

Central Nervous System Findings on Magnetic Resonance Imaging in Children with Epilepsy

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1. Introduction

Epilepsy is a relatively frequent pathology in child populations, with an annual incidence rate ranging from 41 to 67 per 100 000 cases¹⁻⁷. In the past decade, many important advances related to epilepsy have arisen. On one hand, new diagnostic methods (video electroencephalography monitoring, structural and/or functional neuroimaging, metabolic and genetic analysis, etc) facilitate the diagnosis and the syndromic classification; on the other hand, the availability of the new antiepileptic drugs is conditioning new therapeutic possibilities⁸⁻¹¹.

The International League Against Epilepsy classification for epilepsy and epileptic syndromes suggests prognosis consequences, because it allows estimating outcome and therapeutic responses¹²⁻¹⁵. In this way, structural neuroimaging plays an important role in the evaluation, management, and treatment of the child with epilepsy. The role of neuroimaging is to detect an underlying cerebral lesion that may be causally related to the child's seizure disorder. Magnetic resonance imaging (MRI) is the elective of all structural imaging tool. MRI is considerably superior to X-ray CT in terms of its sensitivity and specificity for identifying subtle abnormalities. The principal role of MRI is in the definition of the structural abnormalities that underlie seizure disorders (tumours, malformations of cortical development, hippocampal sclerosis, neurocutaneous diseases, vascular malformations, traumatic lesions, strokes, residual lesions, etc.) and to contribute to the aetiologic diagnosis and classification of the different epilepsies and epileptic syndromes, and thereby provide an accurate prognosis for patients^{11,16-18}. In Spain, there is limited information about its current use in the initial evaluation of pediatric epilepsy and about its performance during the initial diagnosis of epilepsy, which suggests that a descriptive study of MRI findings in epilepsy in children would be necessary.

The aim of this study is to analyze the epidemiological characteristics and proportional distribution of the epilepsy and epileptic syndromes in children, and to describe the central nervous system findings on MRI in these patients.

2. Methods

2.1 Subjects

The study is based on data obtained from 457 medical records of a random selection among the patients diagnosed with epilepsy in the Paediatric Neurology Unit of the Navarre Hospital Complex in Pamplona who were examined from January until December 2009. The patients were included on the condition that MRI was performed at diagnosis according to a standardized paediatric seizure protocol.

The Navarra Hospital Complex of Pamplona is the neuropediatric reference center in Navarra and is the place where the neuropediatric and neurophysiology and magnetic resonance imaging units are located. The functional and structural organization of the health service in Navarra provides referral of all patients with suspected seizures or epilepsy from the health care centers or secondary hospitals (located in Tudela and Estella) to the reference hospital. A neuropediatric examination and follow-up are performed, and, finally, a syndromic diagnosis is established in most patients.

Information recorded from every patient includes epidemiologic data (sex, age at onset, and personal and familial history of epilepsy and febrile seizures) and clinical data (seizure types, neurologic findings, and associated pathologic conditions), as well as the results of complementary studies (electroencephalogram and neuroimaging, including genetic, metabolic, and neurophysiologic studies when required) in order to classify seizures according to etiology as idiopathic, symptomatic or cryptogenic.

The International League Against Epilepsy criteria for epileptic seizures and epileptic syndromes and guidelines for epidemiologic studies have been applied for diagnosis and classification^{12-15,19}. Therefore, epilepsy was diagnosed at the time of a second unprovoked seizure, and multiple seizures in a 24-hour period were considered a single episode. Patients with neonatal seizures only, febrile seizure and other acute symptomatic seizures were excluded. The syndromic diagnosis corresponding to each patient was discussed by members of the neuropediatric unit, and a final diagnosis was reached based on concurrence of the members.

3. Magnetic resonance imaging

MRI was performed in all patients at the onset of diagnosis according to a standardized paediatric seizure protocol. The standardized pediatric seizure protocol consisted of the following scanning sequences:

- T2-weighted fast spin-echo (FSE) images and proton density-weighted in axial plane with 5 mm thick slices.
- T2-weighted Fluid attenuated inversion recovery (FLAIR) images in the coronal plane, with 5 mm thick slices.
- T1-weighted FLAIR images in the sagittal plane, with 5 mm thick slices.
- T1-weighted FLAIR images in the axial plane, with 3 mm thick slices.
- Diffusion-weighted (DW) images in the axial plane.

Complementary sequences:

- T2-weighted gradient-echo images in the axial plane, with 5 mm thick slices, for the detection of calcifications or hemosiderine deposits.
- T2-weighted FSE images in the coronal plane, with 3 mm thick slices, for the study of temporal lobe seizure foci.

The scoring system used for MRI examinations in this study classifies various abnormal features by location²⁰. Abnormal features include volume loss, leukomalacia/gliosis, encephalomalacia, other white-matter lesions, heterotopia, cortical dysplasia, other gray-matter lesions, mass lesions, vascular lesions, ventricular enlargement, prominence of the extra-axial spaces, hippocampal atrophy or signal abnormality, and others structural abnormalities.

Abnormalities on MRI were classified as either significant or nonsignificant based on a system of classification previously developed²¹⁻²³. A significant abnormality was defined as a MRI finding reasonably likely to be related to seizure disorder. These were defined as at least one of the following: leukomalacia/gliosis, encephalomalacia, any gray-matter lesion, mass lesion, hemorrhage, vascular lesion, hippocampal abnormality, ventricular enlargement >1.5 cm, or prominence of extra-axial fluid spaces >1.0 cm.

Some potential overlap in scoring encephalomalacia and leukomalacia/gliosis was recognized. Encephalomalacia was generally thought to signify "cystic encephalomalacia" and to involve cortical regions. If there was some signal abnormality consistent with gliosis adjacent to an area of encephalomalacia, this was scored as encephalomalacia. If there were other discrete areas of abnormal signal consistent with gliosis, these were scored as (additional) areas of leukomalacia/gliosis.

All of these studies were read and coded by two neuroradiologists with experience involved in this study. Rater was blind to other rater scoring and to other clinical data (e.g., electroencephalogram findings), except for knowing that the child had presented with a seizure.

The computer program SPSS 17.0 for Windows (Chicago, Illinois, USA) was used to perform the statistical analysis (descriptive study).

4. Results

Age distribution was 78 infants (from 1 to 12 months of age), 157 in early childhood (from 1 to 6 years), 134 school-aged children (from 6 to 10 years), and 88 adolescents (from 10 to 15 years).

4.1 Infants

The sample consisted of 78 patients (37 males and 41 females). In infants, most of the seizures were symptomatic (53.8%), whereas others were idiopathic (25.6%) or cryptogenic (20.5%). Table 1 shows the distribution of the epilepsies and epileptic syndromes in infants. Epilepsies attributed to and organized by structural or metabolic conditions (34.6%) and West syndrome (30.8%) were the most prevalent syndromes.

Epilepsies attributed to and organized by structural or metabolic conditions (n=27) were secondary to perinatal asphyxia (figure 1), purulent meningitis, congenital malformations of the brain (figure 2), Aicardy syndrome (figure 3), inherited metabolic disorders, phakomatoses (figure 4) and venous thrombosis. Among patients diagnosed with West syndrome, etiology was symptomatic in 62.5% of the cases (n=15); this means, 6 cases related to perinatal ischaemic or anoxic lesions, 3 cases with Down syndrome, 2 cases with tuberous sclerosis, and 1 case related with pathologies as subcortical band heterotopia (figure 5), semilobar holoprosencephaly, neonatal meningoencephalitis (figure 6) and perinatal intracranial hemorrhage.

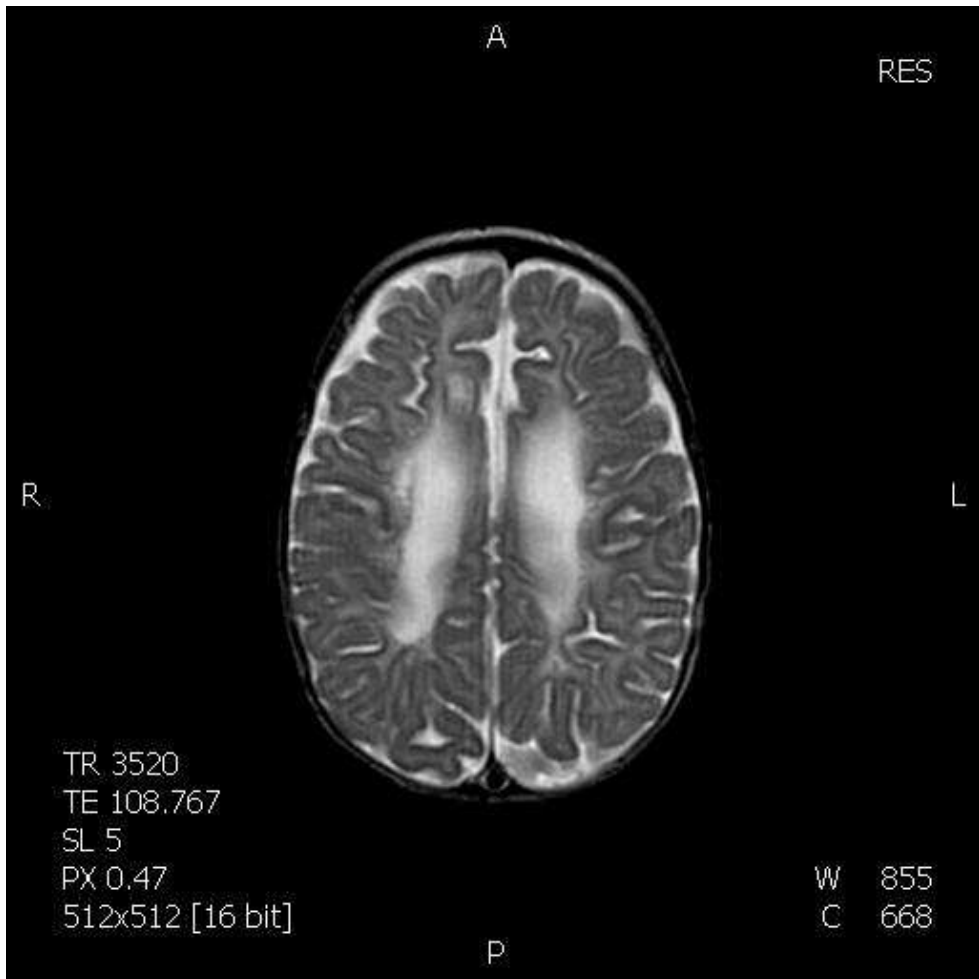


Fig. 1. Chronic-atrophic stage and cystic periventricular leukomalacia: Spin echo (SE) T-2 image showing periventricular white matter atrophy and small cystic lesions adjacent to right ventricle.

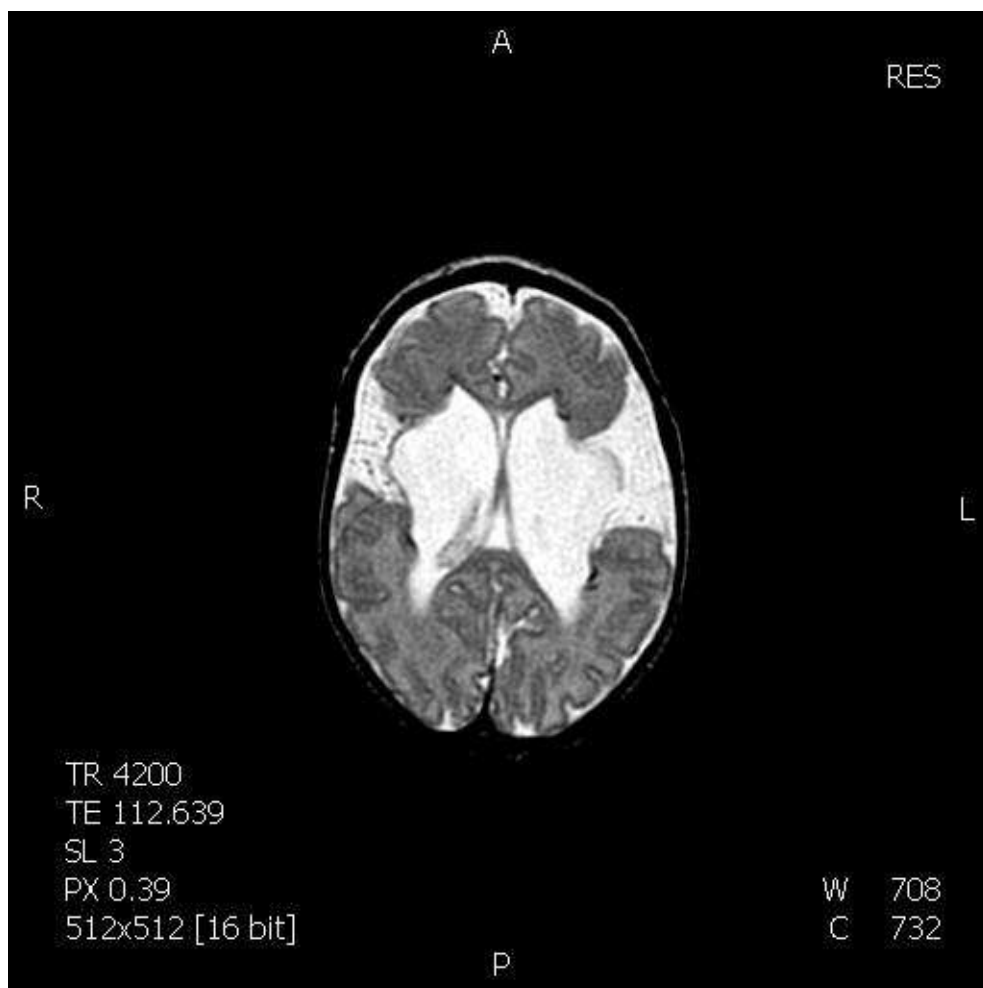
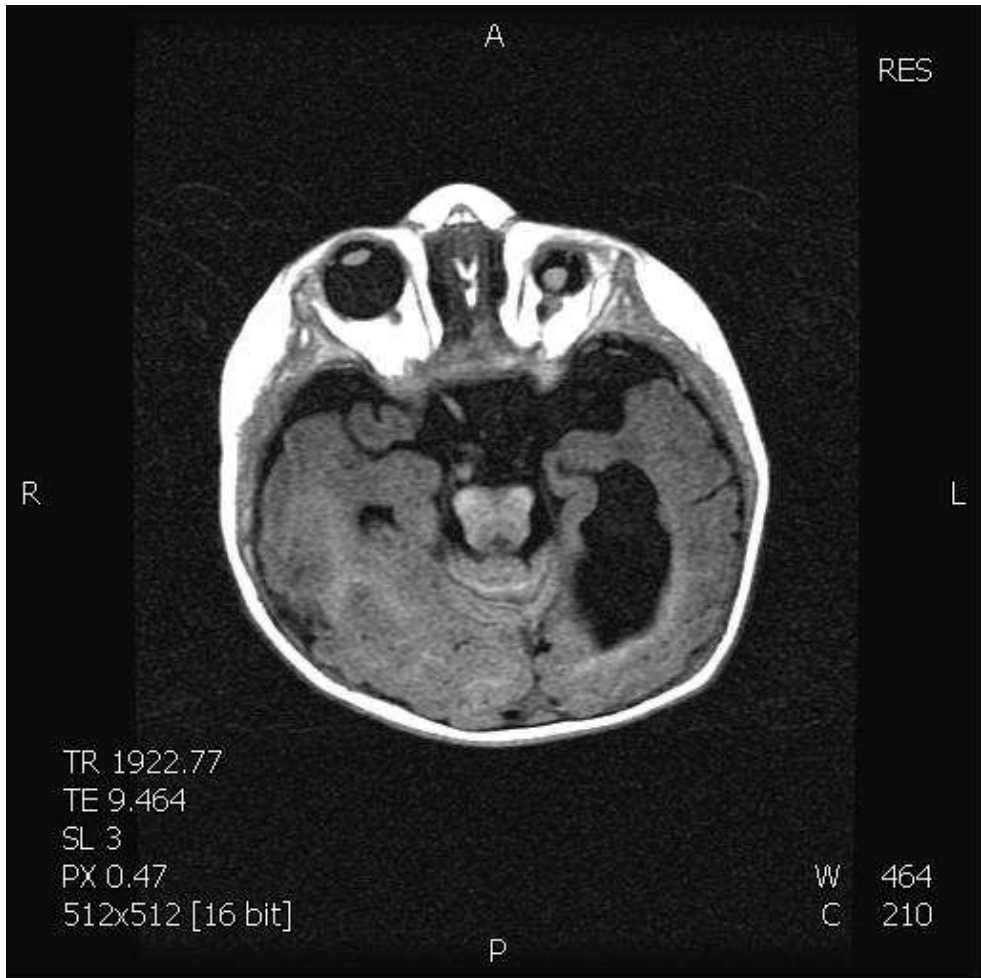
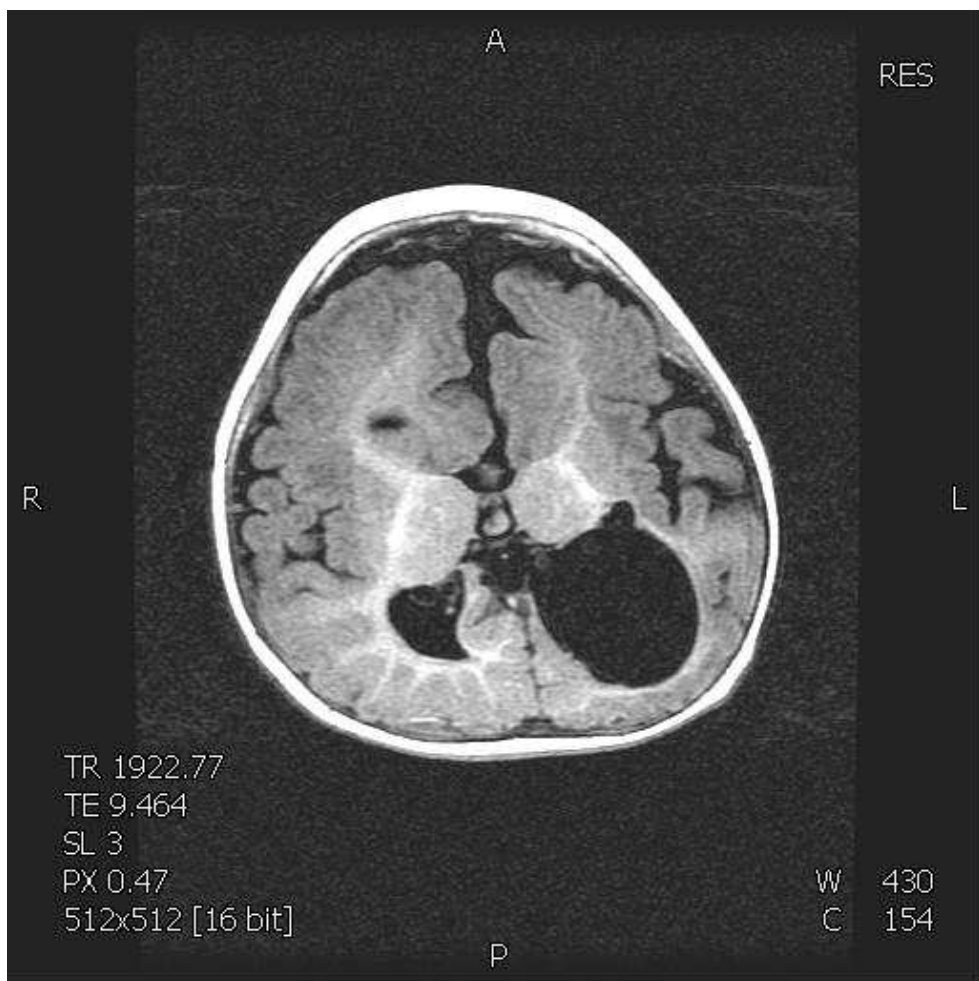


Fig. 2. Open lip schizencephaly: SE T-2 weighted image showing localized parenchymal defects as a split between subarachnoid and ventricular space. Small low-signal periventricular lesions related to calcifications (clinical suspicion of perinatal infection).



(a)



(b)

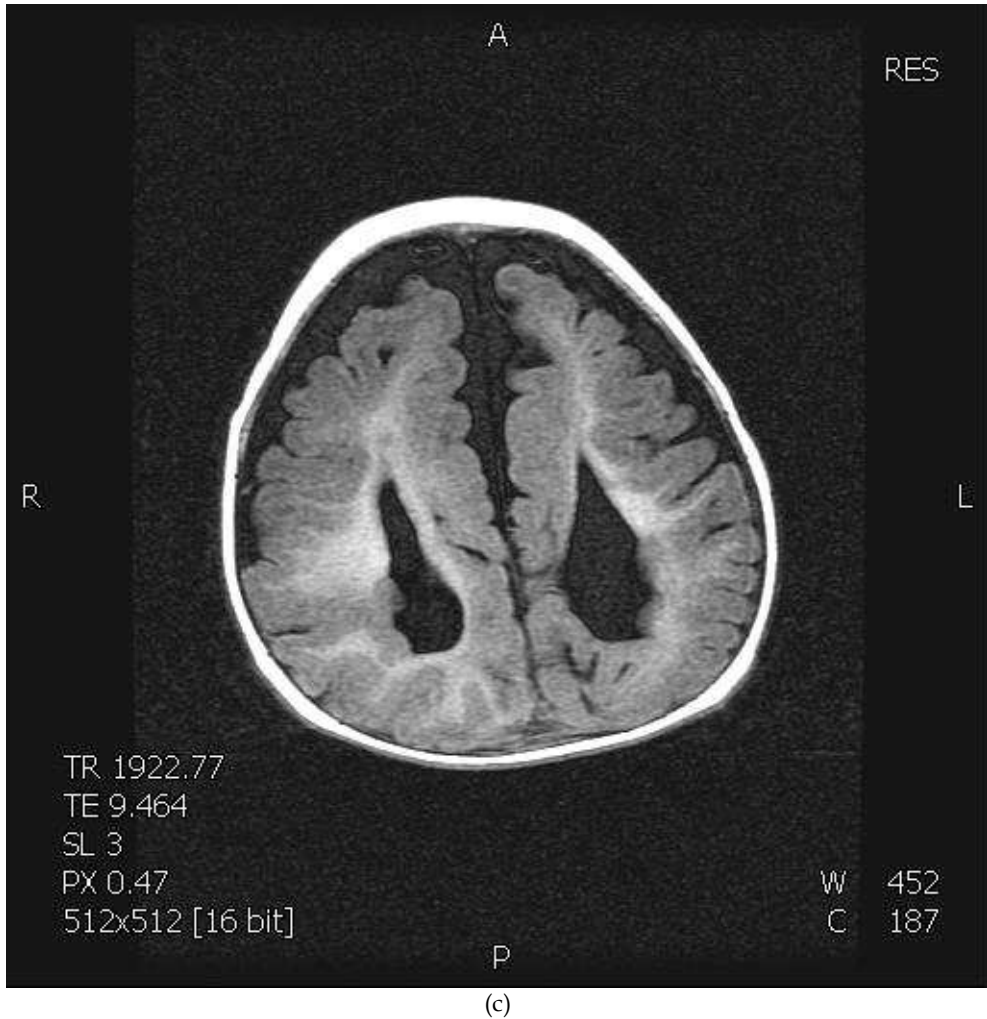
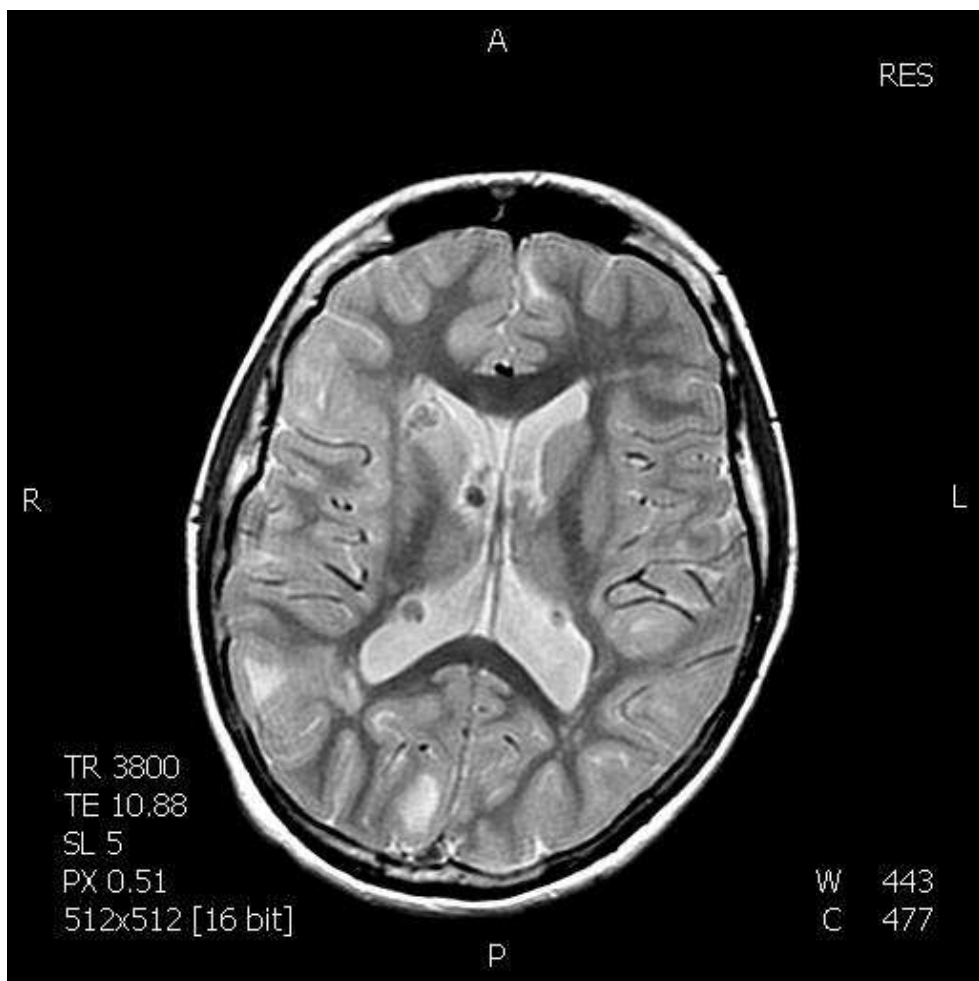


Fig. 3. (a, b, c). Aicardi syndrome: FLAIR T1 images showing choroid plexus cysts that expand the occipital horn in left ventricle, subependymal heterotopia adjacent to both lateral ventricles, agenesis of the corpus callosum that causes a parallel layout of the lateral ventricles and left microphthalmia with posterior lens luxation.



(a)

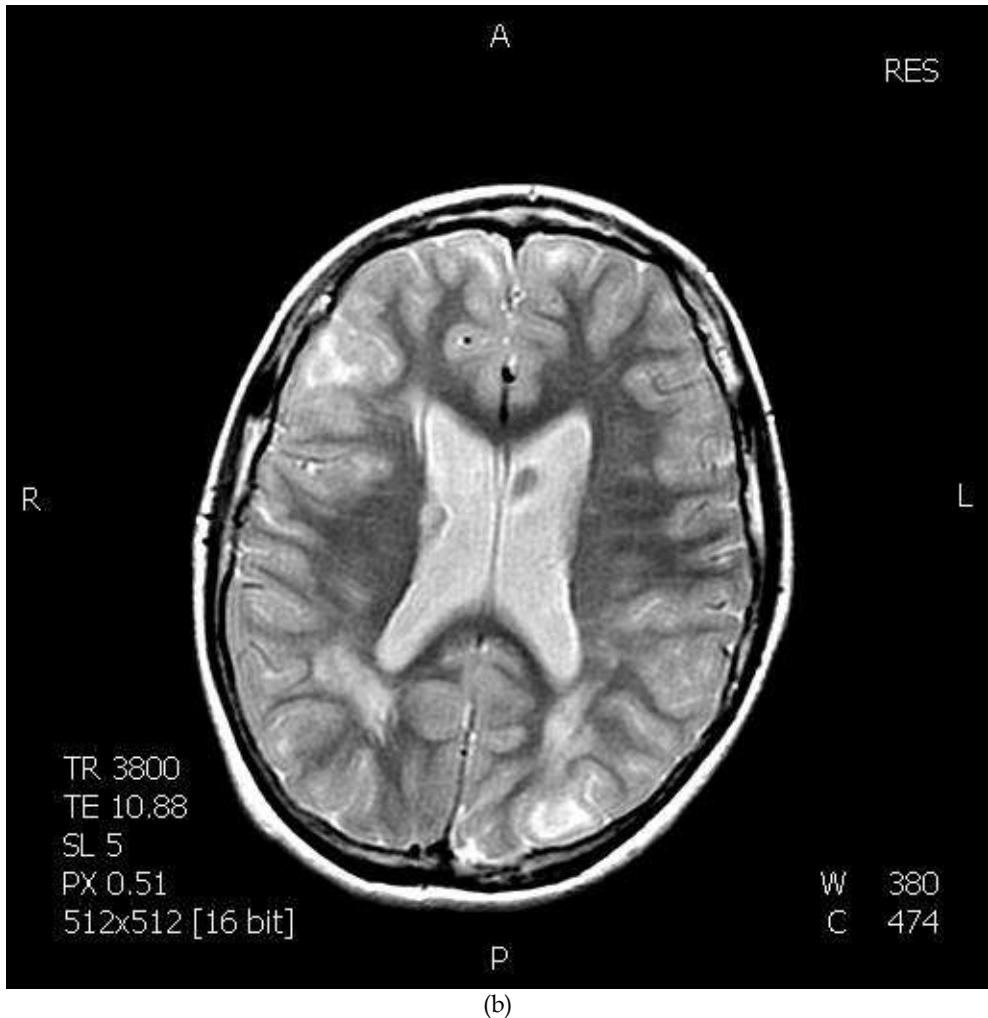


Fig. 4. (a, b). Tuberos sclerosis: SE 3800/11 images displaying subependymal hamartomas bulging towards the ventricular space, giant cell astrocytomas near the foramen of Monro (the right ventricle astrocytoma showing calcifications), brain hamartomas seen as hyperintense subcortical lesions and portions of dysplastic white matter which follow the pathway of neuronal migration, revealed as linear tracks of radial layout in the white matter.

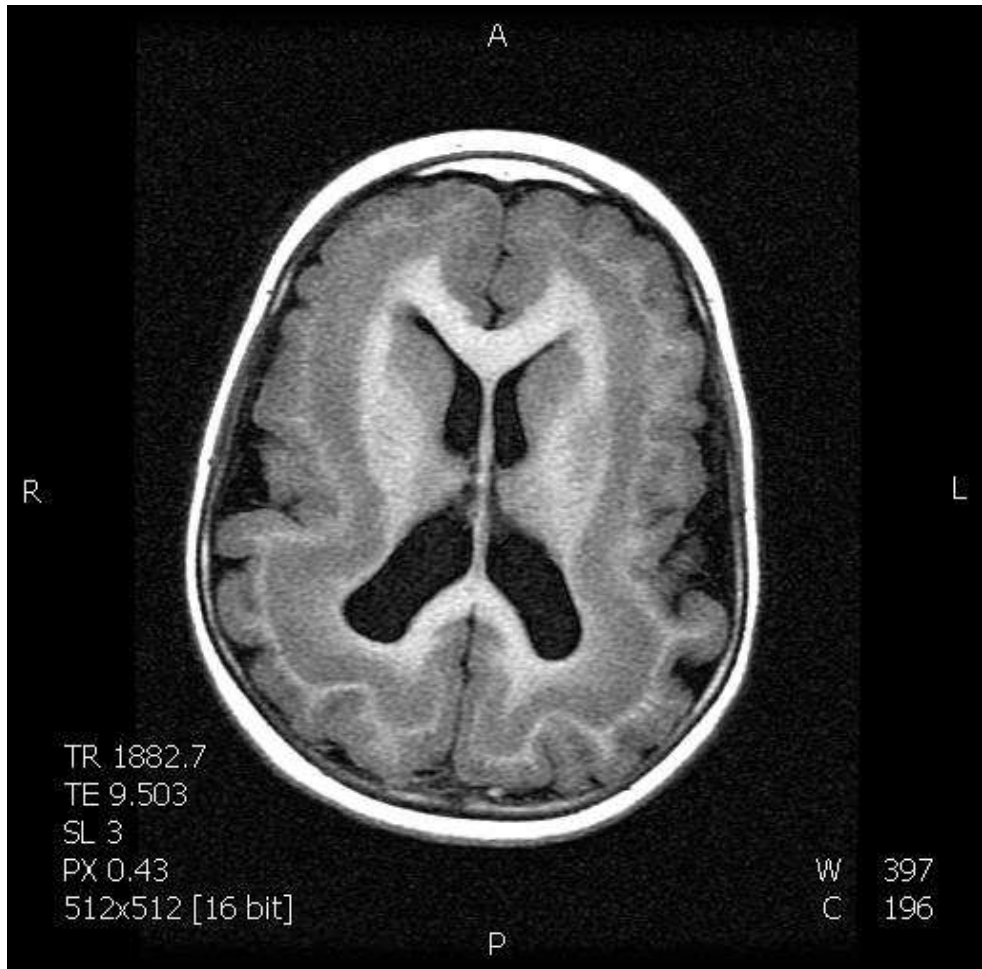


Fig. 5. Band heterotopia: FLAIR T1 images show a thick band of heterotopic grey matter, which is separated from the cortex by a thin layer of myelinated white matter.

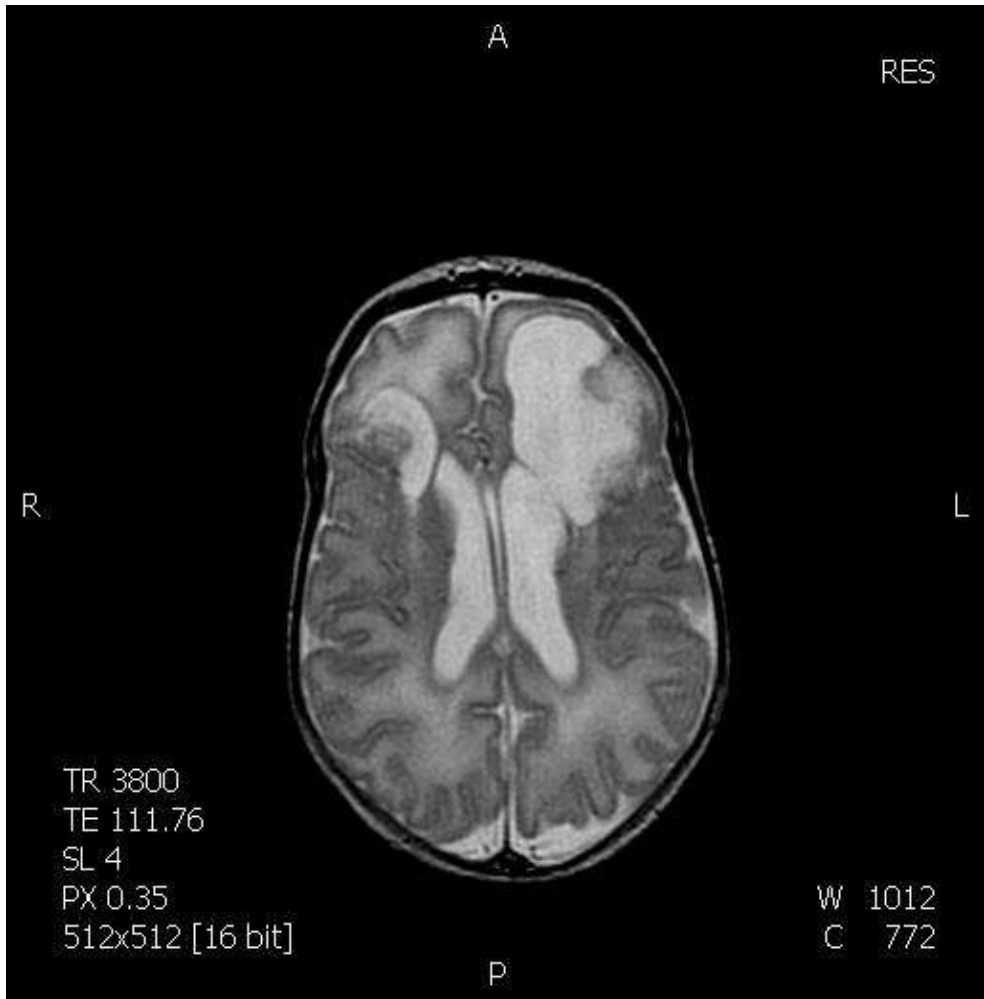


Fig. 6. Frontal bilateral porencephalic lesions as sequelae of meningitis. SE T2 image shows two large frontal porencephalic lesions, being the left one communicated with the frontal horn.

Of 78 infants in this study, 42 (53.8%) demonstrated at least one MRI abnormality. Thirty-three (42.3%) manifested MRI abnormalities that were classified as significant because they were considered to be potentially related to the seizure condition.

Table 2 presents the number of infants with MRI abnormalities. Because different abnormalities can affect the same locations for a given child, the sum of abnormalities may exceed the total number of children. Of 42 children with at least one MRI abnormality, the most common abnormalities included white-matter lesions (28.7%), volume loss (22.8%), gray-matter lesions (18.8%) and ventricular enlargement >1 cm (13.9%).

West syndrome	24
Myoclonic epilepsy in infancy	5
Benign familial infantile epilepsy	3
Benign non-familial infantile epilepsy	1
Dravet syndrome	10
Reflex epilepsy (tactile evoked myoclonic seizures)	1
Epilepsies of unknown cause (generalised or focal)	7
Epilepsies associated with structural or metabolic conditions	27
Perinatal insults	10
Cerebral infections	
Bacterial meningitis (<i>Str. pneumoniae</i>)	1
Malformations of cortical development	
Schizencephalies	2
Focal cortical dysplasia	1
Polymicrogyria	1
Other cerebral malformations	
Aicardi syndrome	1
Holoprosencephaly	2
Inherited metabolic disorders	
Non-ketotic hyperglycinemia	1
Tay-Sachs disease	1
Alpers disease	1
Mucopolysaccharidosis (Hunter syndrome)	1
Neurocutaneous disorders	
Tuberous sclerosis complex	4
Vascular lesion	
Sagittal sinus thrombosis	1

Table 1. Distribution of the different epilepsies and epileptic syndromes in infants (n=78)

MRI abnormality (n=101)	n (%)
Volume loss	23 (22.8%)
Generalized	5
Hemisphere	1
Lobe	5
Cerebelar	3
Corpus callosum	9
White matter lesions	29 (28.7%)
Leukomalacia/gliosis	15
Encephalomalacia	5
Other lesions	9
Gray-matter lesions	19 (18.8%)
Heterotopias	1
Cortical dysplasias	7
Other lesions	11
Vascular lesion	3 (3%)
Hemorrhage	2
Venous thrombosis	1
Ventricular enlargement	14 (13.9%)
<1.5cm	4
>1.5cm	10
Prominence of extra-axial fluid space	1 (1%)
<1.0cm	1
>1.0cm	0
Other structural abnormalities	12 (11.9%)
Agenesis of the corpus callosum	2
Delayed myelination	6
Enlarged perivascular spaces in the corpus callosum	1
Calcifications	3

Boldface rows represented “significant abnormalities”

Table 2. MRI abnormalities found in infants diagnosed with epilepsy

4.2 Early childhood

The sample was made up of 157 patients (85 males and 72 females). In early childhood, distribution was idiopathic (44.6%), cryptogenic (29.9%) or symptomatic (25.5%). Table 3 shows the distribution of the epilepsies and epileptic syndromes in this period. Epilepsies in which nature of the underlying causes is yet unknown (29.9%) and epilepsies attributed to and organized by structural or metabolic conditions (24.8%) were the most prevalent syndromes.

Epilepsies associated to structural or metabolic conditions (n=39) were secondary to perinatal asphyxia (figure 7), cerebral infections (figure 8), congenital malformations of the brain, inherited metabolic disorders, phakomatoses (figure 9), chromosomal abnormalities, arterial infarction (figure 10), arteriovenous malformations and supratentorial tumors.

Of 157 early infants in this study, 45 (28.7%) had at least one MRI abnormality. Thirty-two (20.4%) showed MRI abnormalities that were classified as significant because they were considered to be potentially related to the seizure condition.

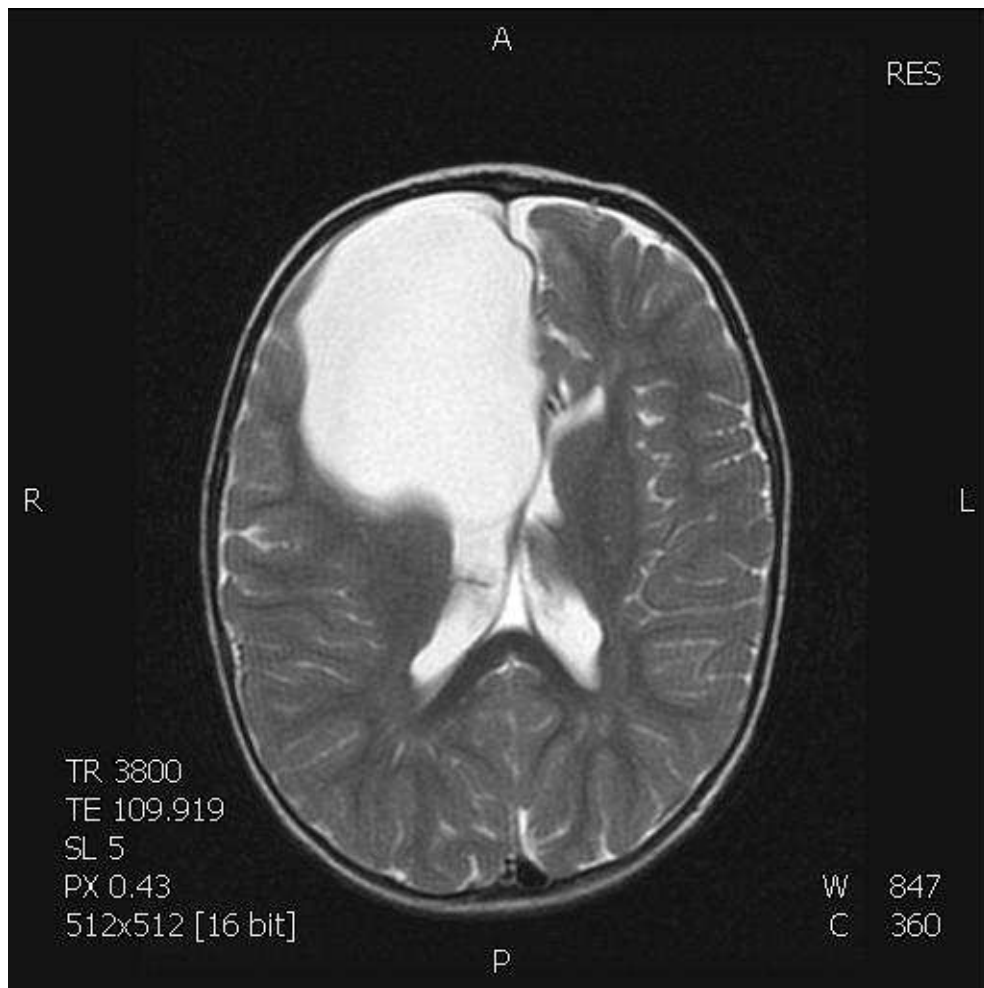
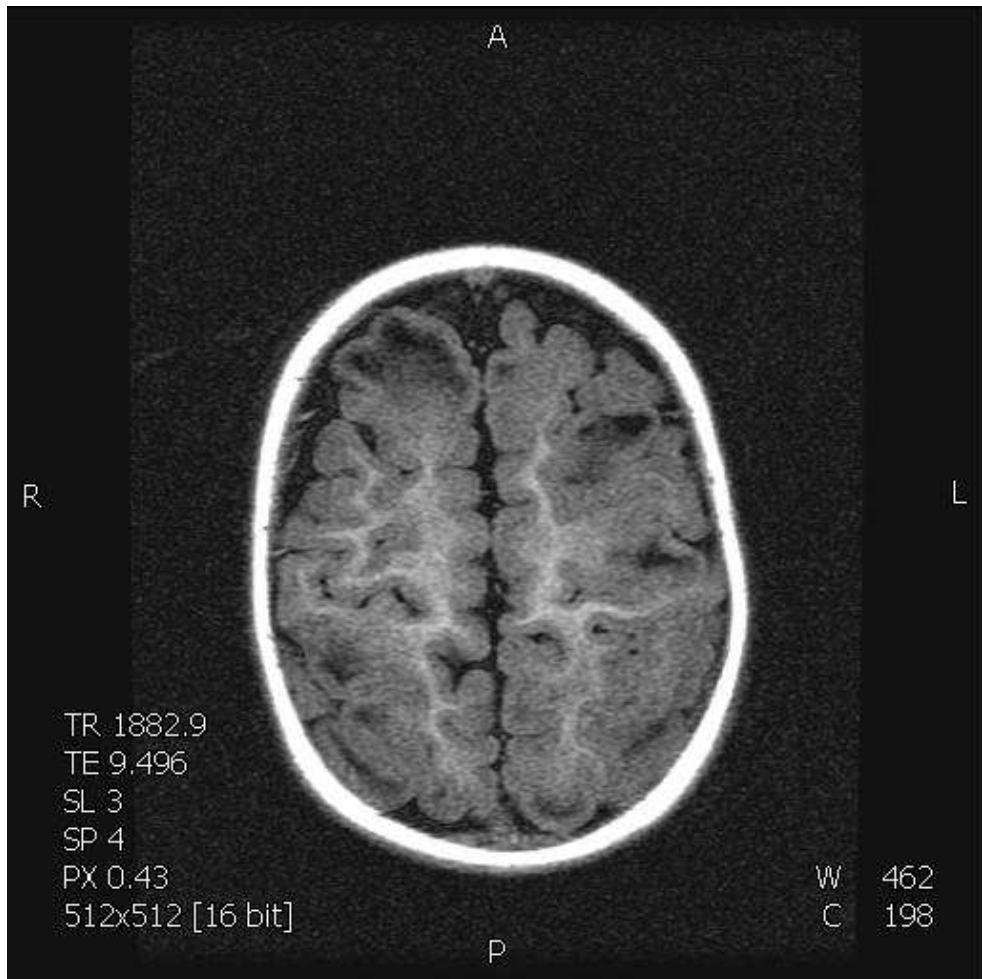


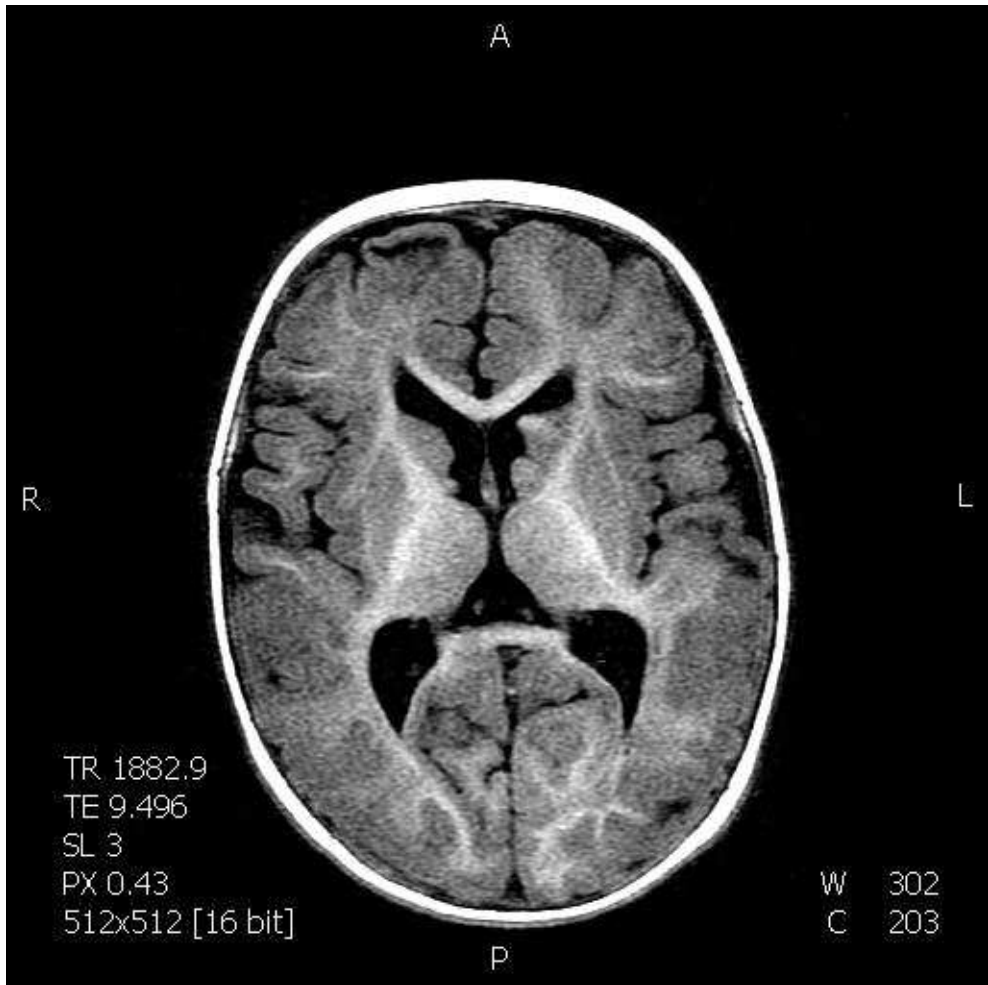
Fig. 7. Porencephalic cyst: T2-weighted SE image displays a wide cyst in the left frontal lobe, which is connected to the lateral ventricle and causes a slight lateral midline displacement of the brain.



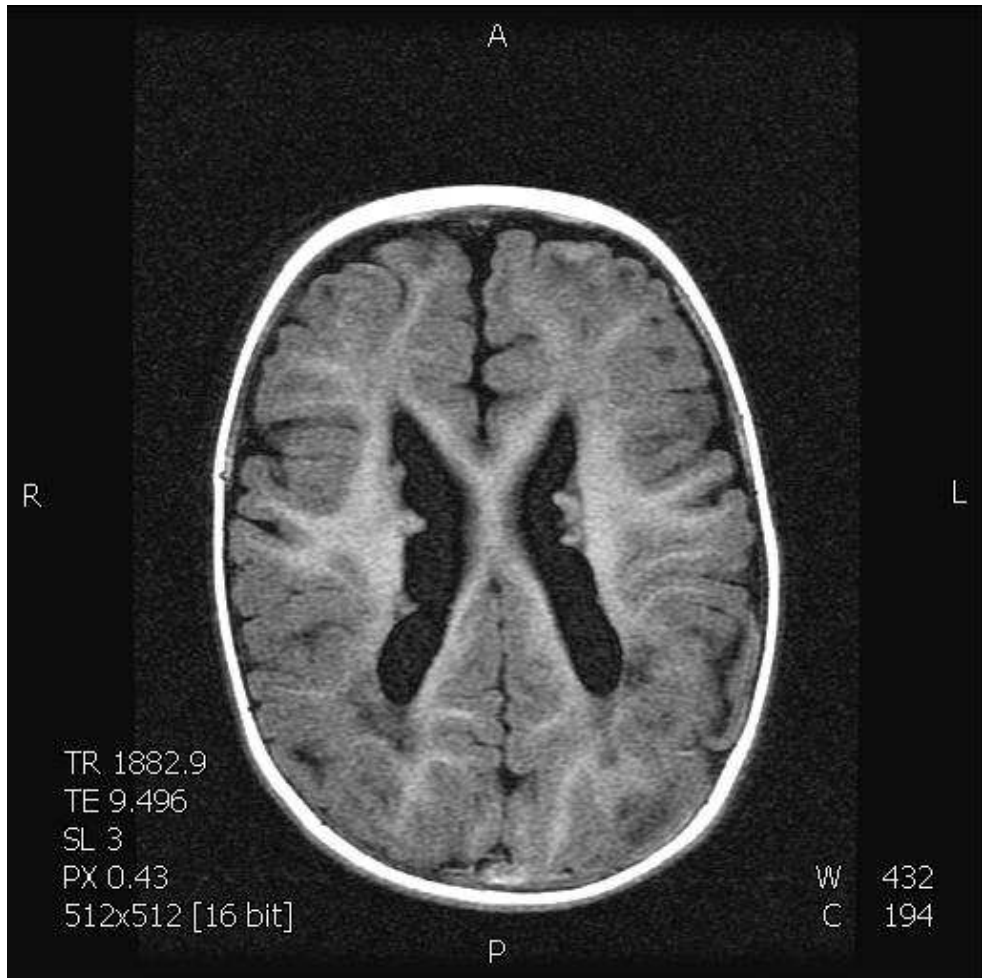
Fig. 8. Neurocysticercosis: T1-weighted SE images (gadolinium-enhanced) shows small cystic intraparenchymal lesions and peripheral enhancement.



(a)



(b)



(c)

Fig. 9. (a, b, c). Tuberous sclerosis: T1-weighted FLAIR images reveal cerebral hamartomas as low signal intensity subcortical lesions, subependymal hamartomas casted on the ventricular space and small giant cell astrocytomas adjacent to the foramen of Monro.

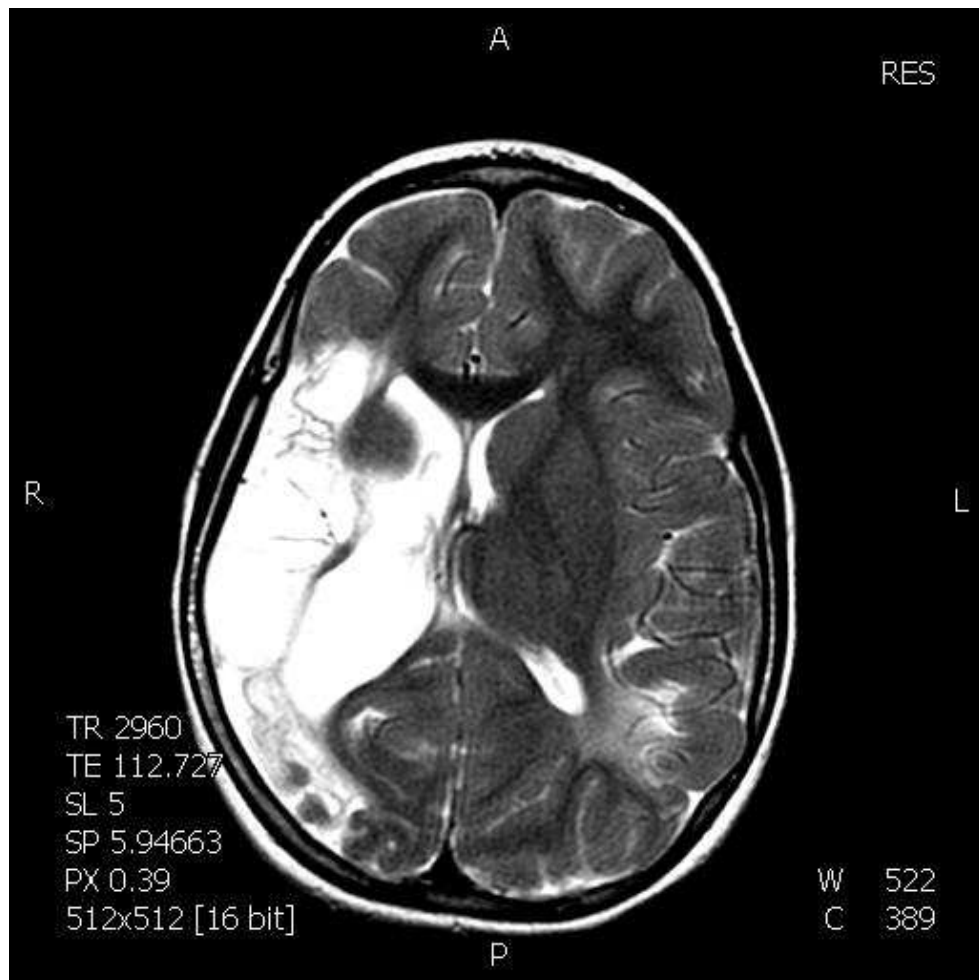


Fig. 10. Post-stroke sequelae in the right middle cerebral artery: T2- weighted SE image showing residual encephalomalacia with volume loss and ex vacuo enlargement of the right ventricle. An area of periventricular leukomalacia in the left occipital lobe can be appreciated.

Table 4 presents the number of early infants with MRI abnormalities (the sum of abnormalities may exceed the total number of children because different abnormalities can affect the same locations for a given patient). In this group of 45 children with at least one MRI abnormality, the most common abnormalities included white-matter lesions (28.7%), volume loss (19.1%), gray-matter lesions (21.3%) and ventricular enlargement (14.9%).

West syndrome	2
Myoclonic epilepsy	4
Febrile seizures plus	1
Panayiotopoulos syndrome	9
Epilepsy with myoclonic atonic seizures	10
Benign epilepsy with centrotemporal spikes	18
Late onset childhood occipital epilepsy (Gastaut type)	1
Epilepsy with myoclonic absences	1
Childhood absence epilepsy	13
Lennox-Gastaut syndrome	1
Epilepsy with continuous spike-and-wave during sleep	7
Landau-Kleffner syndrome	1
Autosomal-dominant nocturnal frontal lobe epilepsy	1
Epilepsies of unknown cause (generalized or focal)	46
Epilepsies associated with structural or metabolic conditions	39
Perinatal insults	11
Cerebral infections	
Cysticercosis	1
Herpes simplex encephalitis	2
Malaria	1
Malformations of cortical development	
Focal cortical dysplasia	2
Heterotopias	1
Polymicrogyria	2
Schizencephalies	2
Others cerebral malformations	
Dandy-Walker malformations	1
Inherited metabolic disorders	
Alpers disease	1
Others	2
Neurocutaneous disorders	
Tuberous sclerosis complex	2
Chromosomal abnormalities	
Down syndrome (trisomy 21)	1
Angelman syndrome	3
Deletion 8p23	1
Deletion 5q syndrome	1
Duplication 15q syndrome	1
Stroke	
Middle cerebral artery infarction	2
Vascular malformations	
Arteriovenous malformation	1
Tumors	
Supratentorial ependymoma	1
Condition with epileptic seizures that do not require a diagnosis of epilepsy	
Infantile convulsions with mild gastroenteritis	3

Table 3. Distribution of the different epilepsies and epileptic syndromes in early childhood (n=157)

MRI abnormality (n=94)	n (%)
Volume loss	18 (19.1%)
Generalized	6
Hemisphere	1
Lobe	2
Cerebellar	1
Corpus callosum	8
White matter lesions	27 (28.7%)
Leukomalacia/gliosis	13
Encephalomalacia	5
Other lesions	9
Gray-matter lesions	20 (21.3%)
Heterotopias	1
Cortical dysplasias	6
Other lesions	13
Vascular lesion	2 (2.1%)
Hemorrhage	2
Ventricular enlargement	14 (14.9%)
<1.5cm	11
>1.5cm	3
Prominence of extra-axial fluid space	1 (1.1%)
<1.0cm	1
>1.0cm	0
Mass lesion	1 (1.1%)
Other structural abnormalities	11 (11.7%)
Hemisphere asymmetry	2
Cerebellar tonsils descent	1
Choroid plexus cyst	1
Pineal cyst	1
Mega cisterna magna	1
Arteriovenous malformations	1
Delayed myelination	2
Agenesis of the corpus callosum	2

Boldface rows represented “significant abnormalities”

Table 4. MRI abnormalities found in early childhood diagnosed with epilepsy

4.3 School-aged children

The sample was made up of 134 patients (72 males and 62 females). In school-age children, seizures were idiopathic in 55.2%, cryptogenic in 25.4% and symptomatic in 19.4%. Table 5 shows the distribution of the epilepsies and epileptic syndromes in school-aged children. Epilepsies in which the nature of the underlying causes is yet unknown (29.1%), benign epilepsy with centrotemporal spikes (25.4%) and childhood absence epilepsy (18.7%) were the most prevalent syndromes.

Epilepsies attributed to structural or metabolic conditions (n=39) were secondary to perinatal asphyxia, cerebral infections, congenital malformations of the brain (figure 11), phakomatoses, arterial infarction, arteriovenous malformations (figure 12), suprasellar arachnoid cyst (figure 13), drug toxicity (figure 14) and desmoplastic neuroepithelial tumors.

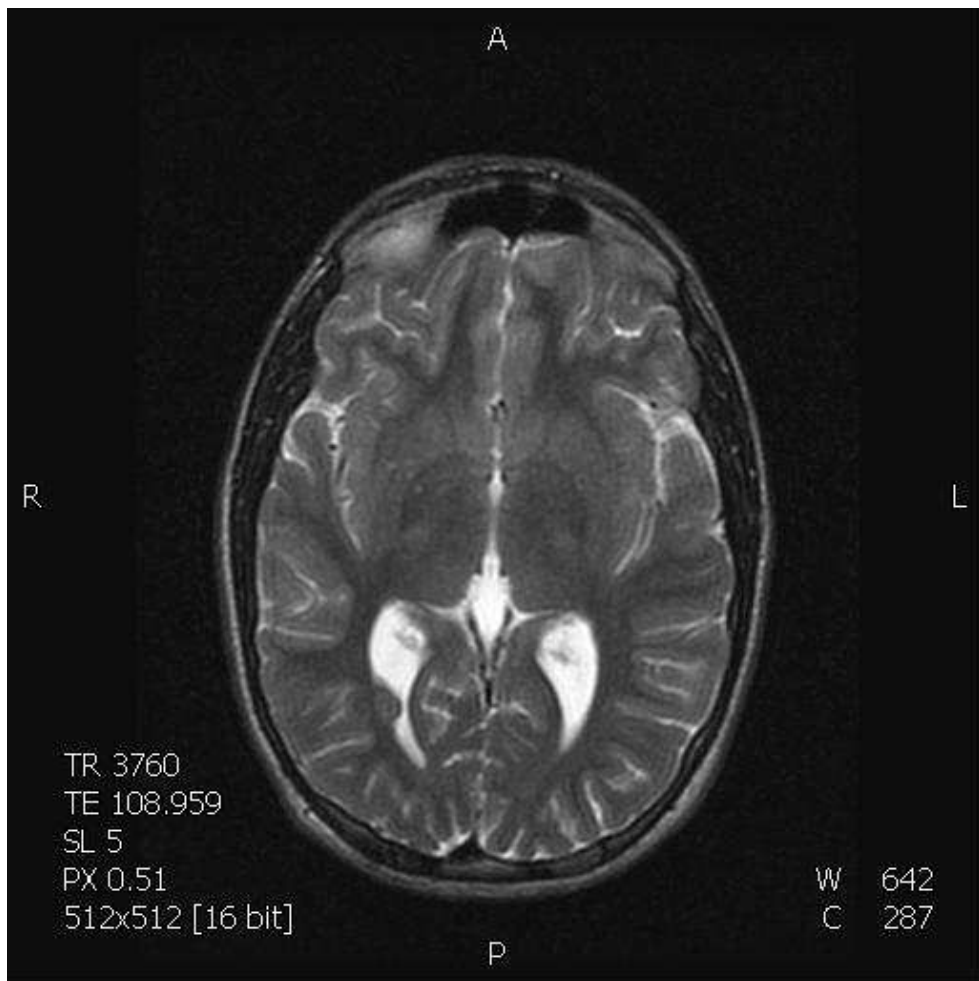
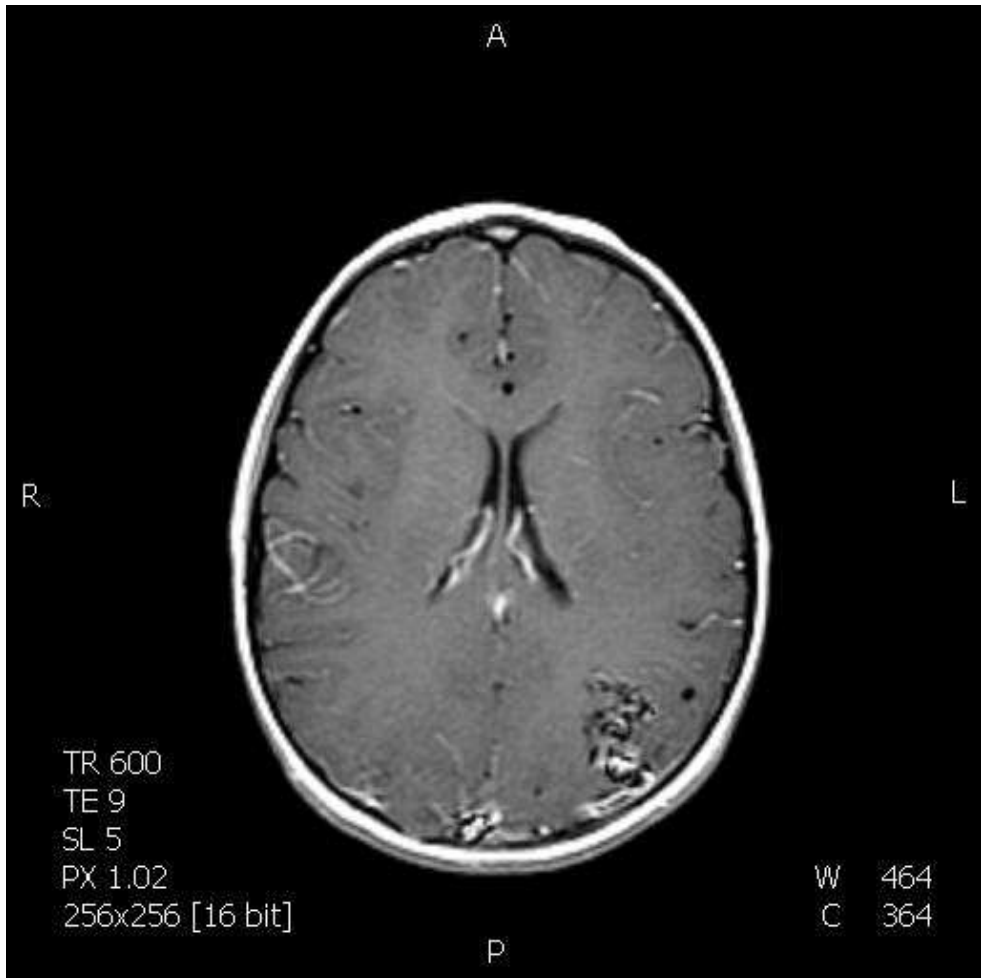


Fig. 11. Subependymal heterotopia: T2-weighted SE image shows a gray matter nodule protruding over the occipital horn of the right ventricle.



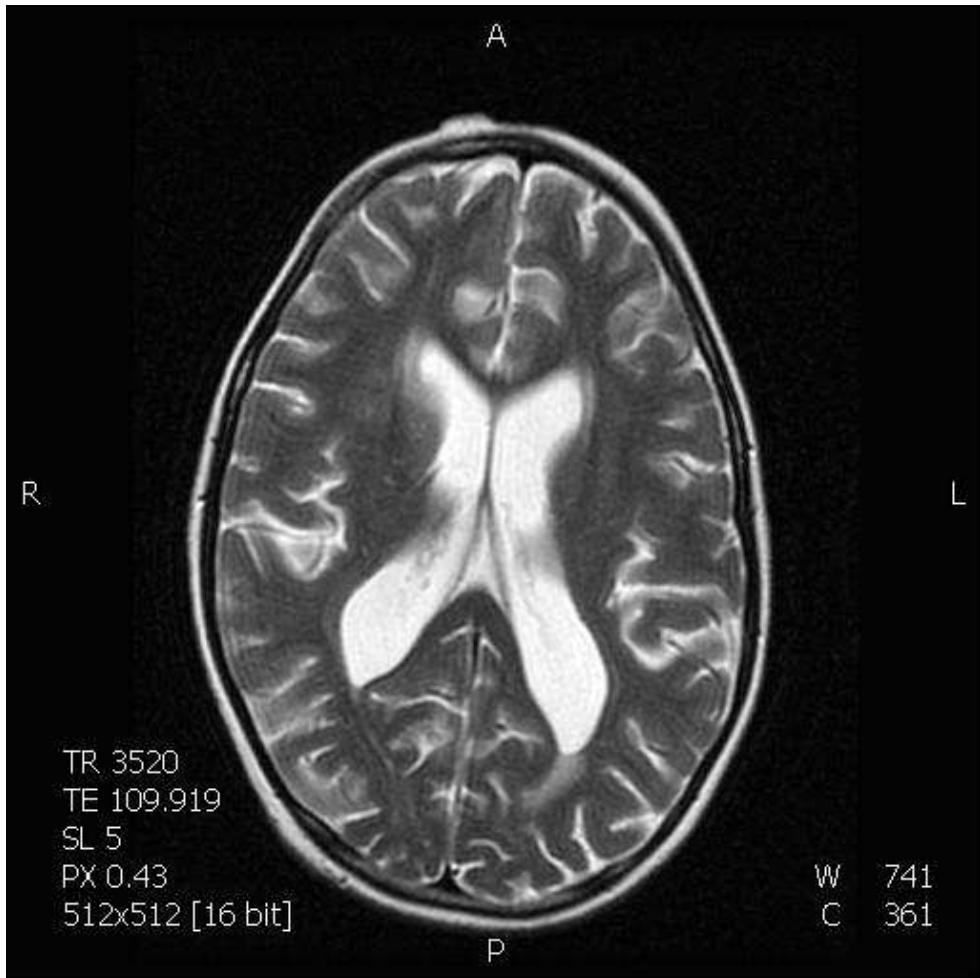
(a)



Fig. 12. (a, b). Arteriovenous malformation (AVM):T1-weighted SE images post contrast-enhancement features a tangle of blood vessels in the left parieto-occipital region. Some of them show enhancement and others show absence of blood flow.



Fig. 13. Suprasellar arachnoid cyst: T2-weighted SE image shows a cystic suprasellar lesion which displaces the III ventricle and causes lateral ventricle hydrocephalus.



(a)

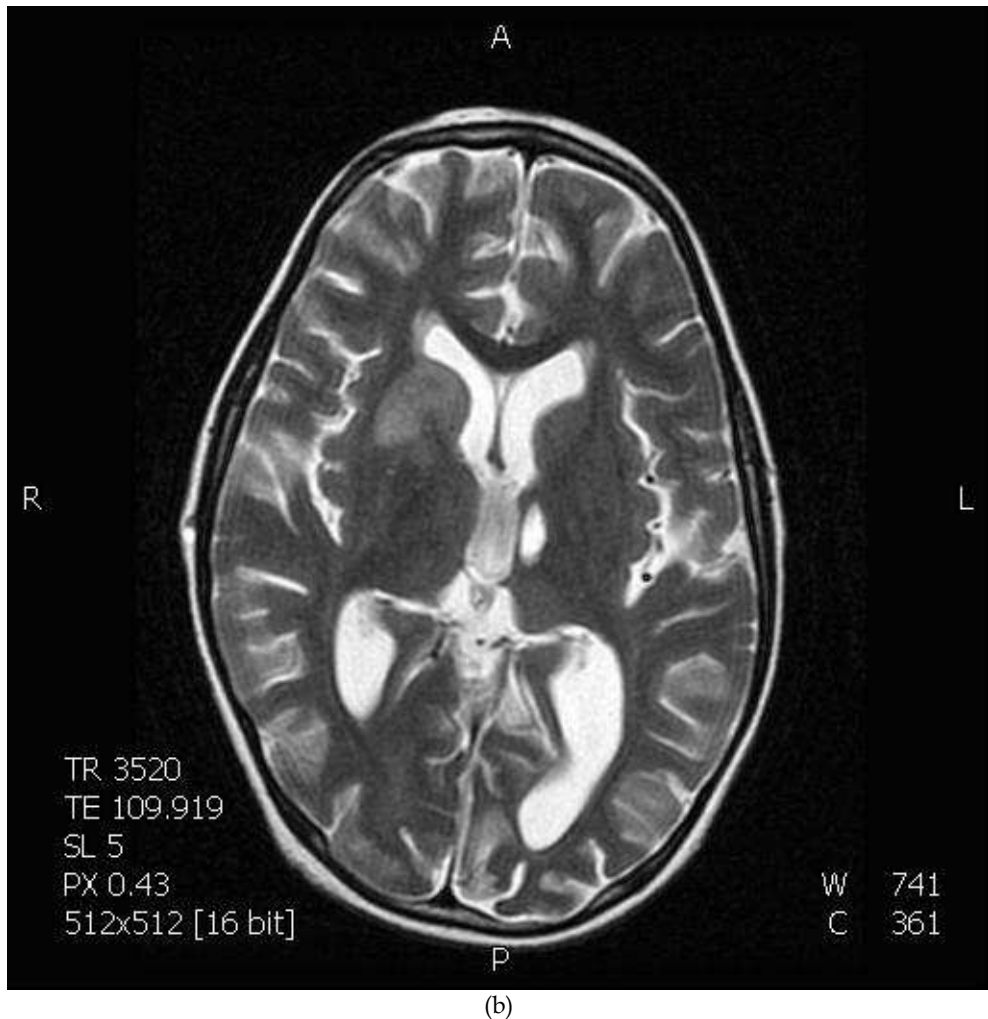


Fig. 14. (a, b). Chemotherapy-induced toxicity in a boy diagnosed with acute lymphoblastic leukemia. T2-weighted SE images reveal cerebral involvement as patches with hyperintense areas in periventricular white matter, right occipital cortico-subcortical area and the right corpus striatum. In addition, there is a porencephalic lesion in the left thalamic region.

After going through the records of the 134 school-aged children, we found that 28 (20.9%) had at least one MRI abnormality recorded. Twenty-one (15.7%) presented MRI abnormalities that again were considered as significant because they were potentially related to the seizure condition.

Table 6 presents the number of school-age children with MRI abnormalities. From the 28 children with at least one MRI abnormality, the findings included white-matter lesions (23.4%), gray-matter lesions (23.4%), volume loss (17%) and prominence of extra-axial fluid space (12.8%)

Panayiotopoulos syndrome	5
Benign epilepsy with centrotemporal spikes	34
Late onset childhood occipital epilepsy (Gastaut type)	4
Reflex epilepsy (photosensitive epilepsies)	1
Childhood absence epilepsy	25
Lennox-Gastaut syndrome	1
Epilepsy with continuous spike-and-wave during sleep	4
Landau-Kleffner syndrome	1
Epilepsies of unknown cause (focal/generalized)	39
Epilepsies associated with structural or metabolic conditions	20
Perinatal insults	3
Cerebral infections	
Subdural empyema	1
EBV encephalitis	1
Malformations of cortical development	
Subependymal heterotopia	2
Band heterotopia (double cortex)	1
Focal cortical dysplasia	1
Polymicrogyria	1
Others cerebral malformations	
Chiary I malformations	1
Tumors	
Desmoplastic neuroepithelial tumors	1
Neurocutaneous disorders	
Tuberous sclerosis complex	1
Stroke	
Middle cerebral artery infarction	3
Vascular malformations	
Arteriovenous malformations	1
Cavernous malformations	1
Prominence of extra-axial fluid space	
Suprasellar arachnoid cyst	1
Drug toxicity	
Leukoencephalopathy due to vinca alkaloids	1

Table 5. Distribution of the different epilepsies and epileptic syndromes in school-aged children (n=134)

MRI abnormality (n=47)	n (%)
Volume loss	8 (17%)
Generalized	3
Hemisphere	3
Corpus callosum	2
White matter lesions	11 (23.4%)
Leukomalacia/gliosis	9
Encephalomalacia	1
Other lesions	1
Gray-matter lesions	11 (23.4%)
Heterotopias	3
Cortical dysplasias	2
Other lesions	6
Mass lesion	1 (2.1%)
Vascular lesion	2 (4.3%)
Hemorrhage	2
Ventricular enlargement	2 (4.3%)
<1.5cm	1
>1.5cm	1
Prominence of extra-axial fluid space	6 (12.8%)
<1.0cm	5
>1.0cm	1
Other structural abnormalities	7 (14.9%)
Calcifications	2
Lobe asymmetry	1
Cerebellar tonsils descent	1
Arteriovenous malformations	2
Pineal cyst	1

Boldface rows represented “significant abnormalities”

Table 6. MRI abnormalities found in school-aged childhood diagnosed with epilepsy

4.4 Adolescents

The sample was consisted of 88 patients (39 males and 49 females). In this group of patients, seizures were idiopathic in 69.3%, cryptogenic in 19.3% and symptomatic in 11.4% of them. Table 7 shows the distribution of the epilepsies and epileptic syndromes in adolescents. Idiopathic generalized epilepsies with variable phenotypes (46.6%) and cryptogenic focal epilepsies and/or unknown cause (19.3%) were the most prevalent syndromes.

Epilepsies associated to structural or metabolic conditions (n=9) were secondary to perinatal asphyxia, malformations of the brain, strokes (figure 15), vascular malformations, chromosomal abnormalities andependimal cyst (figure 16).

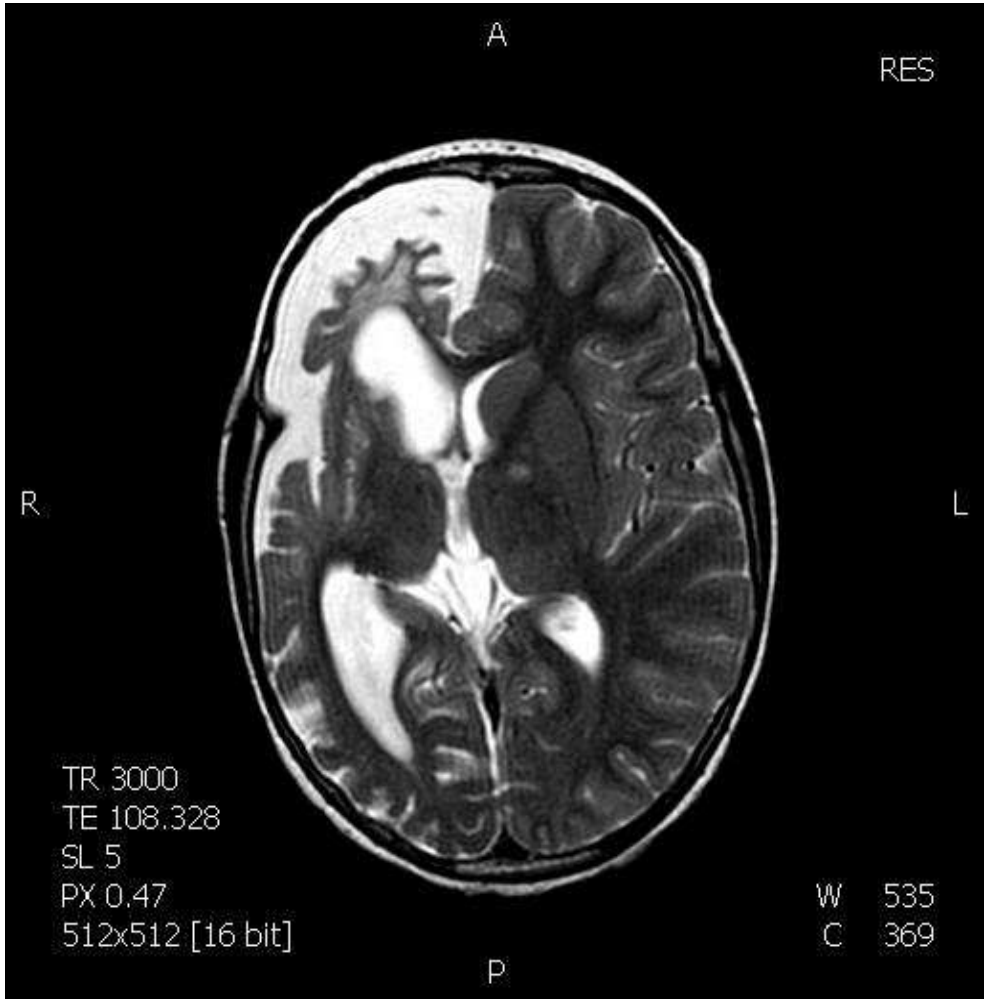


Fig. 15. Right cerebral hemisphere atrophy after ischemic lesion: T2-weighted SE image presents a volume loss in the right hemisphere, atrophy of cortical gyri, leukomalacia and ex vacuo enlargement of lateral ventricle. A hyperintense nodule, compatible with spongiotic intramyelinic change (neurofibromatosis), can be appreciated in the left globus pallidus.

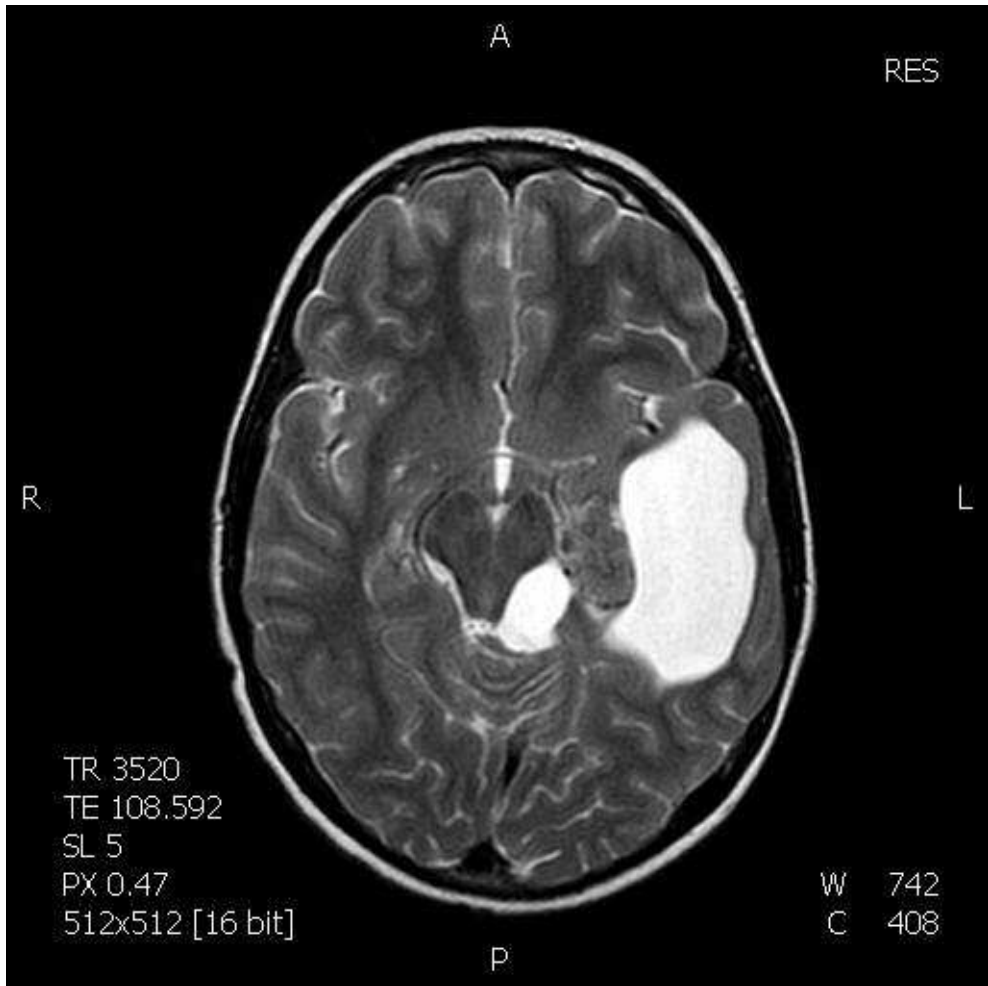


Fig. 16. Ependymal cyst: T2-weighted SE image shows a cystic lesion that expands the left occipital horn and a small brain herniation inside the interpeduncular cistern.

Benign epilepsy with centrotemporal spikes	13
Panayiotopoulos syndrome	3
Late onset childhood occipital epilepsy (Gastaut type)	1
Idiopathic generalized epilepsies with variable phenotypes	41
Juvenile absence epilepsy	20
Juvenile mioclonic epilepsy	13
Epilepsy with GTCSs only	8
Progressive mioclonus epilepsy (Lafora disease)	1
Reflex epilepsies (photosensitive epilepsies)	2
Epilepsies of unknown cause (generalized or focal)	17
Mesial temporal lobe epilepsy with hippocampal sclerosis	1
Epilepsies associated with structural or metabolic conditions	9
Perinatal insults	
Malformations of cortical development	1
Focal cortical dysplasia	1
Stroke	
Vascular malformations	1
Vasculopathies (neurofibromatosis)	1
Vascular malformations	
Venous malformations	1
Chromosomal abnormalities	
Mycodeletion 17p13.3	1
Prominence of extra-axial fluid space	
Arachnoid cyst	1
Ependimal cyst	1
Parenchymal cyst	1

Table 7. Distribution of the different epilepsies and epileptic syndromes in adolescents (n=88)

Of 88 infants in this study, 19 (21.6%) revealed at least one MRI abnormality. Fourteen (15.9%) manifested significant MRI abnormalities (they might to related to the seizure condition).

Table 8 presents the number of adolescents with MRI abnormalities (the sum of abnormalities may be higher than the total number of children). In 19 studies with at least one MRI abnormality, the most common abnormalities included white-matter lesions (28.1%), volume loss (15.6%), gray-matter lesions (12.5%) and prominence of extra-axial fluid space (12.5%).

MRI abnormality (n=32)	n (%)
Volume loss	5 (15.6%)
Generalized	1
Hemisphere	2
Lobe	1
Cerebellar	1
White matter lesions	9 (28.1%)
Leukomalacia/gliosis	7
Encephalomalacia	2
Gray-matter lesions	4 (12.5%)
Cortical dysplasias	1
Other lesions	3
Vascular lesion	1 (3.1%)
Hemorrhage	1
Ventricular enlargement	3 (9.4%)
<1.5cm	2
>1.5cm	1
Prominence of extra-axial fluid space	4 (12.5%)
<1.0cm	3
>1.0cm	1
Other structural abnormalities	6 (18.8%)
Lobe asymmetry	3
Cerebellar tonsils descent	1
Absence of the posterior pituitary	1
Arteriovenous malformations	1

Boldface rows represented “significant abnormalities”

Table 8. MRI abnormalities found in adolescents diagnosed with epilepsy

4.5 Whole sample

The whole group was 457 patients (233 males and 224 females). Etiology was considered idiopathic in 225 (49.2%), cryptogenic in 114 (24.9%), and symptomatic in 118 (25.8%). Table 9 shows the distribution of the epilepsies and epileptic syndromes in the overall sample.

There was at least one MRI abnormality in 134 patients (29.3%). One hundred (21.9%) had significant MRI abnormalities (potentially related to the seizure condition).

Table 10 presents the number of children with MRI imaging abnormalities. As we previously said, the sum of abnormalities may exceed the total number of children, since different abnormalities can affect the same locations in one given patient. Of 134 children with at least one MRI abnormality, the most common abnormalities included white-matter lesions (27.6%), volume loss (19.6%), gray-matter lesions (19.6%) and ventricular enlargement (12%). Table 11 shows the distribution of MRI abnormalities found according to age.

Neuroimaging studies achieved in two patients diagnosed with benign epilepsy with centrottemporal spikes, two patients with childhood absence epilepsy, one patient with juvenile myoclonic epilepsy, and other patient with juvenile absence epilepsy revealed MRI abnormalities classified as significant: leukomalacia periventricular (4 cases) or areas of gliosis (2 cases).

Infancy	
West syndrome	26
Myoclonic epilepsy in infancy	9
Benign familial infantile epilepsy	3
Benign non-familial infantile epilepsy	1
Dravet syndrome	10
Childhood	
Febrile seizures plus	1
Panayiotopoulos syndrome	17
Epilepsy with myoclonic atonic seizures	10
Benign epilepsy with centrotemporal spikes	65
Autosomal-dominant nocturnal frontal lobe epilepsy	1
Late onset childhood occipital epilepsy (Gastaut type)	6
Epilepsy with myoclonic absences	1
Lennox-Gastaut syndrome	2
Epilepsy with continuous spike-and-wave during sleep	11
Landau-Kleffner syndrome	2
Childhood absence epilepsy	38
Adolescence	
Juvenile absence epilepsy	20
Juvenile mioclonic epilepsy	13
Epilepsy with generalized tonic-clonic seizures alone	8
Progressive mioclonus epilepsy (Lafora disease)	1
Less specific age relationship	
Reflex epilepsies	4
Distinctive constellation	
Mesial temporal lobe epilepsy with hippocampal sclerosis	1
Epilepsies that the nature of the underlying cause is yet unknown (generalized or focal)	109
Epilepsies associated with structural or metabolic conditions	
Perinatal insults	25
Cerebral infections	7
Cerebral malformations	22
Inherited metabolic disorders	7
Neurocutaneous disorders	7
Tumors	2
Stroke	7
Vascular malformations	4
Vascular lesions	1
Chromosomal abnormalities	8
Prominence of extra-axial fluid space	4
Drug toxicity	1
Condition with epileptic seizures that do not require a diagnosis of epilepsy	
Infantile convulsions with mild gastroenteritis	3

Table 9. Distribution of the different epilepsies and epileptic syndromes arranged by age at onset (n=157)

MRI abnormality (n=275)	n (%)
Volume loss	54 (19.6%)
Generalized	15
Hemisphere	7
Lobe	8
Cerebellar	5
Corpus callosum	19
White matter lesions	76 (27.6%)
Leukomalacia/gliosis	44
Encephalomalacia	13
Other lesions	19
Gray-matter lesions	54 (19.6%)
Heterotopias	5
Cortical dysplasias	16
Other lesions	33
Vascular lesion	8 (2.9%)
Hemorrhage	7
Venous thrombosis	1
Ventricular enlargement	33 (12%)
<1.5cm	18
>1.5cm	15
Prominence of extra-axial fluid space	12 (4.4%)
<1.0cm	10
>1.0cm	2
Mass lesion	2 (0.7%)
Other structural abnormalities	36 (13.1%)
Hemisphere asymmetry	2
Lobe asymmetry	4
Cerebellar tonsils descent	3
Choroid plexus cyst	1
Pineal cyst	2
Mega cisterna magna	1
Arteriovenous malformations	4
Delayed myelination	8
Agenesis of the corpus callosum	4
Absence of the posterior pituitary	1
Calcifications	5
Enlarged perivascular spaces in the corpus callosum	1

Boldface rows represented “significant abnormalities”

Table 10. MRI abnormalities found in children diagnosed with epilepsy

Age group	Type of abnormalities	
	Significant n (%)	Overall n (%)
Infants	33 (42,3%)	42 (53,8%)
Early infants	32 (20,4%)	45 (28,7%)
School-aged childhood	21 (15,7%)	28 (20,9%)
Adolescents	14 (15,9%)	19 (21,6%)
Total	100 (21,4%)	134 (29,6%)

Table 11. Distribution of MRI abnormalities found according to age

5. Discussion

The community of Navarra has a population of 605 876 inhabitants (2008 census, National Institute of Statistics), 88 055 of whom are children (<15 years of age; 45 105 boys [51.2%] and 42 950 girls [48.5%]). Although there are no data about the prevalence of infantile epilepsy in Spain, the extrapolation of published data^{7,24-26} allows estimating that the selected population would account for a high percentage of epilepsy diagnosed children in Navarra. That means, it is a wide enough population to consider as representative for this territory, and, also, the results would contribute to determining the epidemiological characteristics of epilepsy in children. A routine RMI has been requested in all patients with epilepsy as it has been our practice for several years in this Pediatric Neurology Unit in order to aid the formulation of syndromic and etiological classification and, therefore, there is no reason to suspect any statistical bias in the results and conclusions.

According to the data, we confirm that age seems to represent a main factor in the clinical expression of the different childhood epilepsy phenotypes. In fact, relative distribution of the different seizure types and epileptic syndromes was different for each age group, as seen in our series. For example, some epileptic syndromes were predominant in some age groups, such as epilepsies associated to structural or metabolic conditions and West syndrome in infants, epilepsies in which the nature of the underlying causes is yet unknown and epilepsies associated to structural or metabolic conditions in early childhood, or absence and focal benign epilepsies with centrottemporal spikes in school-aged children and idiopathic generalised epilepsies with variable phenotypes in adolescents. Thus, when referring to childhood epilepsy, it would be useful to make reference to the age group of the patients, because characteristics for the epilepsies and epileptic syndromes during childhood seem to be close to the structural and functional changes in the brain since birth to adolescence²⁷⁻³⁰.

Our major finding of this study was that the use of MRI at diagnosis of epilepsy in children demonstrated a high rate of abnormalities findings. There was an inverse relationship between the prevalence of significant MRI abnormalities and age at diagnosis. Thus, the prevalence in the first year of life was 42.3%, in early childhood was 20.4%, in schoolchildren was 15.7%, and in adolescents was 15.9%. White-matter lesions were more

commonly associated with epilepsies and epileptic syndromes in children at any age, whereas many other children displayed epileptogenic lesions involving the cortex or gray matter. In addition, volume loss, considered a priori to be a non significant abnormality, was also very frequent in this population. Ventricular enlargement, especially mild, was also fairly frequent (12% of total sample).

Structural neuroimaging is recommended for all children with recently diagnosed localization-related or generalized epilepsy who do not have the clinical and electrographic features characteristic of classical idiopathic focal or generalized epilepsy (these include benign epilepsy with centrotemporal spikes, childhood absence epilepsy, juvenile absence epilepsy, and juvenile myoclonic epilepsy)^{16,31-33}. However, this series shows how structural abnormalities judged to be etiologically related to the seizure conditions have been found in idiopathic focal or generalized epilepsy, which are consistent with other published data^{23,34,35}. This possibility suggests that clinicians should consider obtaining structural neuroimaging with an MRI when feasible for all patients with epilepsy, because MRI abnormalities may be present even in children with apparently benign syndromes or cryptogenic seizures, and the discovery of an epileptogenic lesion has potential implications for diagnosis, prognosis and treatment.

Our data cannot be easily compared with those in other studies because the populations are somewhat different^{23,31-33,36}. Our study attempted to acquire MRI scans on all children, whereas previous studies excluded some syndromes or children with seizure onset in infancy and early childhood. Therefore, this series extends earlier work by other investigators in several ways. First, imaging was limited to MRI, the current anatomic “gold standard”. Second, imaging was performed at diagnosis. Third, we applied a standardized classification system to MRI findings which permits to present a comprehensive and systematic description of imaging findings. Finally, data were coded directly from magnetic resonance images by two neuroradiologists who read the images firsthand.

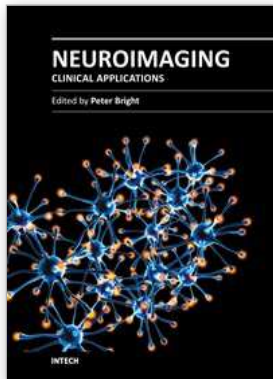
In conclusion, the use of MRI and a reliable standardized scoring system in a large sample of children after their diagnosis of epilepsy identified a high rate of abnormalities (134 of 457, 29.3%). This may have important implications for practice guidelines in this population. First, some findings that might have been regarded as incidental in the past (e.g., volume loss/ventricular enlargement, and others white-matter abnormalities) appear to be present at the onset of seizures and may therefore be clinically significant. Second, the detection of abnormalities in epileptic syndromes other than localization-related symptomatic/cryptogenic syndromes supports an argument for routine MRI at the onset of any seizure condition.

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Modern neuroimaging tools allow unprecedented opportunities for understanding brain neuroanatomy and function in health and disease. Each available technique carries with it a particular balance of strengths and limitations, such that converging evidence based on multiple methods provides the most powerful approach for advancing our knowledge in the fields of clinical and cognitive neuroscience. The scope of this book is not to provide a comprehensive overview of methods and their clinical applications but to provide a "snapshot" of current approaches using well established and newly emerging techniques.

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