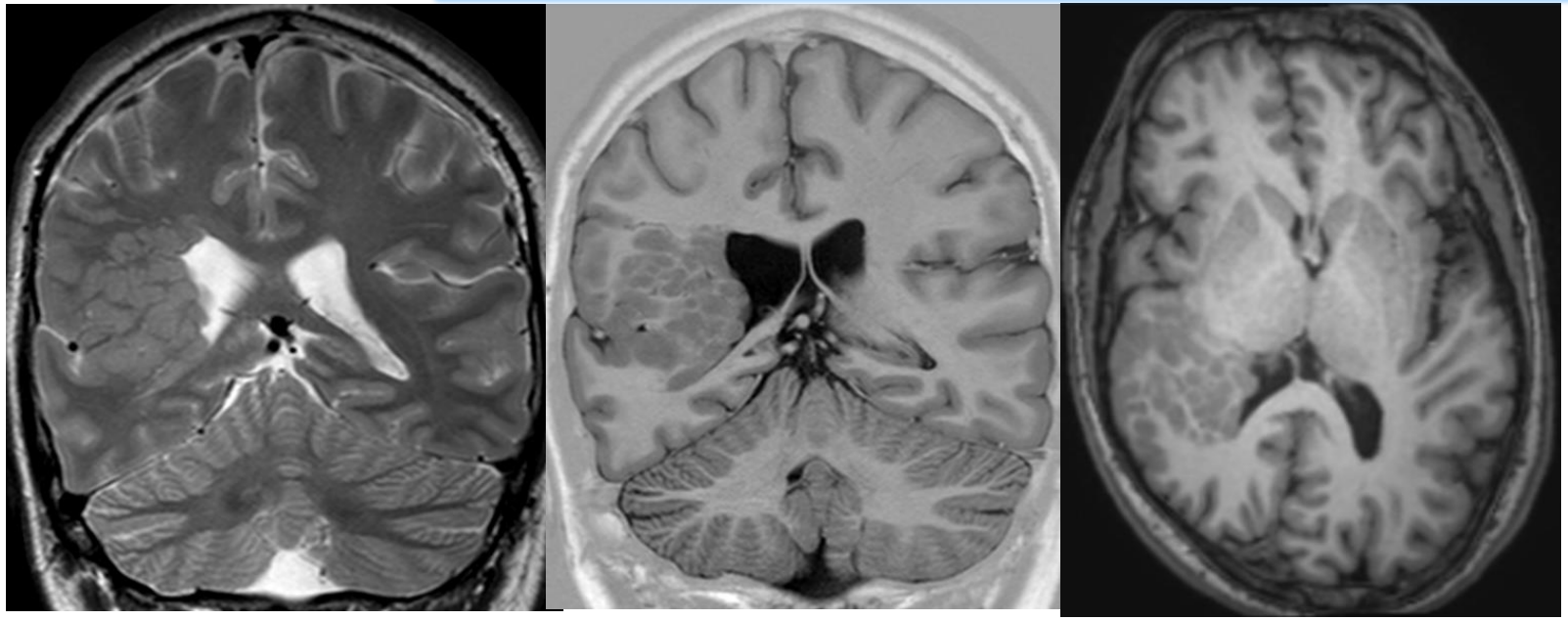
* "Ribbon-like heterotopia": SG heterotópica aspecto polimicrogírico, bilateral y simétrica,

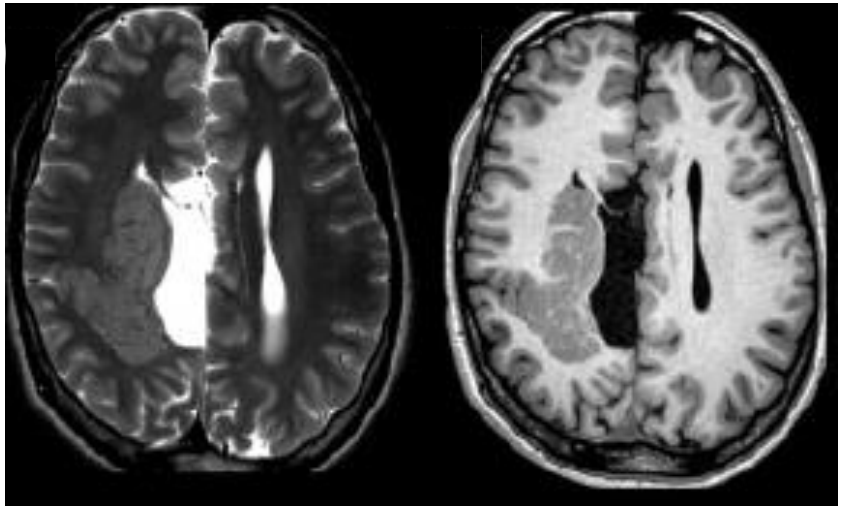
- Si es muy importante: pseudomasas, distorsión ventricular, distorsión de ganglios de la base

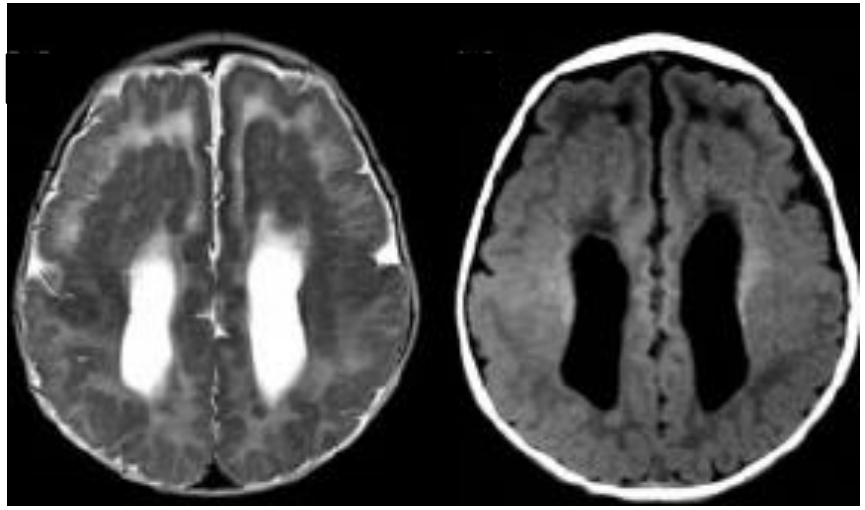
- Lóbulo afectado más pequeño: ↓ volumen de SB .

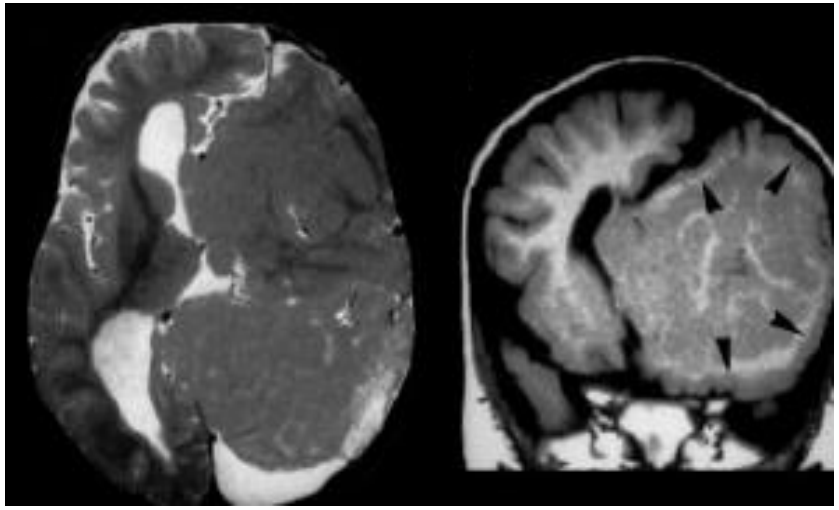
HETEROTOPIA SUBCORTICAL

H.S. Curvilínea en paciente de 26 años con ERT









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GRUPO II

HETEROTOPIA SUBCORTICAL EN BANDA

~~"Doble córtex"~~

Forma parte del **Espectro de la Lisencefalia** (= etiología y alteración genética)

Banda isointensa de SG a nivel subcortical :

> bilateral y simétrica

> completa o incompleta (ANT/POST)

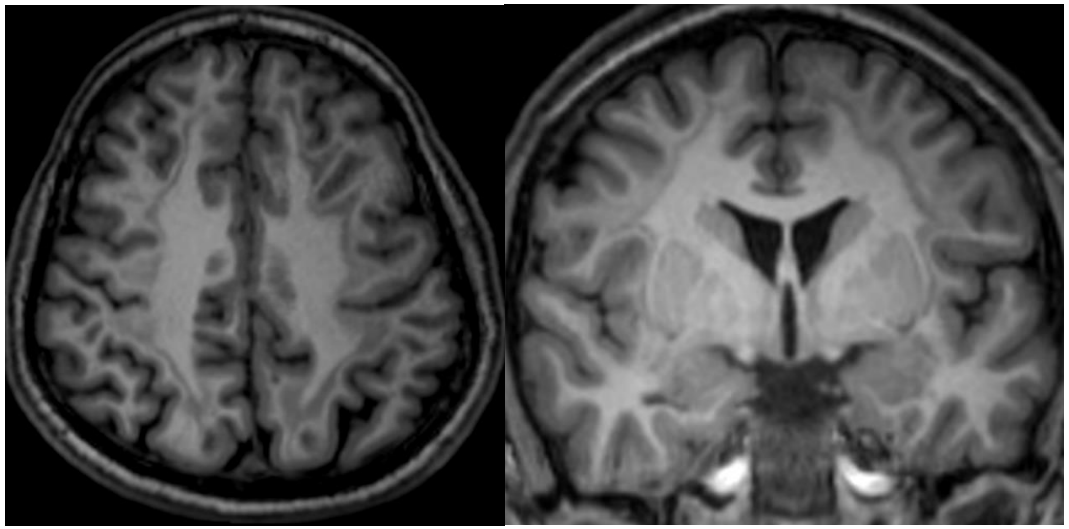
> Fina (<7 mm): yuxta-corticales o Gruesa (> 7 mm): profundas a fondo de surco

> Córtex NORMAL / ENGROSADO-SURCOS POCO PROFUNDOS / PAQUIGÍRCO

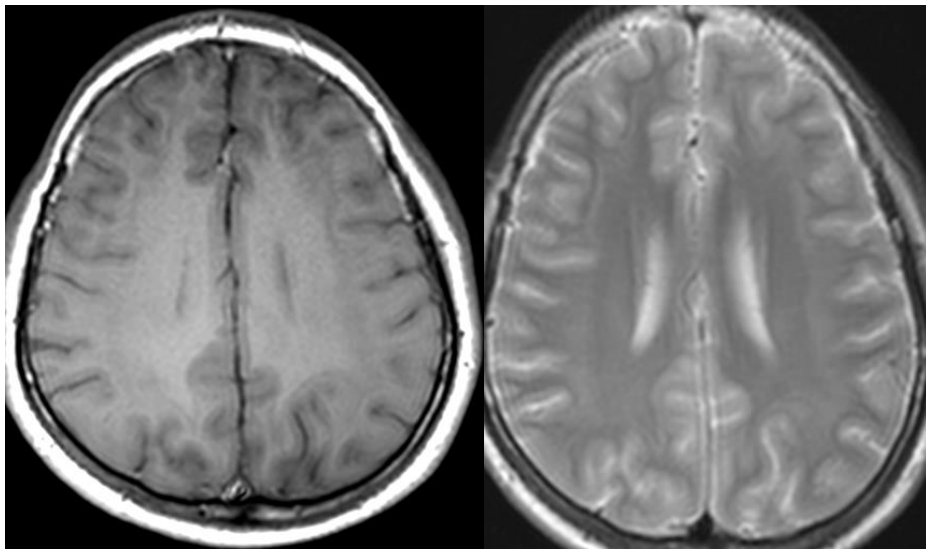
* Todos estos aspectos: indicados en informe (> implicaciones de severidad clínica y mutaciones genéticas)

HETEROTOPIA SUBCORTICAL EN BANDA

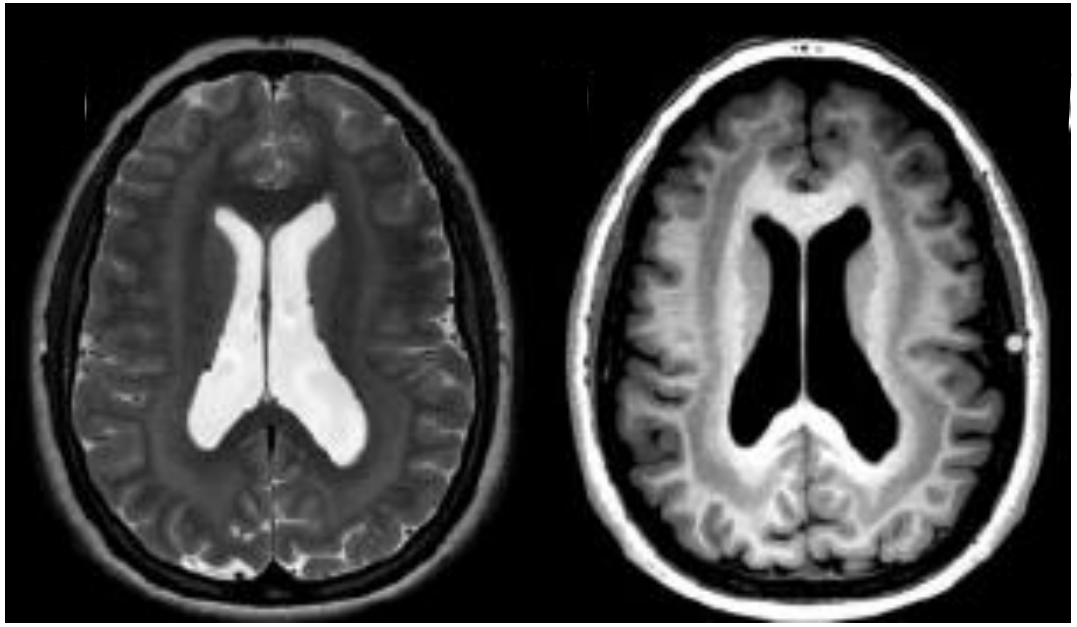
Niña 14 años ERT y retraso mental

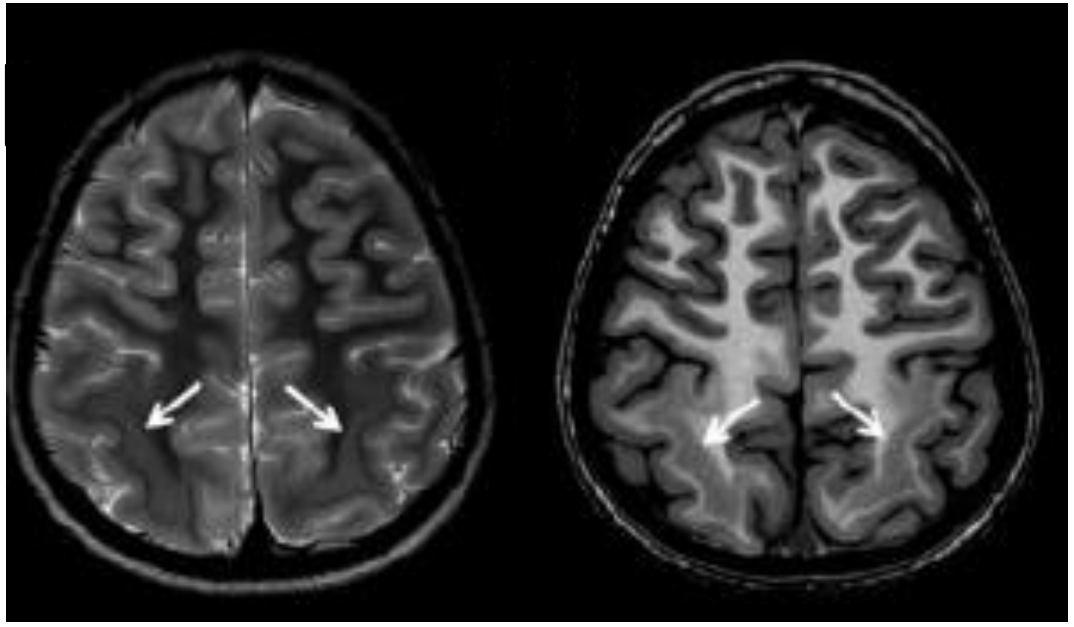


Cortes finos 1 mm (T13D)



Cortes estándar (5 mm)





Severino M et al. Definitions and classification of malformations of cortical development: practical guidelines. Brain. 2020;143(10):2874-2894

LISENCEFALIA

GRUPO II

Córtex grueso asociado a disminución de girificación

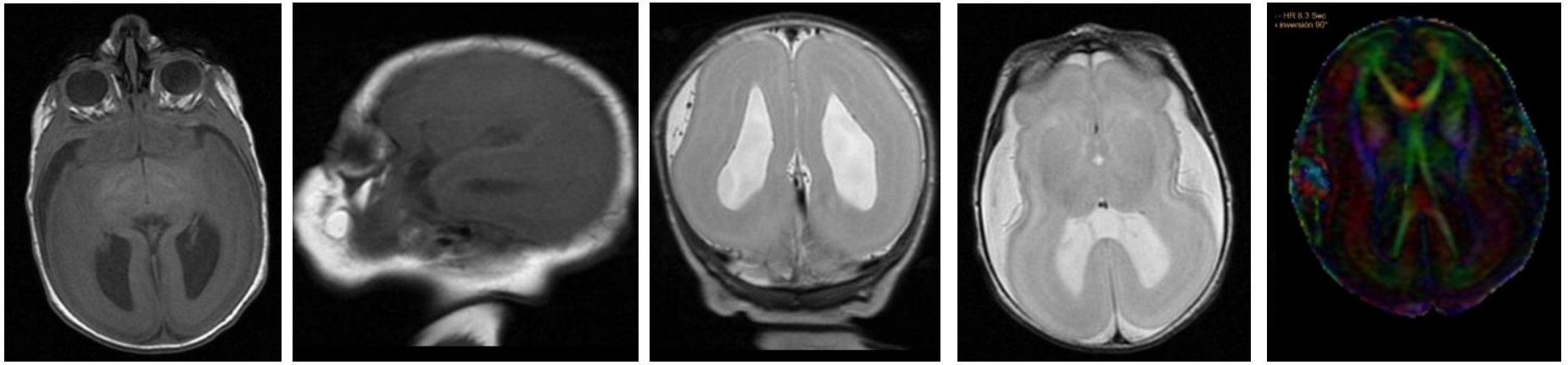
Distintas variantes:

- Severidad (agiria/oligiria)
- Gradiente (Ant/Post)
- Grosor de córtex (grueso/fino)
- Asociación de otras malformaciones

Dependiente de estas > subtipo genético

"Heterotopia subcortical en banda" > forma más leve del espectro

- Unión cortico-subcortical: **LISA,** bien definida (Dco. Dif. Con la PMC)
- Secundariamente: ↓volumen sustancia blanca ↓tamaño surcos y ventriculomegalia



Niño de 9 años con espasmos infantiles: **Lisencefalia LIS1**

Cortesía Dr. Muchart

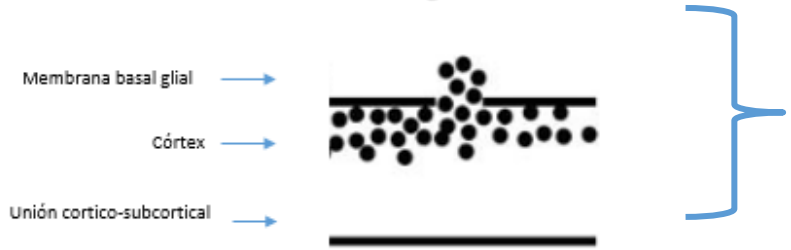
COMPLEJO EMPEDRADO "COBBLESTONE"

GRUPO II

Varias mutaciones > vía de glicosilación > alteración de la membrana basal ("glial limitans") > migración neuronal terminal anómala > "sobremigración"

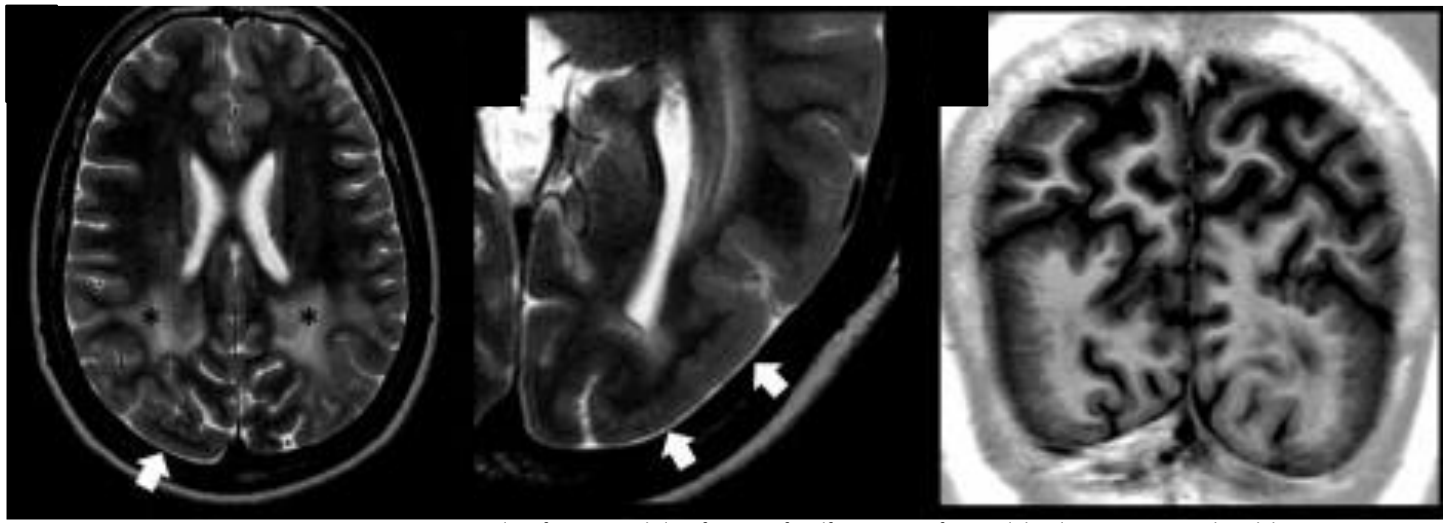
Hallazgos de RM variables

(múltiples fenotipos)



gap pequeño / neuronas: RM NORMAL
gap mediano / neuronas ≈ RM ALTERADA

- Alteraciones bilaterales y simétricas / Afectación todo el cerebro-grandes áreas / **Anterior** o Posterior
- Superficie cerebral irregular ("empedrado"), córtex engrosado, unión córtico-subcortical IRREGULAR (estrías verticales)
- Hiperseñal de SG (por SB intracortical) y de la SB subcortical (puede normalizarse con la edad)
- Asociación de alteraciones en fosa posterior (hendiduras del tronco encefálico y microquistes cerebelosos)



Severino M et al. Definitions and classification of malformations of cortical development: practical guidelines. Brain. 2020;143(10):2874-2894

POLIMICROGIRIA

GRUPO III > GRUPO II

* Estudios histopatológicos recientes > defectos en la zona limitante membrana pial y meninges > SOBREMIGRACIÓN > *heterotopía leptomeníngea*
* Malformación heterogénea: Genética (1ª; varios genes relacionados) y No Genética (2ª) (infección, isquemia, teratogenia)
* Variabilidad de topografía y extensión: Focal/Unilateral/Bilateral/Generalizada Simétrica/No simétrica Bilateral simétrica/Bilateral asimétrica
* Se han descrito varios subtipos **PERISILVIANA (bilateral)*

RM

> Múltiples pequeños giros densamente empaquetados

> Cortes finos > T13D (~~paquigiria~~)

> Unión cortico-subcortical irregular/ondulada > clave para diferenciar de paquigiria

> Córtex señal normal

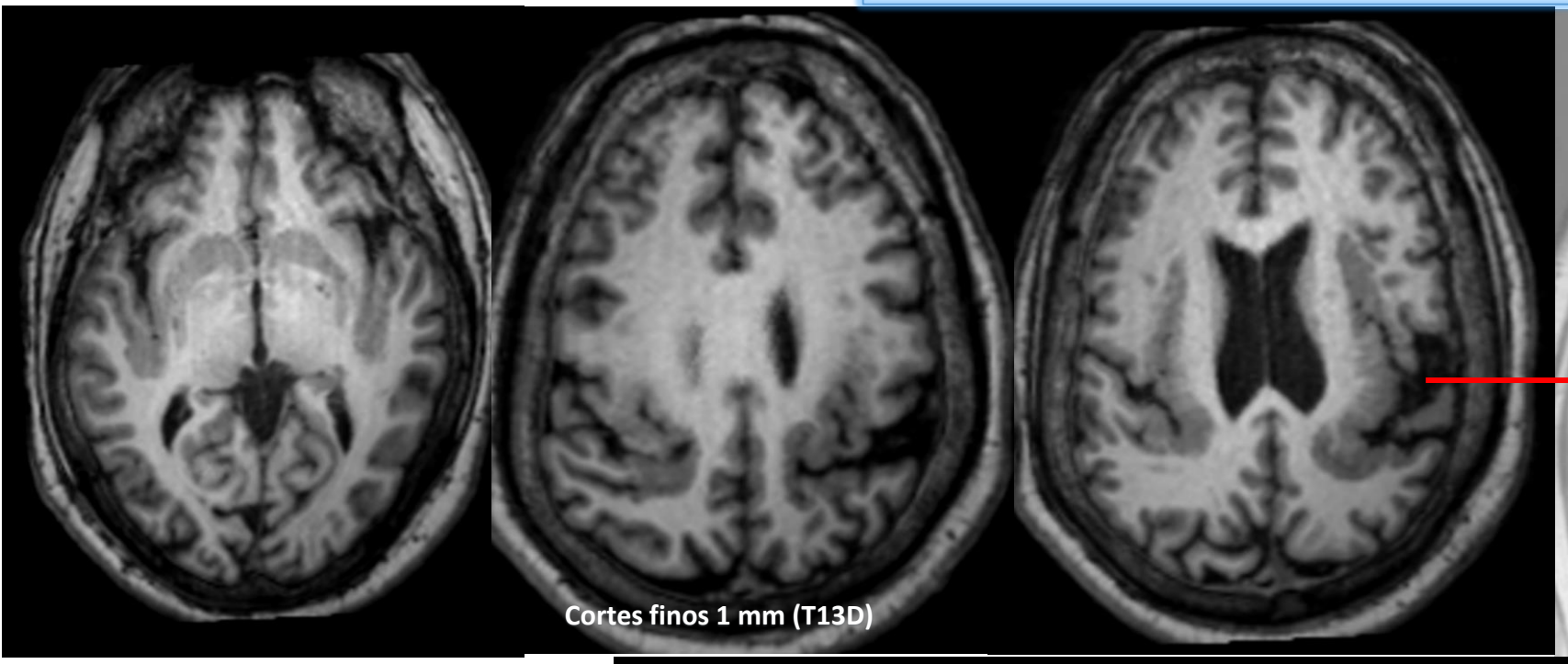
> Sustancia blanca: señal normal o hiperintensa (T2/FLAIR), en relación con espacios perivasculares dilatados.

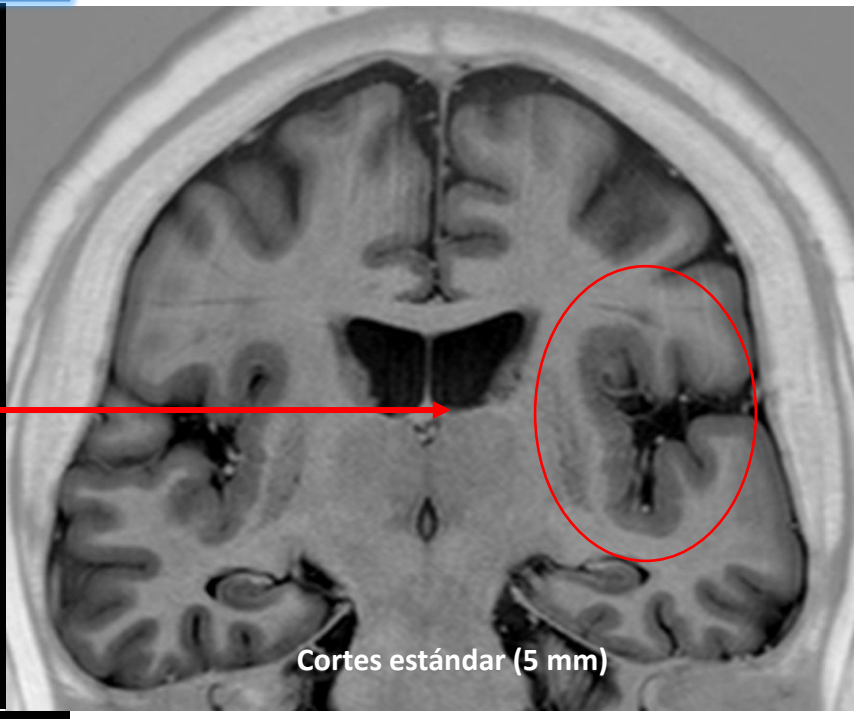
> Ocasionalmente (<5%) calcificación (infección congénita)

DIAGNÓSTICO DIFERENCIAL : poligiria, microgiria, ulegiria, complejo empedrado "cobblestone"

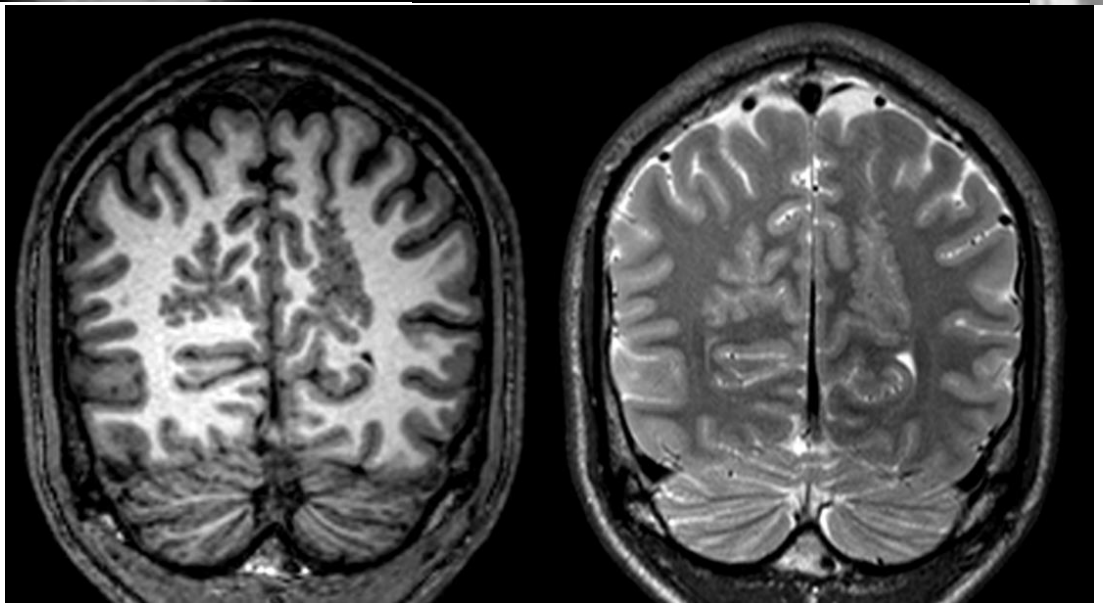
* "Cobblestone/polymicrogyria- like": difícil de diferenciar (pueden compartir mutaciones y mecanismos fisiopatológicos)

POLIMICROGIRIA





Mujer 44 . ERT



Hombre 19 a. con ERT

ESQUIZENCEFALIA

GRUPO III > GRUPO II

Variante severa de PMG (retraso mental, déficit motor, epilepsia)

Ausencia cuidado prenatal , consumo –OH y sustancias > (~~genética~~) agresión perinatal temprana

HALLAZGOS RM:

- Hendidura tapizada de SG > superficie ventricular (epéndimo) a > superficie cortical (superficie pial)

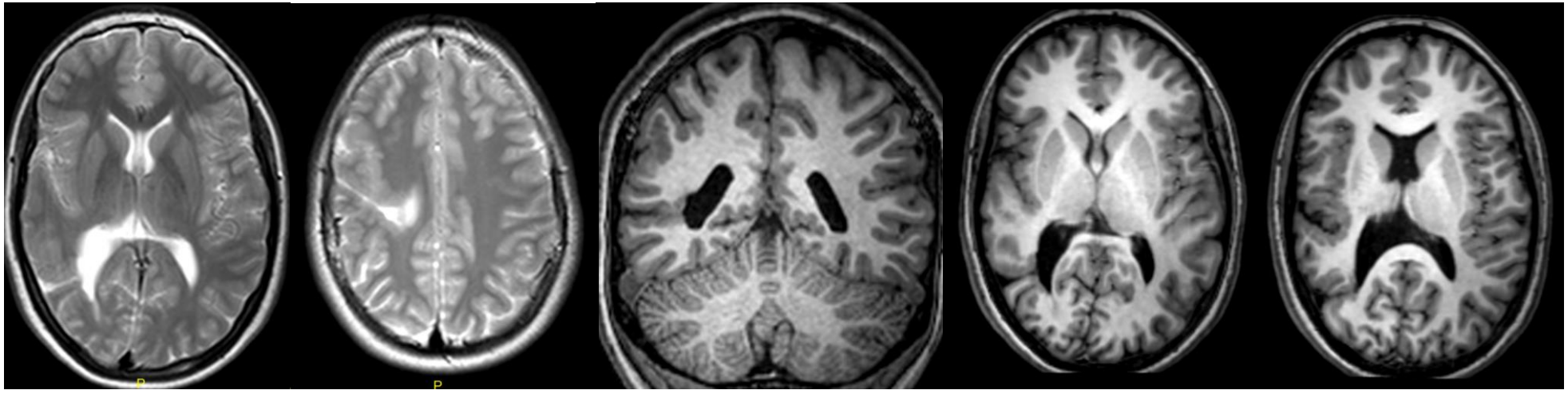
- SG que tapiza o está adyacente a la hendidura > PMG

- Hendidura: * sin LCR (E. labio cerrado) * con LCR (E. labio abierto) * vasos sanguíneos (menos frec.)

- Muesca en la superficie ependimaria ventricular (crucial utilizar secuencias de RM de alta resolución para identificar hendiduras sutiles y/u hoyuelos ventriculares que pueden indicar la presencia de esquizencefalia)

- Múltiples, 1/3 Bilateral - Coexistencia de otras alteraciones (fórnix y septum pellucidum: displasia septo-óptica plus)

Dco. Dif > porencefalia o lesiones cicatriciales: hendidura recubierta de SB y/o gliosis



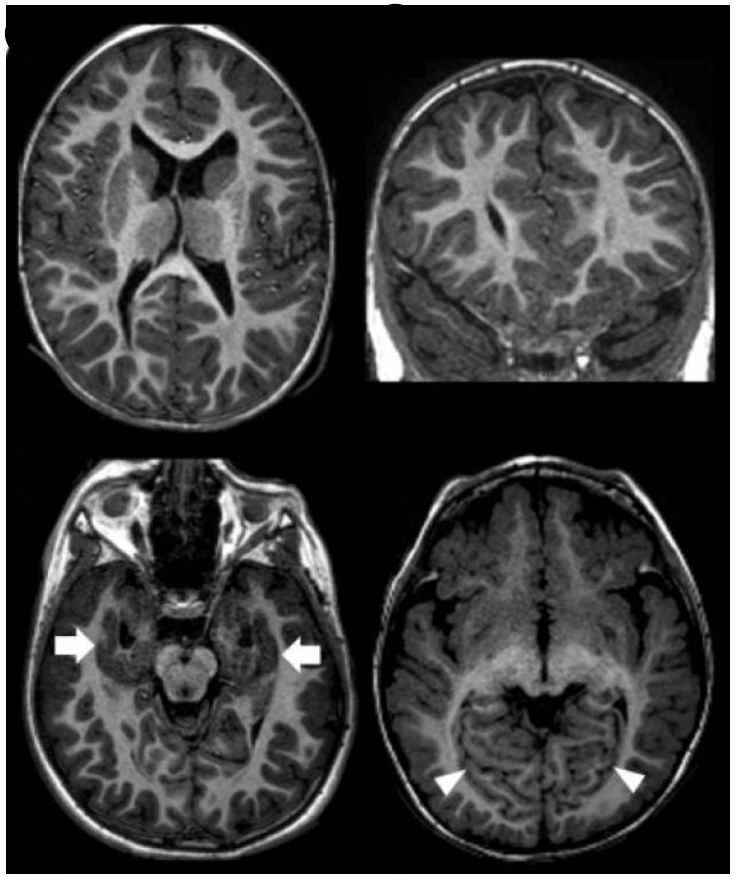
DISGIRIA

GRUPO III

Recientemente descrita: malformación no específica en la que la corteza cerebral es dismórfica

Primaria (alteración genética: genes tubulina) o Secundaria

Difusa o Focal (zonas específicas, simétricas)



S. Subramanian et al. AJNR 2022, 43 (1) 146-150

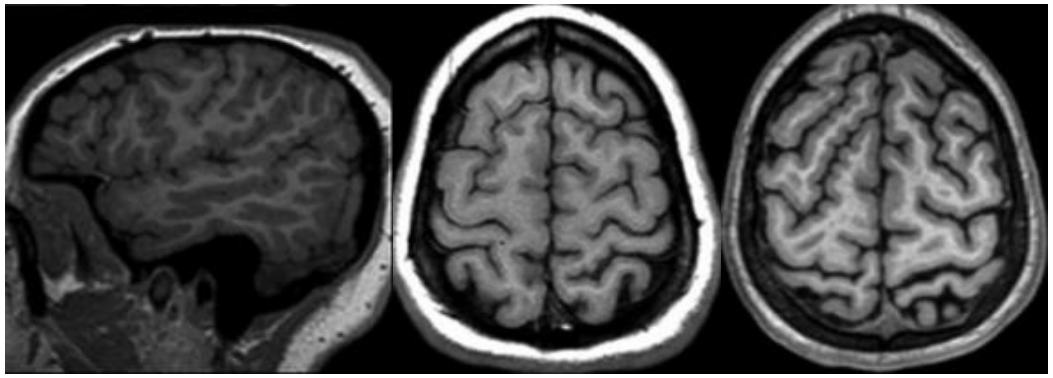
RM

GROSOR CORTICAL NORMAL, PERO CON ALTERACIÓN EN PATRÓN GIRAL > PROFUNDIDAD Y ORIENTACIÓN

- superficie cortical lisa con giros orientados radialmente
- giros estrechos separados por surcos poco profundos

- **considerarlo** > apariencia cortical "rara" (no típica de polimicrogiria, paquigiria o un patrón de giros simplificado)

* Dco. Difícil dada la variabilidad de la girificación intra e inter-individual



S. Subramanian et al. AJNR 2022, 43 (1) 146-150

DISPLASIA CORTICAL FOCAL

GRUPO I/III

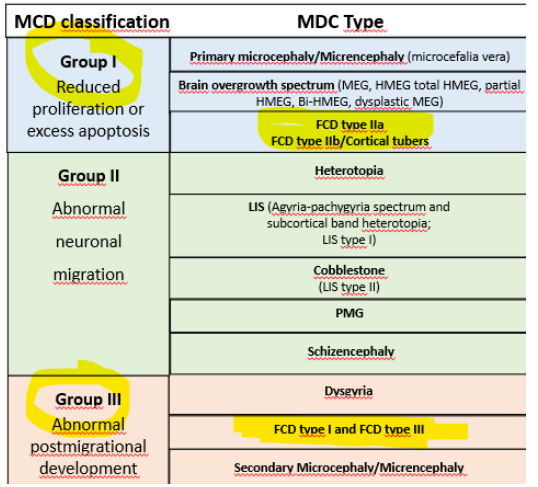
ERT: 1ª causa de en edad pediátrica y 2ª casusa en adultos

TABLE 1 The histopathology-based FCD classification update (new categories highlighted in gray)

FCDI[a]	FCDIa abundant microcolumns	FCDIb abnormal layering	FCDIc vertical and horizontal abnormalities	
FCDII[a]	FCDIIa dysmorphic neurons		FCDIIb dysmorphic neurons and balloon cells	
FCDIII[a]	FCDIIIa cortical dyslamination associated with hippocampal sclerosis	FCDIIIb cortical dyslamination adjacent to brain tumor	FCDIIIc cortical dyslamination adjacent to vascular malformation	FCDIIId cortical dyslamination adjacent to lesion acquired during early life, e.g. stroke
White Matter[a]	mMCD[b] with excessive heterotopic neurons[a]		mMCD with oligodendroglial hyperplasia in epilepsy (MOGHE)[c]	
No definite FCD on histopathology[a]	Abnormality of cortical organization remains ambiguous and histopathological findings not compatible with FCDI, II or III[d]			

"The ILAE consensus classification of focal cortical dysplasia 2022" Najm I et al. *Epilepsia*. 2022

Entidades diferentes??



DISPLASIA CORTICAL FOCAL

GRUPO I/III

Las DCF > difíciles de visualizar en neuroimagen > su detección sigue siendo un desafío:

- Estudios de calidad (protocolo específico (HARNESS), 3T), leídos en pantallas de alta resolución
- NRX especializados, equipos multidisciplinares con información clínica
- Lectura sistémica y “Second look”

Combinación de varios signos radiológicos (no todos deben estar presentes, ninguno específico)

DISPLASIA CORTICAL FOCAL: TIPO I

La RM es normal en la mayoría de los pacientes con FCD tipo I

LÓBULO TEMPORAL

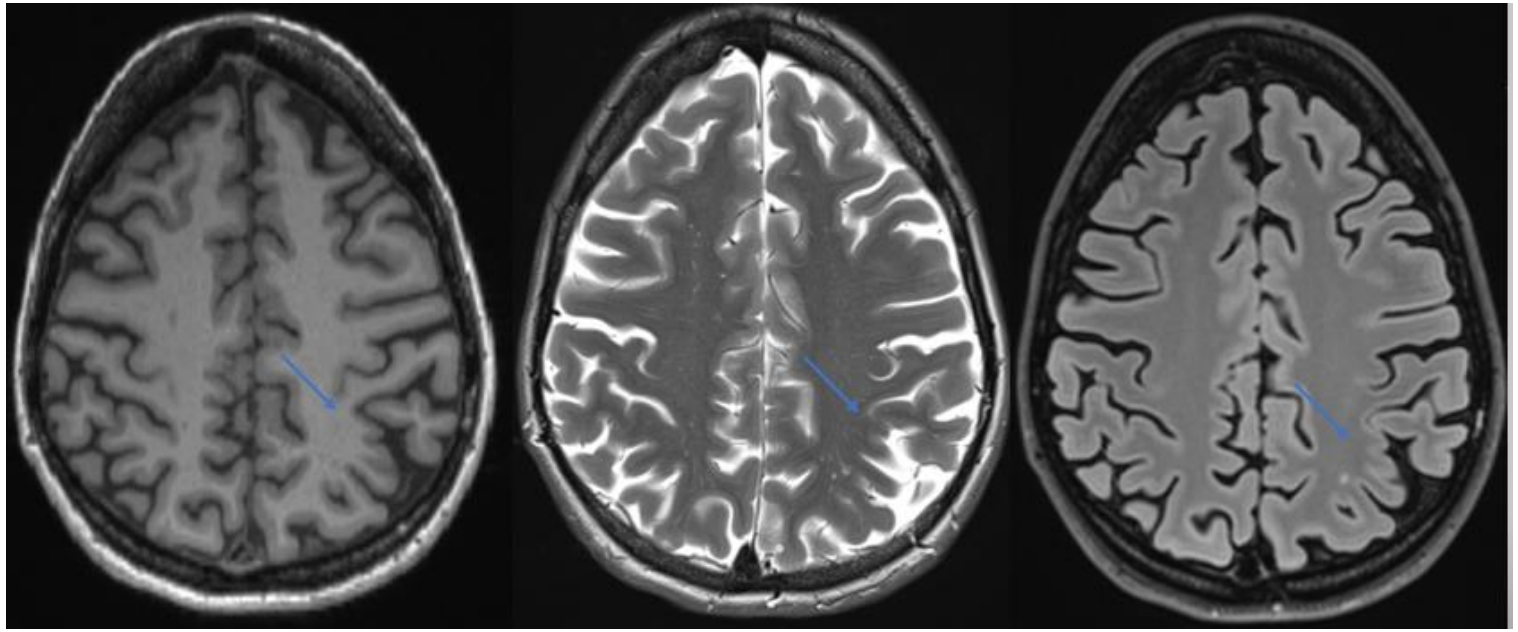
Hallazgos sutiles/no totalmente bien establecidos:

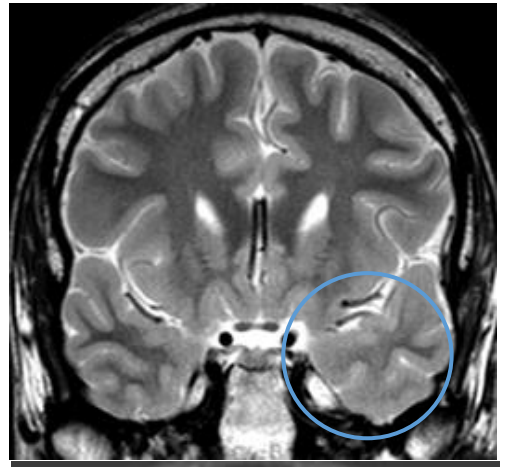
- hipoplasia o atrofia lobar/sublobar
- pérdida de volumen de la SB subcortical
- leve borramiento de la unión SB/SG con espesor cortical normal
- aumento sutil de la señal en T2/FLAIR en SB subcortical

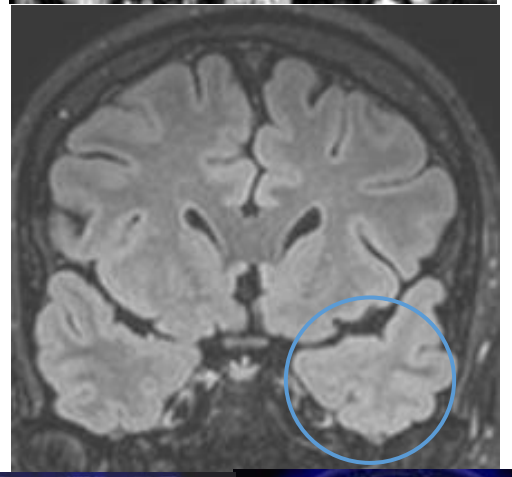
TIPO III > asociado a otra lesión:

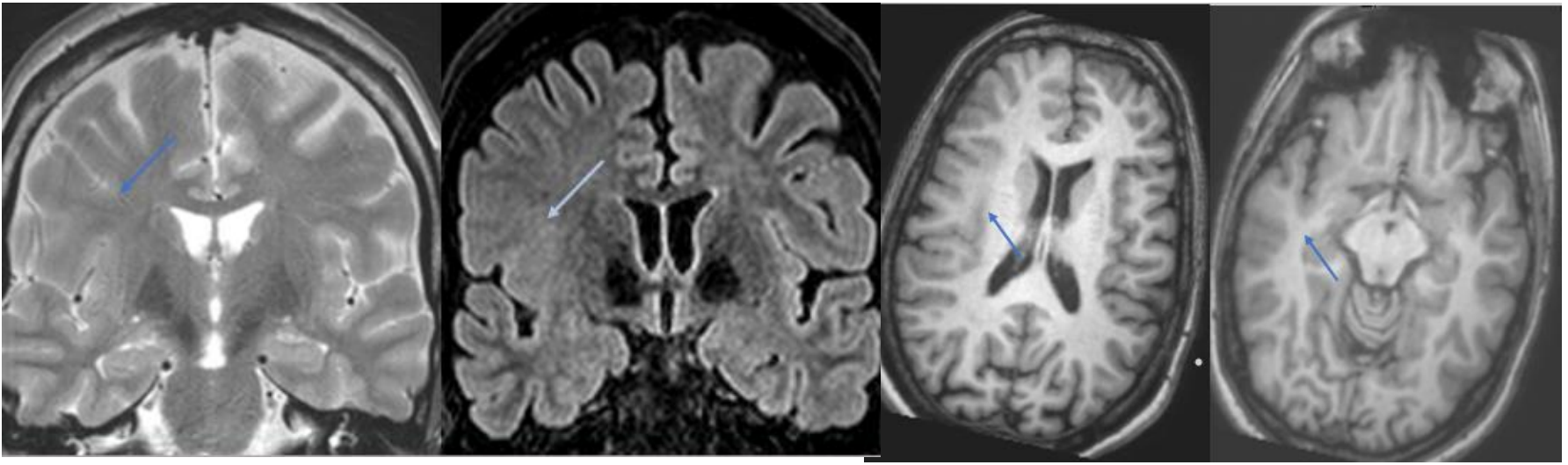
Esclerosis hipocampal / Lesión tumoral / Malformación vascular

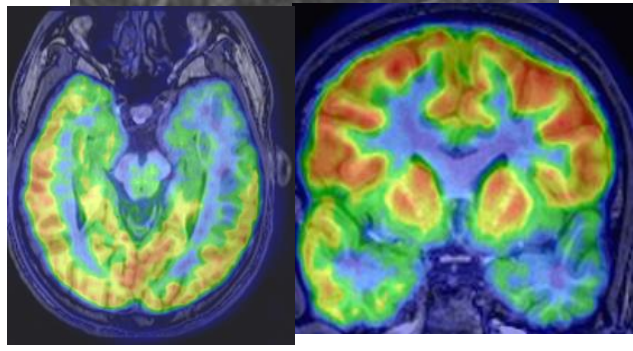
DISPLASIA CORTICAL FOCAL: TIPO I











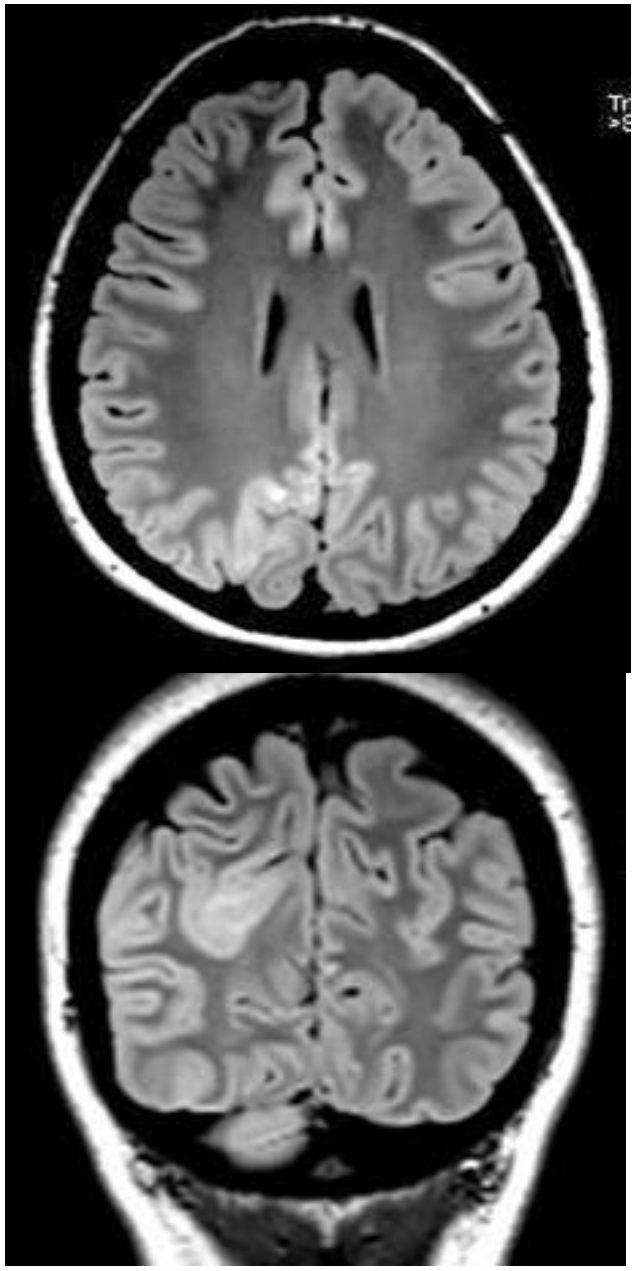
DISPLASIA CORTICAL FOCAL: TIPO II

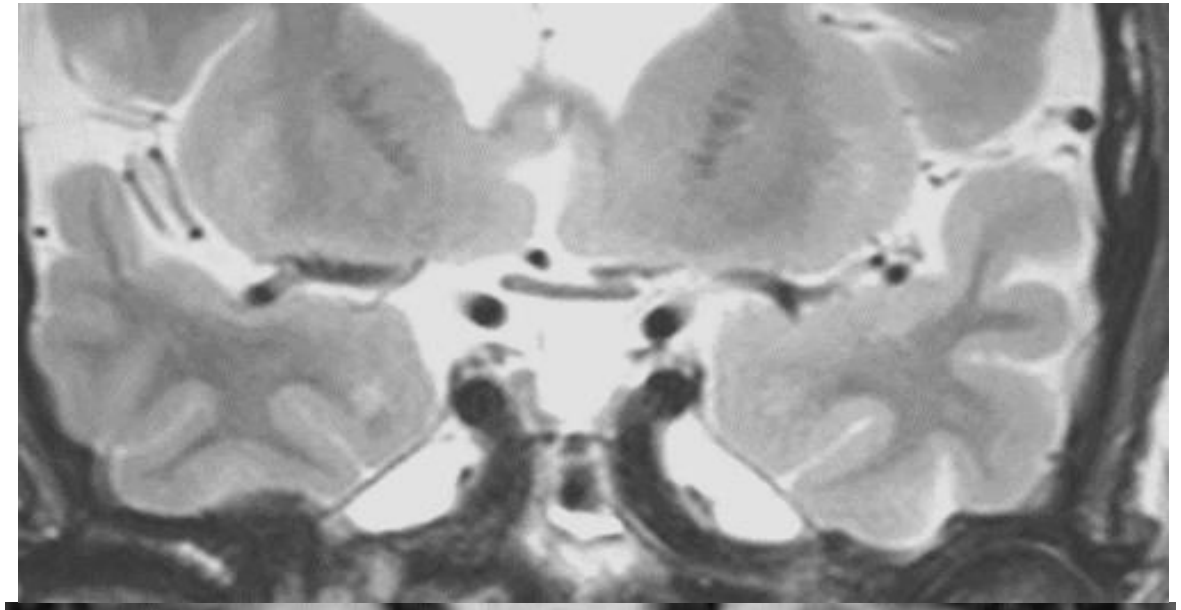
Mutación > vía mTOR

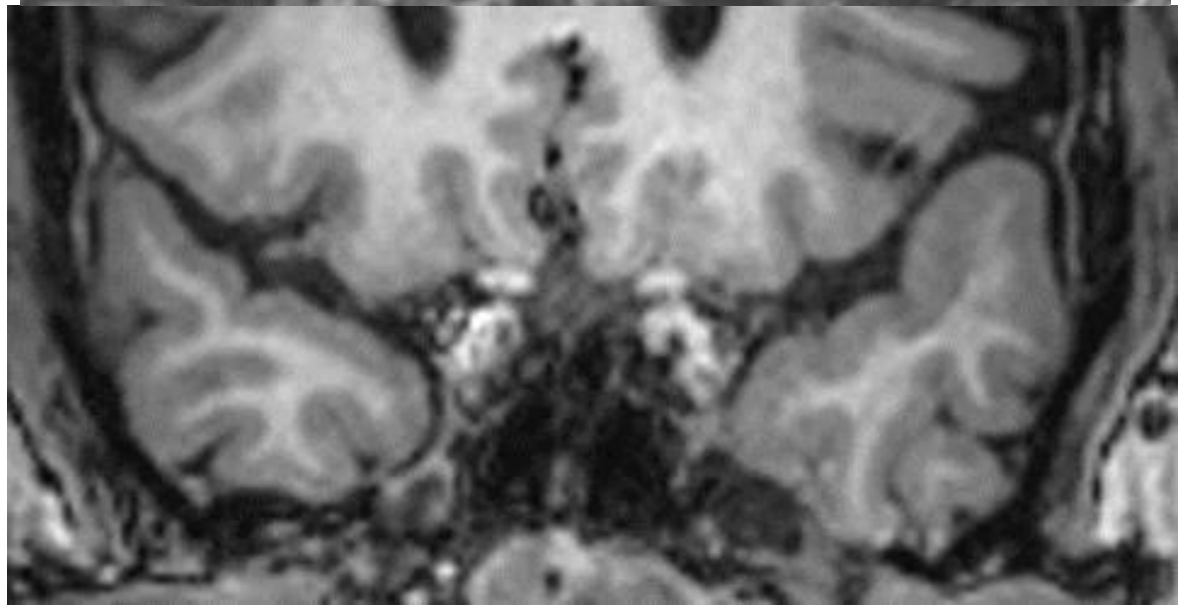
LÓBULO FRONTAL

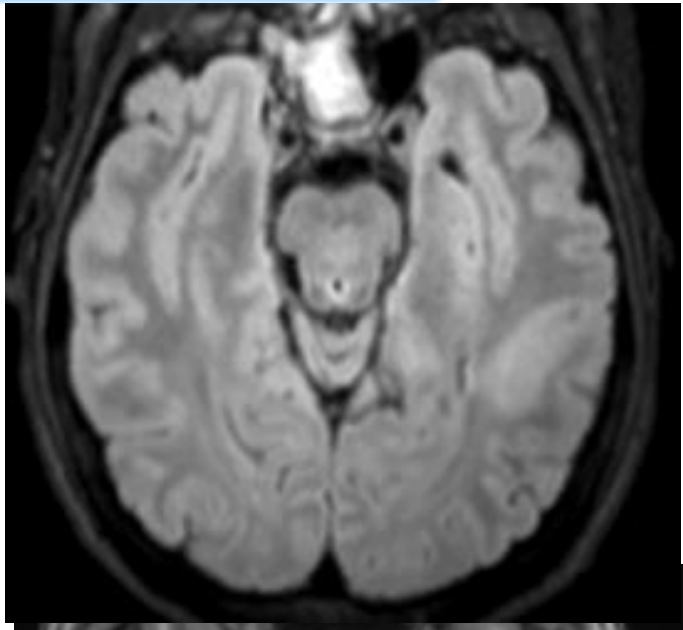
- aumento de señal en T2/FLAIR en SB subcortical/córtex
- aumento del grosor / pseudoengrosamiento cortical
- borramiento de la unión cortico-subcortical
- Patrones anormales de giros/surcos
- signo de "transmantle": disminución gradual de la alteración de la señal de SB hacia el ventrículo (IIB)
- "displasia de fondo del surco"

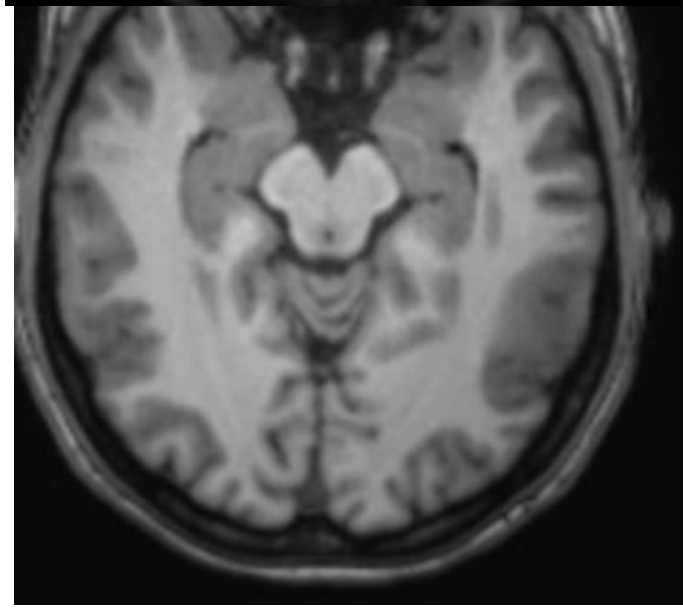
DISPLASIA CORTICAL FOCAL: TIPO II



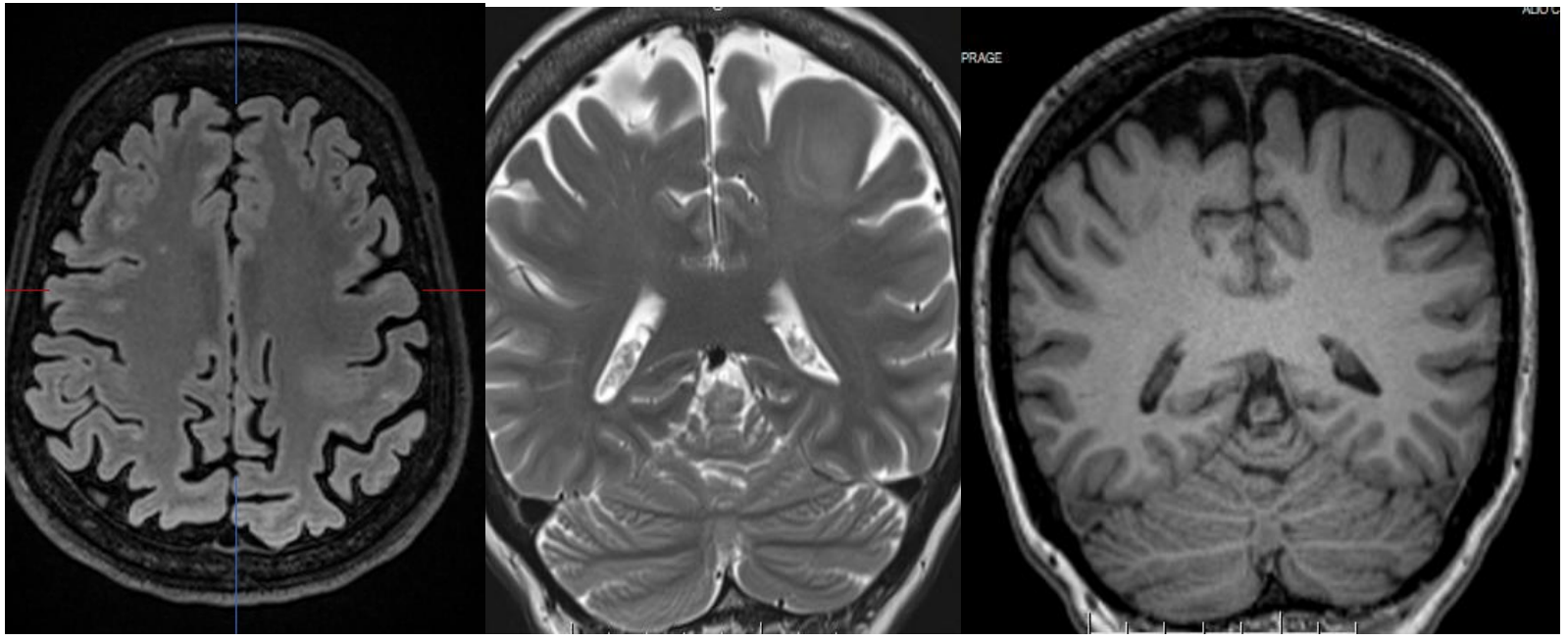


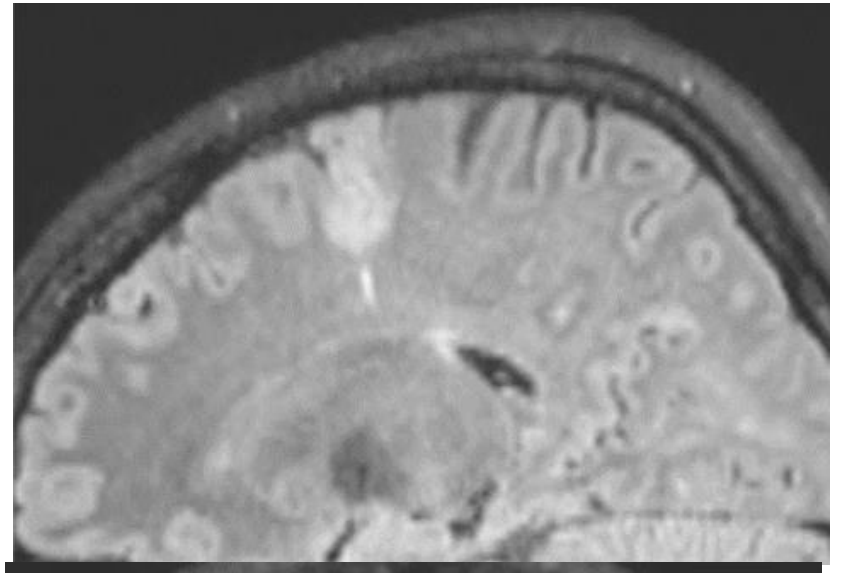


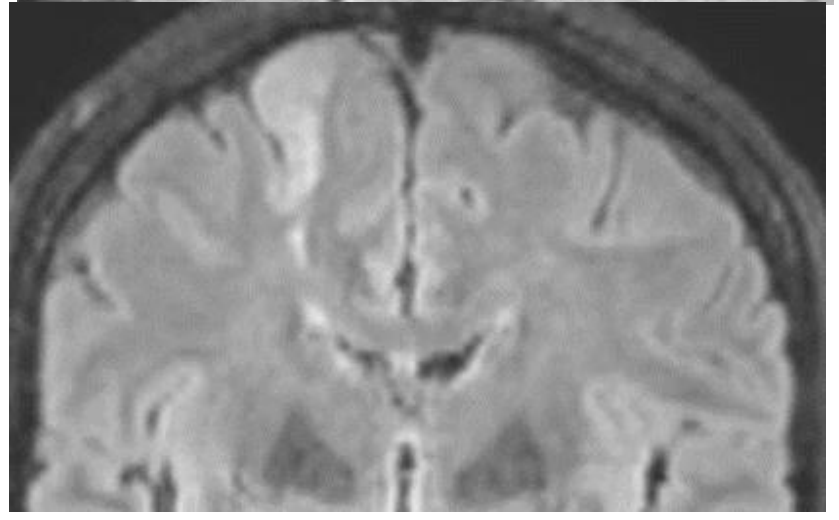


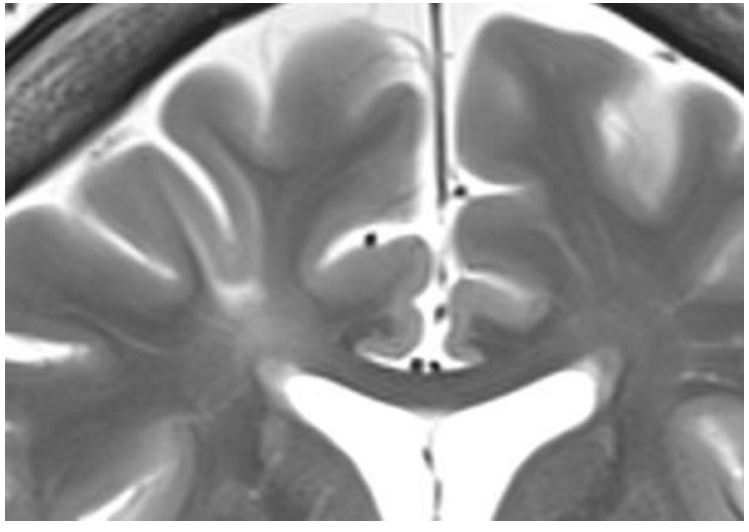


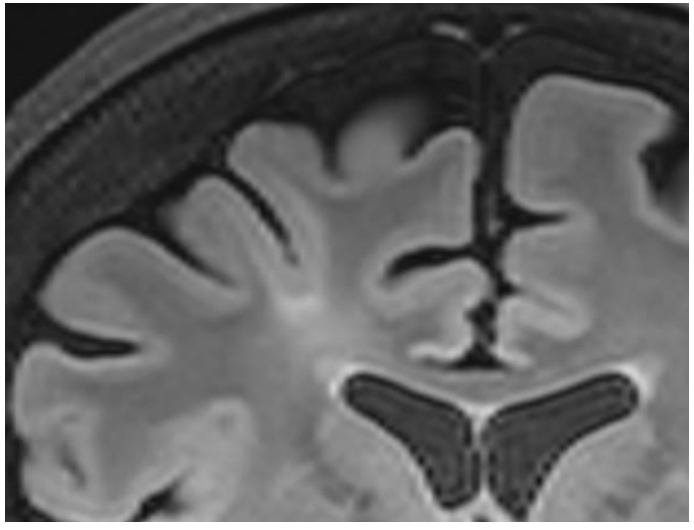
DISPLASIA CORTICAL FOCAL: TIPO II











NEUROIMAGEN: PERSPECTIVAS DE FUTURO

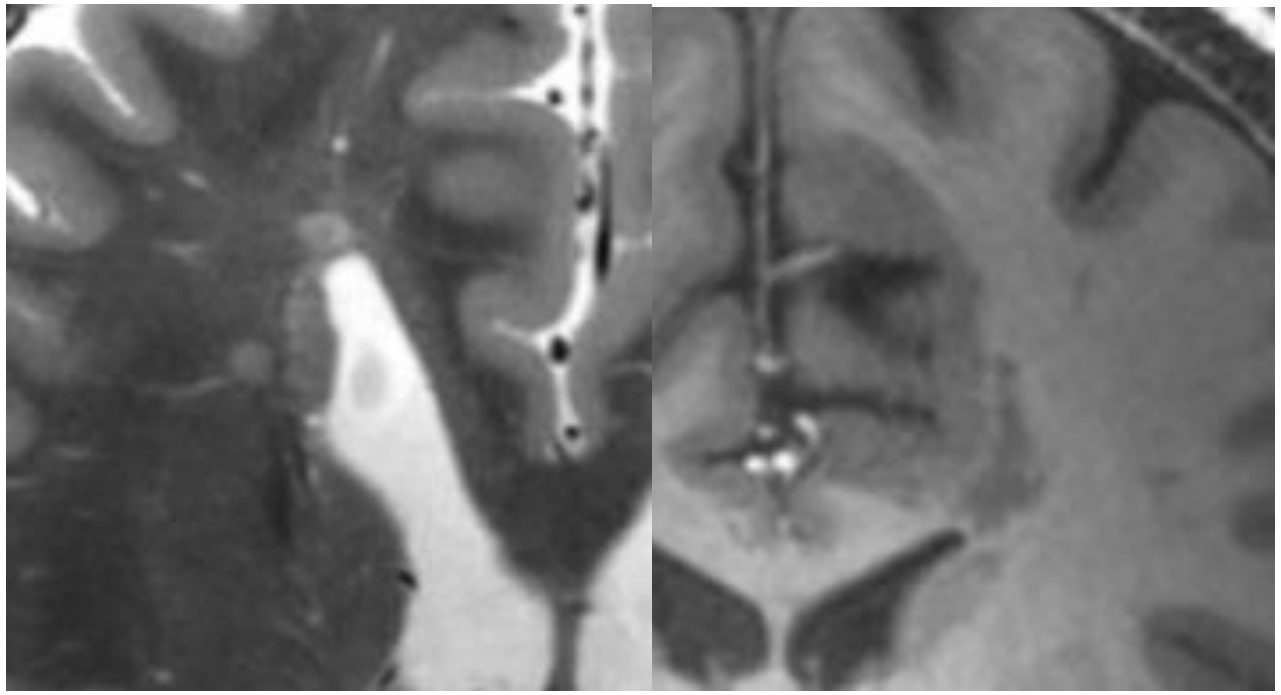
EQUIPOS DE RM 7 TESLA

POST-PROCESADO RM/MACHING LEARNING/DEEP LEARNING

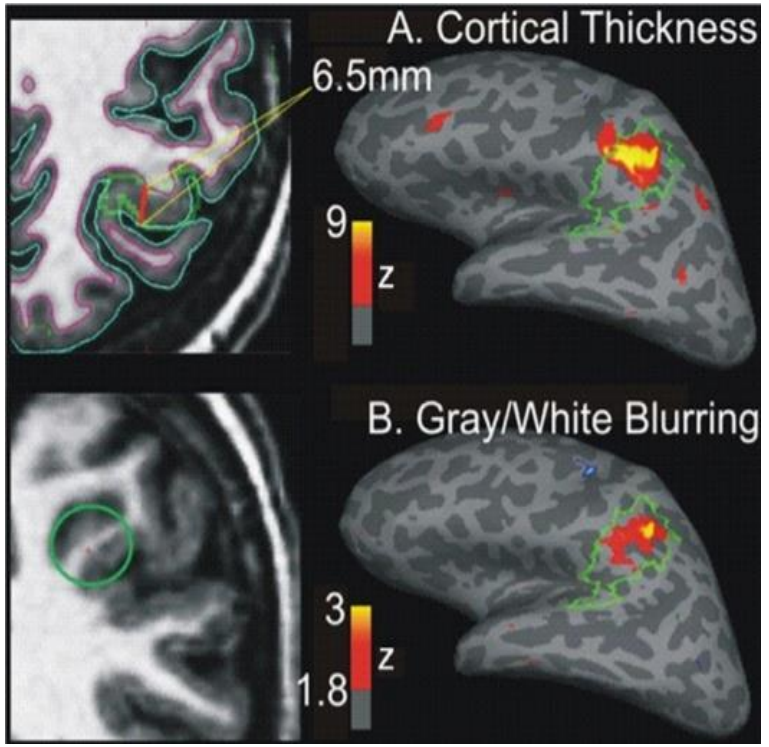
- Surface-based morphometry (SBM): Índices de morfología cortical > volumen, grosor, área y girificación

- Voxel-based morphometry (VBM): Índices de grosor cortical, borramiento de unión cortico-subcortical y profundidad de surcos > MAP program “mapas z-score”: Thickness, Junction, Extension

RM 7 TESLA



SURFACE BASED MORPHOMETRY

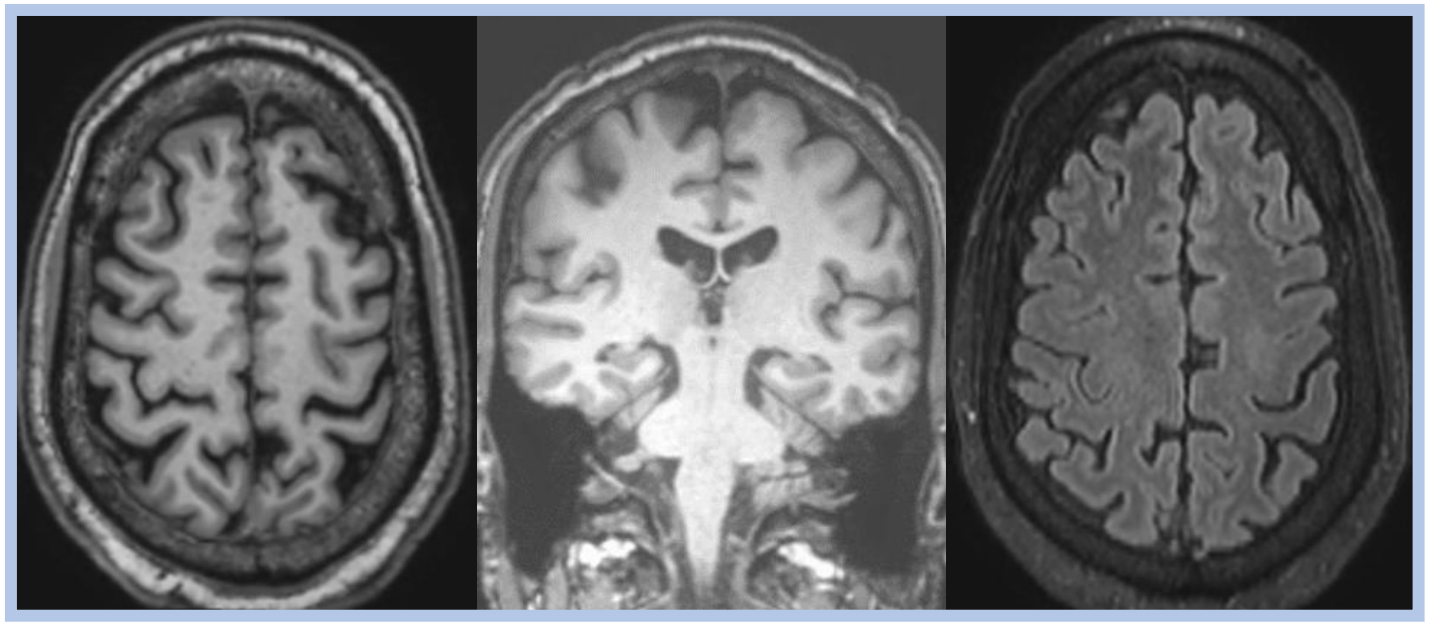


Thesen T et al. Detection of epileptogenic cortical malformations with surface-based MRI morphometry. *PLoS One*. 2011;6(2):e16430

NEUROIMAGEN: MEJORÍA DETECCIÓN

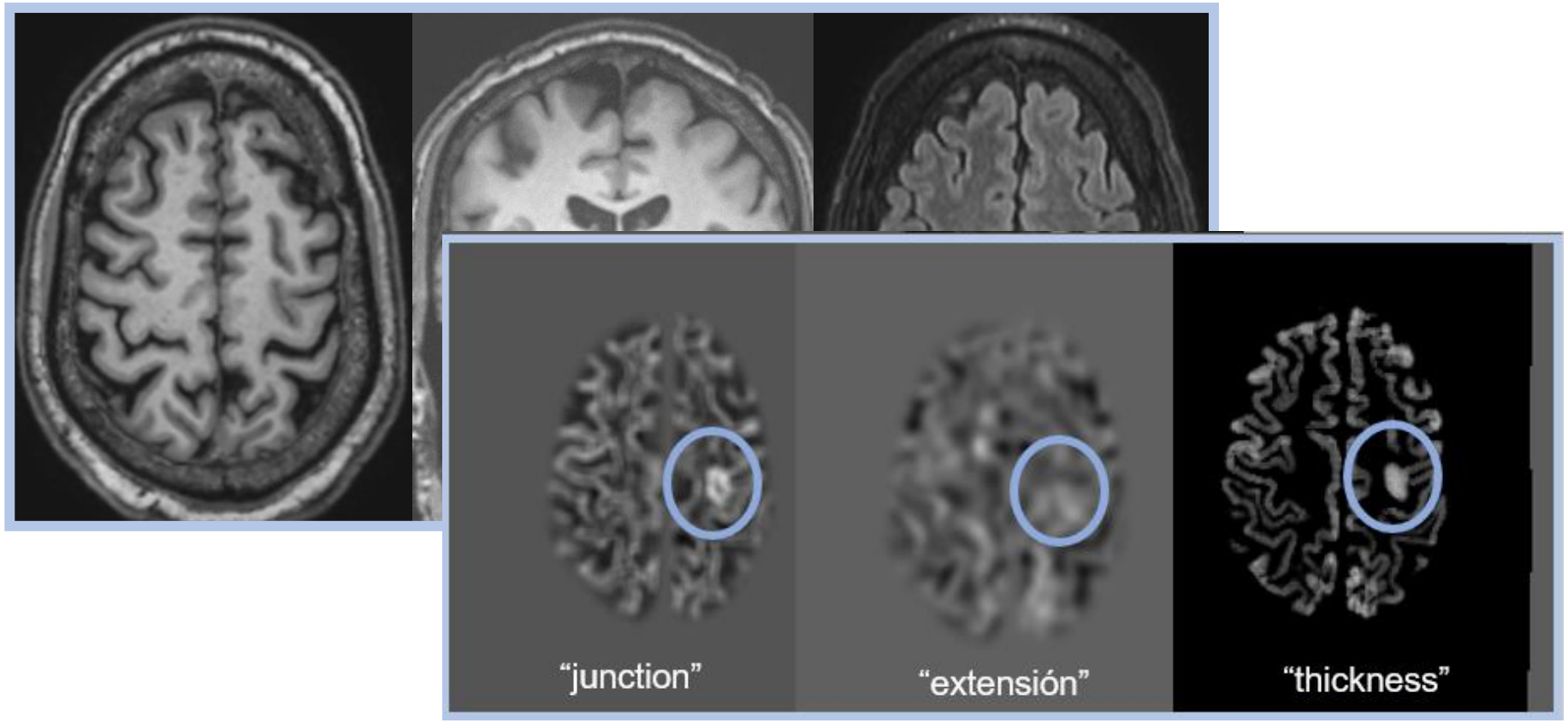
POST-PROCESADO RM : VOXEL BASED MORPHOMETRY

MAP program mapas z-score (Thickness, Junction, Extension)



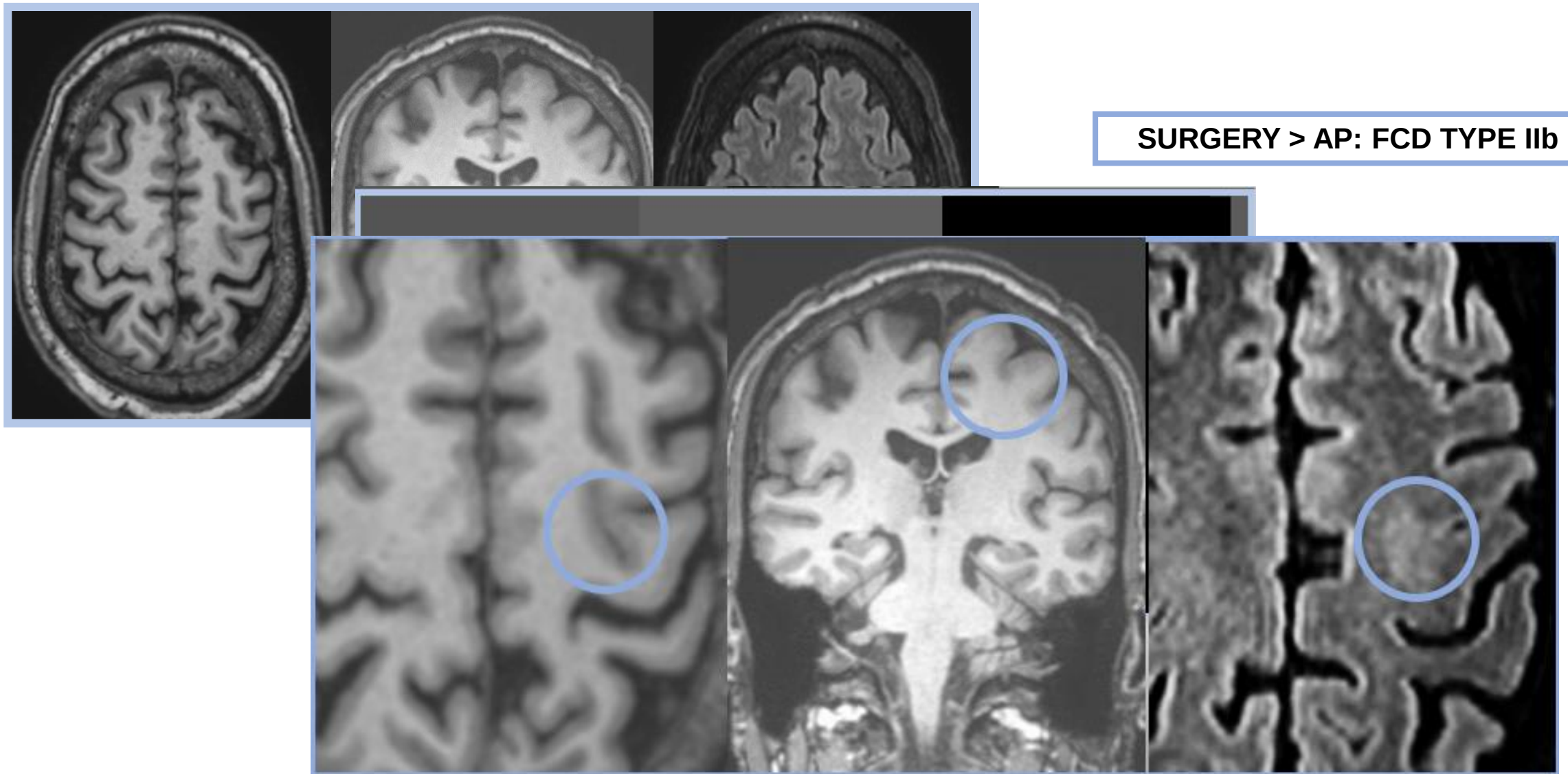
NEUROIMAGEN: MEJORÍA DETECCIÓN

POST-PROCESADO RM : VOXEL BASED MORPHOMETRY



NEUROIMAGEN: MEJORÍA DETECCIÓN

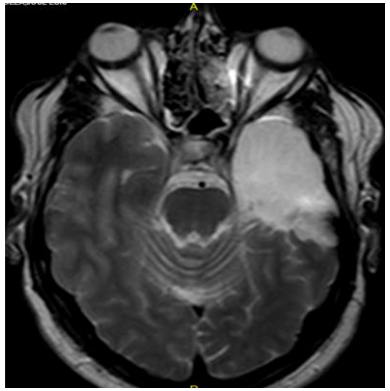
POST-PROCESADO RM : VOXEL BASED MORPHOMETRY

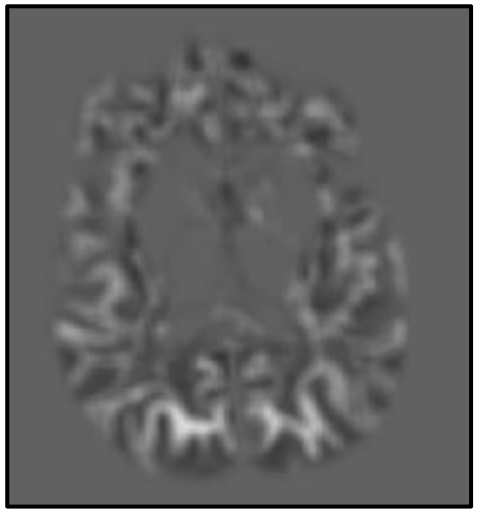


SURGERY > AP: FCD TYPE IIb

NEUROIMAGEN: MEJORÍA DETECCIÓN

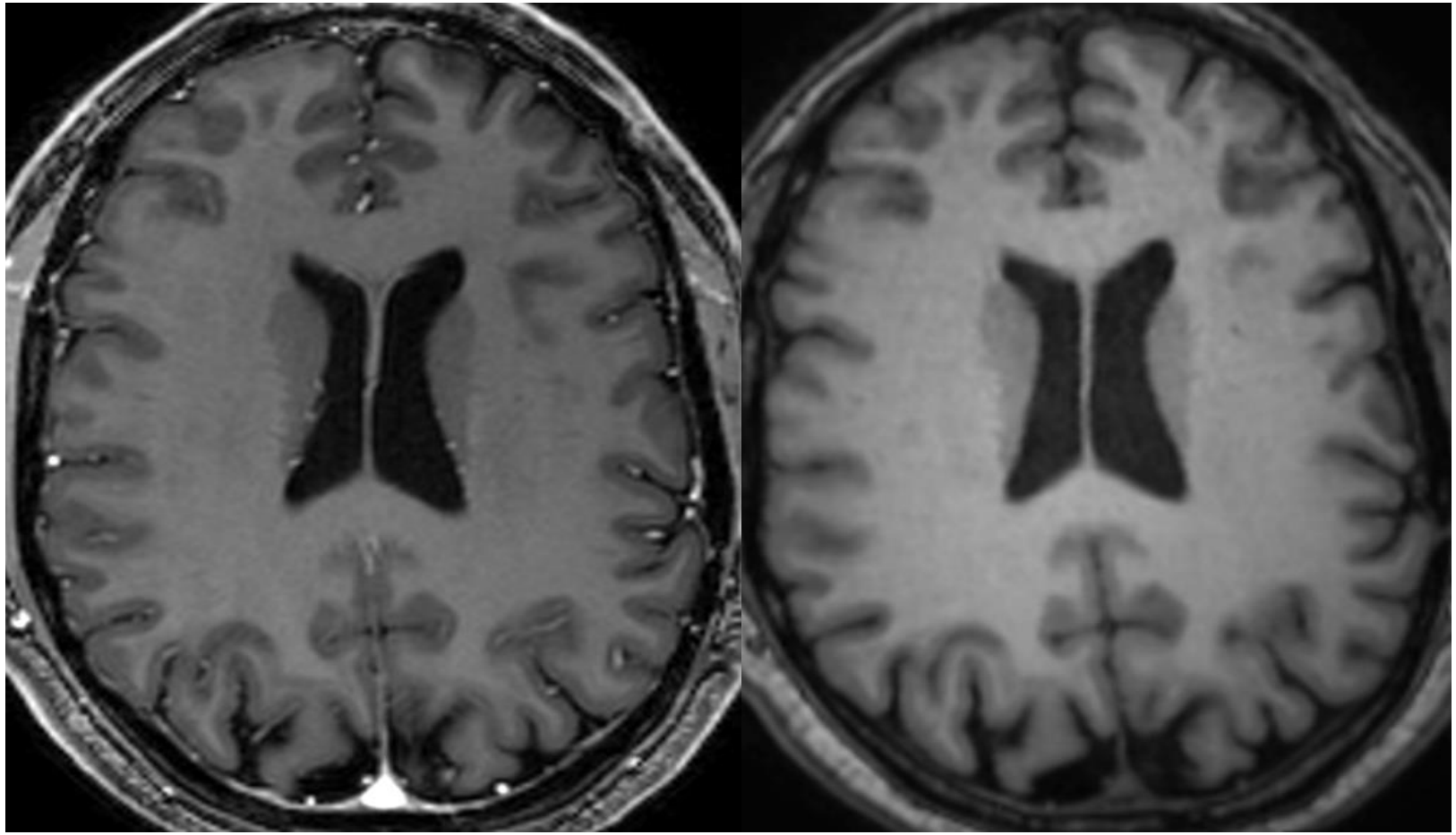
POST-PROCESADO RM : VOXEL BASED MORPHOMETRY





MAP: Juntcion

Heterotopia subcortical en Banda



Mujer 45 a. ERT temporal con manifestaciones visuales

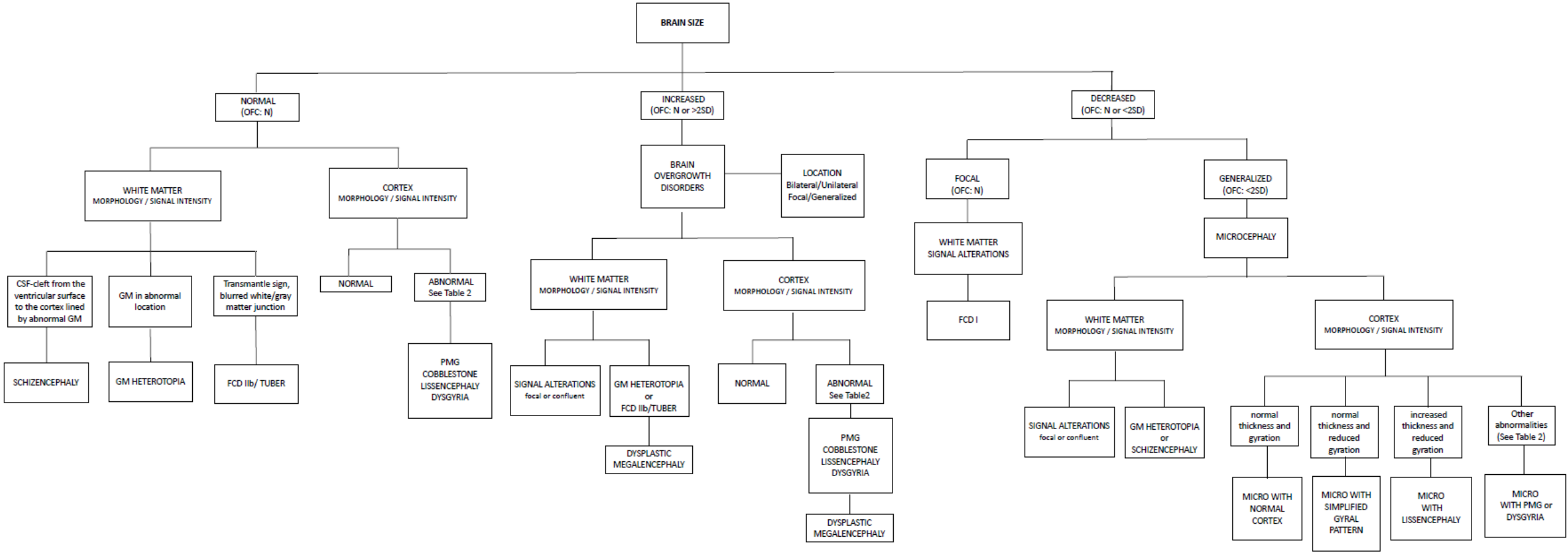
CONCLUSIONES NEUROIMAGEN DE LAS MDC

- ESTAR FAMILIARIZADO CON LAS CLASIFICACIONES Y ÚLTIMAS ACTUALIZACIONES

- ESTUDIO Y PROTOCOLO ADECUADO SEGÚN EDAD

- DESCRIPCIONES DETALLADAS Y ESPECÍFICAS > mejorar el diagnóstico

CONCLUSIONES



VARIABLY ASSOCIATED FEATURES:

- CALCIFICATIONS
- BASAL GANGLIA MALFORMATIONS
- VENTRICULAR SHAPE ABNORMALITIES
- BRAINSTEM & CEREBELLAR MALFORMATIONS
- CEREBELLAR CYSTS
- CALLOSAL ABNORMALITIES