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Developmental Abnormalities of the Medial Temporal Lobe in Patients with Temporal Lobe Epilepsy

Stéphane Lehéricy, Didier Dormont, Frank Sémah, Stéphane Clémenceau, Olivier Granat, Claude Marsault, and Michel Baulac

PURPOSE: To evaluate MR temporal lobe malformations and their frequency in patients with temporal lobe epilepsy. **METHODS:** Two hundred twenty-two consecutive adult patients with temporal lobe epilepsy of varying severity were investigated with 1.0-T or 1.5-T MR units using three-dimensional T1-weighted acquisition protocol. **RESULTS:** Sixteen patients (7.2%) presented with malformations of the temporal lobe. Four patterns of malformations were encountered: (*a*) heterotopia (n = 1), lining the temporal horn of the lateral ventricle; (*b*) focal neocortical dysgenesis (n = 6), which consisted of cortical thickening, poor gray/white matter demarcation, abnormal gyration (n = 5), or limited schizencephaly (n = 1); (*c*) hippocampal malformations (n = 5), which presented as abnormal hippocampal formation associated with a cyst (n = 2), isolated malformation of the subiculum (n = 1), or bilateral hippocampal malformation (n = 2) consisting of an abnormal shape and a misplaced fimbria; (*d*) complex malformations of the temporal lobe, combining categories *a, b,* and *c* (n = 4). The age at onset, severity of the disease, and occurrence of generalized tonicoclonic seizures were not significantly different between patients with malformations and the entire population of patients with temporal lobe epilepsy. **CONCLUSION:** MR analysis of temporal lobe malformations allowed a precise determination of the extent of the malformations and the presence or absence of associated hippocampal disease, all of which are of great help in the preoperative evaluation of patients with intractable epilepsy.

Index terms: Brain, magnetic resonance; Brain, temporal lobe; Seizures

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The contribution of magnetic resonance (MR) imaging to the investigation of patients with temporal lobe epilepsy has considerably increased during recent years. In adult patients, MR has proved highly sensitive to the detection of hippocampal sclerosis and small structural lesions, such as tumors and vascular malformations, which are the major neuropathologic substrates of temporal lobe epilepsy (1–3). The visibility of these lesions with MR imaging, in addition to clinical and electrophysiologic data, has greatly improved the epileptogenic focus.

Malformations of the cerebral cortex represent another category of brain structural disorders that can be associated with epilepsy. Several MR studies have shown cortical malformations, ranging from very extensive disorders, such as lissencephaly, polymicrogyria, or double cortex (4–6), to more restricted lesions such as focal cortical dysplasia (7–9). The incidence of brain malformations in temporal lobe epilepsy has been evaluated in surgically resected specimen of patients with refractory seizures (1, 2).

In the present study, 222 consecutive adult patients with temporal lobe epilepsy of variable severity were examined with MR for malformations of the temporal lobe. The aim of the study was to identify the MR features of these malformations and their frequency, and

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whether they were associated with particular clinical features.

Subjects and Methods

The present study included 222 consecutive patients with temporal lobe epilepsy. The patients were referred to the Department of Neurology at la Sâlpetrière hospital in Paris for seizure disorders between January 1991 and May 1993. The diagnosis of temporal lobe epilepsy was established on the basis of seizure and electroencephalographic data, according to the International League Against Epilepsy international classification (10). Mean age of the patients at onset of the seizures and at first examination was 15.2 ± 12 years (age range, 0 to 68 years) and 36 ± 11 years (age range, 16 to 70 years), respectively (mean ± standard error of the mean). History of febrile seizures was recorded in 52 patients (23.4%). One hundred fifty patients had intractable epilepsy (67.6%). Generalized tonicoclonic seizures occurred in 147 patients (66.2%).

All studies were performed on a 1.0-T (until September 1992) or 1.5-T (after upgrading of the system) MR unit. After scout sequence to ensure symmetric positioning of the head of the subject, three series of scans were taken at each examination: (*a*) sagittal, T1-weighted; (*b*) oblique coronal, T1-weighted, spin-echo (400/15/4 [repetition time/echo time/excitations], 5-mm section thickness, no gap) at 1 T or turbo fast low-angle shot three-dimensional Fourier transform (10/4, flip angle 10°; 1.6-mm section thickness) at 1.5 T; and (*c*) coronal, T2-weighted (spin-echo with repetition time of 2200 to 2500 at 1 T or fast spin-echo with repetition time of 6000 at 1.5 T, with echo time of 30 to 90, 7-mm section thickness). The oblique coronal plane imaging sequence was acquired perpendicular to the long axis of the hippocampus, which was defined on the sagittal images. One section was chosen so as to contain the anterior commissure. Gadopentetate dimeglumine enhancement was performed with the coronal T1-weighted protocol in patients 4 to 8 and 13 to 15 of the present study.

On MR scans, the medial temporal lobe was compared with normal anatomy. MR scans were evaluated for: (*a*) the presence or absence of abnormalities of the temporal lobe cortical ribbon, including its morphology, location, extension and severity; (*b*) the presence or absence of heterotopia, its location and extension; (*c*) the shape, the orientation, and the size of the hippocampal formation; and (*d*) the signal intensity of these abnormalities on T2-weighted images. Precise delineation of the hippocampal formation boundaries was made after magnification on a work station. Two patients with refractory seizures (patients 5 and 13) were evaluated for surgical treatment and underwent intracranial electroencephalographic monitoring.

Results

Imaging Studies

Sixteen (7.2%) of the 222 patients with temporal lobe epilepsy had MR abnormalities suggestive of malformations of the temporal lobe. Four patterns of malformations were encountered: (*a*) heterotopia; (*b*) focal neocortical malformations; (*c*) hippocampal malformations; and (*d*) complex malformations of the temporal lobe, combining categories *a, b,* and *c*.

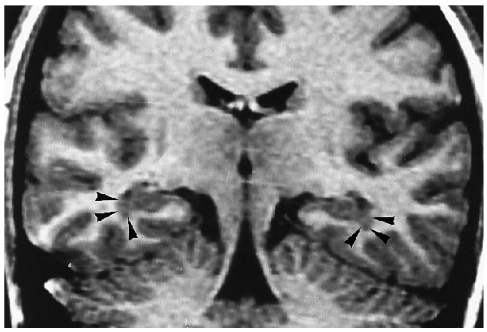

Fig 1. Patient 1: heterotopia. Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. Bilateral small clusters of heterotopic gray matter were present in the white matter of the temporal lobes lining the lateral borders of the temporal horn of the lateral ventricles (*arrows*). The hippocampal formations and the neocortex of the temporal lobes had normal appearance.

Heterotopia (n = 1). Patient 1 presented bilateral, almost symmetric, heterotopia, lining the lateral edges of the temporal horn of the lateral ventricle, extending from the uncus of the temporal lobe to the atrium (Fig 1). Ectopic tissue was isointense to gray matter on all sequences, with no gadopentetate dimeglumine enhancement.

Focal neocortical malformations (n = 6). In five patients (patients 2 through 6), the abnormality consisted of a small area of thickened neocortex involving either the parahippocampal or occipitotemporal gyri. At this level, gray/white matter demarcation was poor. In all cases, the area was isointense to the surrounding gray matter on T1-weighted images (Fig 2). In one patient (patient 2), the abnormal area was isointense on T2-weighted images, whereas areas of hyperintensity were found in the other four patients (patients 3 through 6, Fig 3). No modification of the signal was observed with gadolinium in any of these patients. These abnormalities were obvious on coronal sections, whereas they were less visible on axial sections. The rostrocaudal extension was small in three patients (about 1.5 cm in patients 2 and 4) and larger in patients 3, 5, and 6 (extending rostrocaudally from the anterior part of the temporal lobe or of the uncus, anteriorly, to the lingual and fusiform gyri, posteriorly). Patients 3 and 6

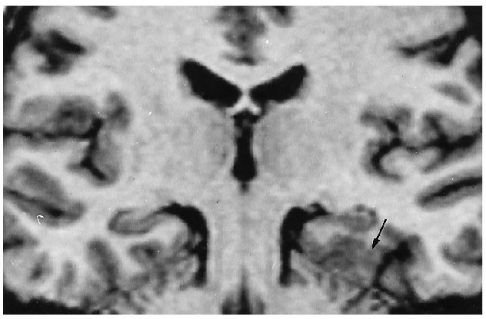

Fig 2. Patient 2: focal cortical malformation of the temporal cortex. Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. The cortical ribbon of the left occipitotemporal gyrus was thickened (*arrow*). No area of increased signal was visible on T2-weighted images (not shown). The hippocampal formation had a normal morphology.

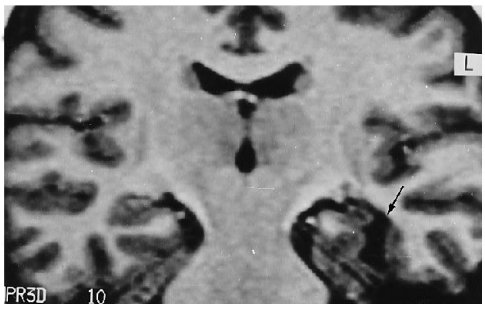

Fig 4. Patient 7: cleft of the left temporal lobe. Oblique coronal T1-weighted section: a cleft occupied the left occipitotemporal gyrus (*arrow*). This cleft extended from the temporal horn to the surface of the brain and was suggestive of a limited form of schizencephaly. The left hippocampal formation was atrophic.

also had an ipsilateral atrophic hippocampal formation.

One patient (patient 7) presented a cleft occupying the white matter of the left occipitotemporal gyrus (Fig 4). The cleft communicated with the temporal horn of the lateral ventricle. The cleft extended rostrocaudally over 25 mm. At the surface of the brain, a thin, cortex-like ribbon partially closed the cleft. Despite the superficial closure, this aspect was thought to correspond to a limited form of schizencephaly.

Malformations of the hippocampal formation (n = 5). Malformation of the subiculum was observed in one patient. Patient 8 had a focal abnormality situated at the junction between the subiculum and the hippocampus (Fig 5). At this level, the gray matter of the left subiculum was thickened and protruded into the underlying white matter. This aspect extended rostrocaudally over a total length of 9 to 10 mm.

Abnormal hippocampal formation associated with a cyst was observed in two patients. In these patients (patients 9 and 10), the hippocampal formation was deformed by the presence of a cyst in the choroidal fissure and the perimesencephalic cistern (Fig 6). The cysts were oval shaped in the rostrocaudal direction and extended from the uncus to the tail of the hippocampus. On coronal images, the hippocampal formation was reduced to a small crescent. No hyperintensity was visible in the hippocampal formation on T2-weighted images.

Bilateral hippocampal formation folding disorders, either isolated (patient 12) or included into larger brain malformation (patient 11), were encountered in two patients. In patient 11, hippocampal formation had a globulous shape (Fig 7). The fimbria was poorly delineated and shifted laterally. Areas of extratemporal neocortex appeared thicker than normal with shallow sulci. Patient 12, presented an isolated abnormality of the hippocampal formation (Fig 8). The hippocampal formation had a round shape, the tail of the hippocampus lost its transverse enlargement, and the fimbria was shifted laterally. These changes were roughly symmetric and predominated in the posterior half of the hippocampus. The fornix and the neocortex were morphologically normal.

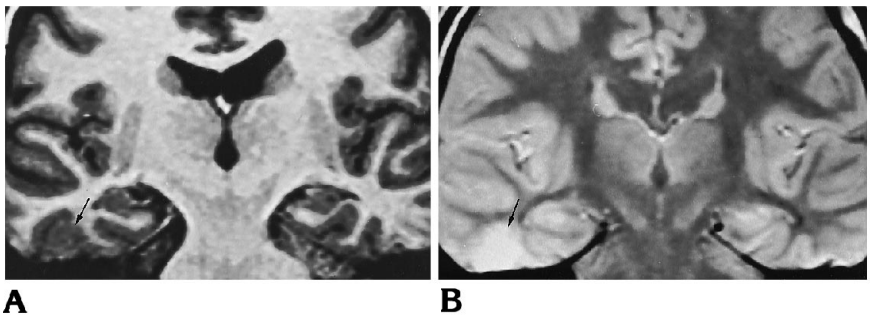

Fig 3. Patient 4: focal cortical malformation of the temporal cortex.

A, Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. The cortex of the right lateral occipitotemporal and inferior temporal gyri was thickened (*arrow*).

B, Oblique coronal proton density–weighted section showing area of hyperintensity at the same level (*arrow*).

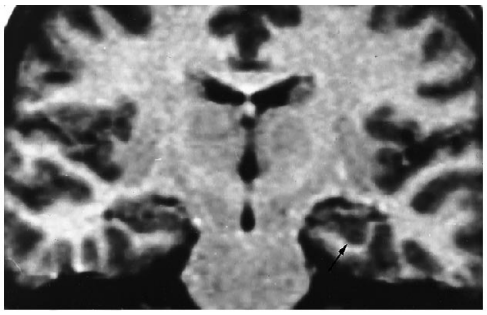

Fig 5. Patient 8: focal abnormality of the subiculum. Oblique coronal T1-weighted section: at the level of the junction between the left subiculum and Ammon's horn, the gray matter of the subiculum was thickened and protruded into the white matter of the underlying parahippocampal gyrus (*arrow*). The ipsilateral hippocampal formation was atrophic. No hyperintensity was visible on T2-weighted images (not shown).

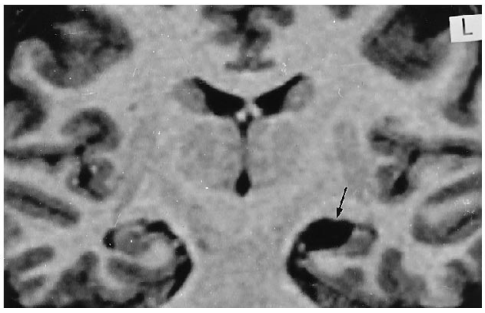

Fig 6. Patient 9: abnormal hippocampal formation associated with a cyst. *A,* Oblique coronal T1-weighted section. The cyst was present in the left choroidal fissure and the perimesencephalic cistern (*arrow*). The hippocampal formation was reduced to a small crescent; the hippocampal fissure was broadly opened; and its normal folding, which brings the dentate gyrus in contact to the subiculum, was not complete.

Complex malformations of the temporal lobe (n = 4). Three patients (patients 13, 14, and 15) presented large clusters of heterotopic gray matter of the right temporal lobe, extending from the medial to the lateral temporal edges (Fig 9). These clusters were isointense to gray matter on all sequences, with no gadopentetate dimeglumine enhancement. The cortex of the adjacent temporal gyri was also abnormal. The three patients had an atrophy of the ipsilateral hippocampal formation. The largest heterotopia (patient 13) extended from the temporal pole to the occipital horn of the lateral ventricle. The atrium of the ventricle was also lined by similar ectopic tissue. Patient 16 presented bilateral, almost symmetric, malformations of the temporal lobe, without heterotopia (Fig 10). The cortex of the medial part of the temporal lobe was thickened with abnormal sulci. Malformations of the amygdala and the hippocampal formation were also present. In all of these patients, extratemporal neocortex had normal appearance.

Clinical and Encephalographic Data

The clinical and electroencephalographic characteristics of these 16 patients are presented in the Table. Personal and familial histories of these patients were unremarkable. Compared to the entire population of patients with temporal lobe epilepsy, mean age at onset of the disease (14.1 ± 2.5 and 15.2 ± 12 for patients with malformations and the entire population, respectively; $P = .82$), percentage of patients with intractable epilepsy (62.5 and 67.6%, respectively; $\chi^2 = 0.173$), and occurrence of generalized tonicoclonic seizures (68.8 and 66.2%, respectively; $\chi^2 = 0.042$) were not significantly different in the two groups. In the two patients who underwent intracranial encephalographic monitoring, the electrodes located the seizure onset in the right hippocampal formation (patient 13) and at the level of the cortical malformation (patient 5).

Neuropathology

Patients 13 and 5 underwent operations. In patient 5, pathologic examination confirmed the presence of cortical dyslamination and clusters of abnormal heterotopic neurons in the molecular layer (Fig 11A). The patient remained seizure-free after surgery (at 6 months follow-up). In patient 13, pathologic examination con-

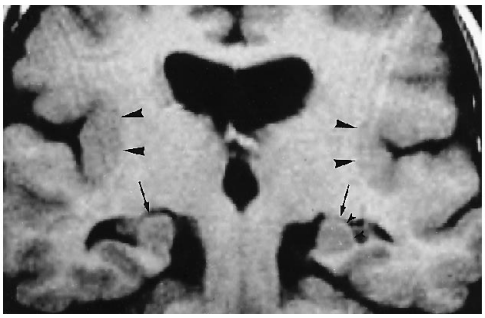

Fig 7. Patient 11: bilateral malformation of the hippocampal formation. T1-weighted oblique coronal section: the hippocampal formation had an unusual vertical orientation and a globular shape (*arrows*). The fimbria and the alveus were poorly delineated (*small arrowheads*). Ventricles were enlarged. The cortex of the temporal lobe had an apparently normal gyration. Areas of extratemporal neocortex appeared thicker than normal with shallow sulci (*large arrowheads*).

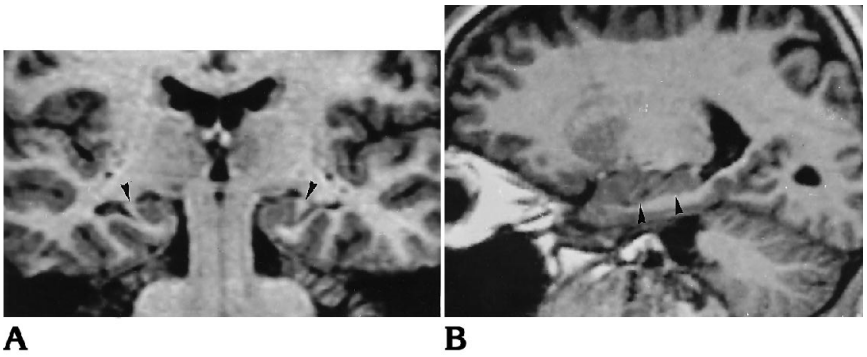

Fig 8. Patient 12: bilateral isolated abnormality of the hippocampal formation.

A, Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. The hippocampal formations have a round shape and a vertical orientation (*arrows*). The indentation of the hippocampal fissure was absent. The fimbria was also shifted laterally.

B, Parasagittal T1-weighted reconstructed section showing an unusual irregular shape of the body of the hippocampal formation (*arrow*).

firmed the presence of heterotopic neuronal-glial tissue in the temporal lobe white matter and of marked cortical dysplasia in the inferotemporal neocortex (Fig 11B). The inferotemporal gyrus presented cortical dyslamination, and abnormal neurons were present in the molecular layer. The patient had only one provoked seizure after surgery (at 15 months follow-up).

Discussion

Analysis of the frequency and of the different types of malformations of the temporal lobe in patients having temporal lobe epilepsy with varying severity is difficult on the sole basis of neuropathologic data. Many of these patients are not candidates for surgery because they do not have intractable epilepsy, because they have bilateral malformations, or because they are not willing to undergo surgery. Accordingly, neuropathologic confirmation of the diagnosis was obtained in only 2 of the 16 patients of the present series; however, MR imaging represents the most sensitive alternative to detect malformations of the medial temporal lobe. Numerous studies have greatly contributed to the knowledge of the MR anatomy of the medial temporal lobe structures in normal (11–15) and pathologic conditions, such as temporal lobe epilepsy (16–22), amnesic syndrome (23, 24), Alzheimer disease (15, 25–27), and schizophrenia (28). In temporal lobe epilepsy, atrophy of the hippocampal formation can be quantified, but visual analysis on coronal sections has a very high sensitivity (16). In the present study, MR imaging of the temporal lobe allowed recognition of not only major abnormalities, such as heterotopia (patients 1, 13, 14, and 15), or large cortical abnormalities (patients 7 and 16), but also of subtle morphological changes, such as malformations of the hippocampal formation (patients 8 through 12). However, the type of cortical abnormalities found in patients 2 through 6, which was considered to correspond to focal neocortical dysgenesis, was more controversial and will be discussed below.

Three types of malformations were encountered in the present study: (*a*) heterotopia in the white matter of the temporal lobe; (*b*) focal or more diffuse dysplasia of the neocortex of the temporal lobe; and (*c*) hippocampal malformations. The 16 patients in the series had either one of these types of malformations (patients 1

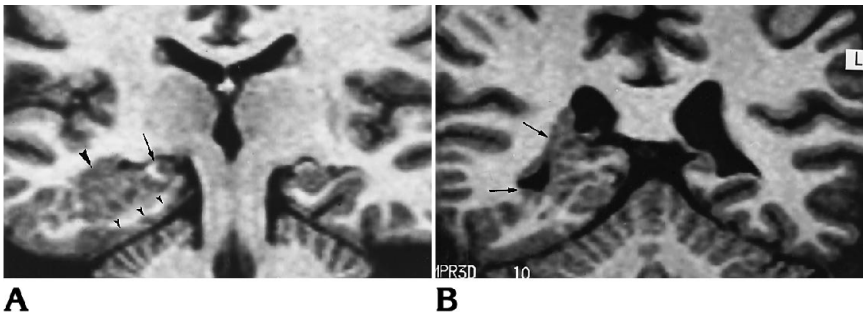

Fig 9. Patient 13: complex malformation of the right temporal lobe.

A, Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. A large cluster of heterotopic gray matter was present in the white matter of the right temporal lobe, lining the inferior border of the temporal horn of the lateral ventricle (*arrowhead*). The cortex of the parahippocampal, medial, and lateral occipitotemporal gyri does not have its normal gyration, and there is disappearance of the collateral sulcus (*small arrowheads*). The hippocampal formation was atrophic and had an abnormal shape. The fimbria was misplaced, shifted laterally (*arrow*).

B, Oblique coronal T1-weighted section at the level of the atrium: heterotopia was visible around the atrium, lining its medial inferior and lateral edges (*arrows*).

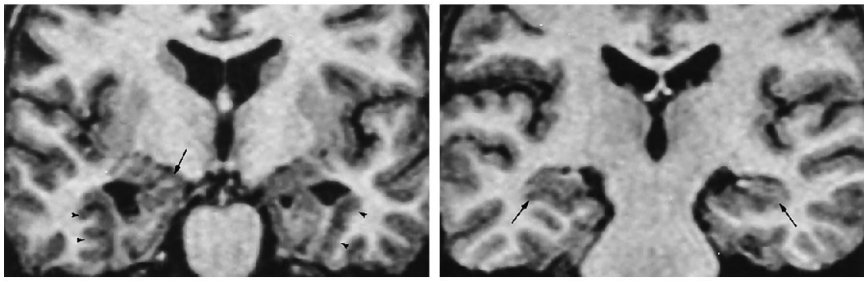

Fig 10. Patient 16: bilateral medial temporal lobe malformation.

A, Oblique coronal T1-weighted section at the level of the uncus. The cortex of the medial part of the temporal lobe was thickened with an abnormally deep inferior temporal sulcus (*arrowheads*). The head of the hippocampal formations had an abnormal shape and the right hippocampal formation was atrophic (*arrow*).

B, Oblique coronal T1-weighted section at the level of the body of the hippocampal formation. Malformation of the hippocampal formation was suggested by abnormal morphology of the subiculum and hippocampus and an enlargement of the hippocampal fissure (*arrows*).

through 12) or complex malformations, combining two or three of these malformations (patients 13 through 16). Nodular heterotopia was found in 4 patients of this series. As defined by Friede (29), nodular heterotopia consisted of clusters of neurons occupying the white matter in proximity to the ventricular wall. According to the classification proposed by Barkovich and Kjos (30), who divided heterotopia into subependymal, focal subcortical, and diffuse subcortical, these cases corresponded to the focal subcortical group. In patient 13, pathologically confirmed, small subependymal nodules were also visible at the posterior extremity of the malformation beneath the ependyma of the ventricular atrium. This abnormal tissue had all of the MR characteristics of heterotopia: the typical location; isointensity to cortical gray matter on all imaging sequences; and no contrast enhancement.

Neocortex of the parahippocampal and occipitotemporal gyri were the site of cortical abnormalities in 10 of the 16 patients. These abnormalities were either focal and restricted to a small part of the temporal neocortex (patients 2 through 6) or more diffuse and associated with other changes, such as heterotopia or hippocampal formation malformations (patients 13 through 16). These areas of cortical abnormalities were detected by either an abnormal thickness of the cortex or unusual gyral formation. Normal cortical thickness has been estimated at 3 to 5 mm, whereas thickened, macrogyric cortex was about 5 to 9 mm (31). Gray/white matter demarcation of the abnormal cortex was poor. In most of the cases, the signal intensity of the macrogyric cortex was the same as the adjacent neocortex, whereas areas of increased signal intensity on T2-weighted images were present in 4 patients (patients 3 to 6), mostly in the underlying white matter. No change in signal intensity was observed after gadopentetate dimeglumine administration.

Neuropathologic examination of the resected neocortex in patient 5 showed that the focal cortical malformation corresponded to the histologic abnormalities identified by Taylor et al (32) (Fig 11), which they called "focal cortical dysplasia." These abnormalities consisted of clusters of large, "bizarre" neurons, cortical dyslamination, and abnormal cells, probably of glial origin in the depth of the affected cortex and the underlying white matter. Subsequently, this entity has been expanded to include mild forms of cortical and subcortical abnormalities, including microdysgenesis of the cortex (33); and this has been reported in patients with refractory complex partial seizures of various location. In the present series, the lesions observed in patients 2, 3, 4, and 6 (Figs 2 and 3) were very similar to the MR findings reported in the literature (7–9, 34) and to that observed in patient 5, suggesting that their cortical abnormalities also corresponded to focal cortical dysplasia. Patients with mild histologic changes may, however, have an apparently normal cortical surface, as assessed histologically (32) or by MR (7). Thus, the possibility that mild forms of focal cortical dysplasia may not be detected macroscopically is an important issue regarding the frequency of these malformations as evaluated by MR.

Although the term *focal cortical dysplasia* is often tentatively used, other malformations may correspond to these MR neocortical abnormalities. Tuberous sclerosis has a broad spectrum during life, ranging from clinically silent, through formes frustes, to the classical disease. Histologically, the distinction between focal cortical dysplasia and forme fruste of tu-

Sixteen patients with temporal lobe epilepsy and MR abnormalities in the temporal lobe

Patient/ Sex	Age, y	Age at onset, y	Seizure Type	Seizure Frequency and Severity	Electroencephalographic Focus	Mental Status	Location of the Malformation	Extension (anteroposterior), cm	Hippocampal Formation
1/F	35	10	CP, SGTC	Intractable	Bilat T	Normal	Bilat temporal heterotopia	5	
2/F	48	17	CP, GTC	Seizure-free under treatment	L T	Normal	L PH thickened	1.5	
3/M	21	8	SP, CP, GTC	20/mo, intractable	L T	Normal	L temporal pole, PH thickened; T2 hyperintense	3.5	L HF atrophy
4/F	26	19	CP	5/mo, intractable	R T	Normal	R lOT, iT thickened; T2 hyperintense	1.5	
5/F	24	1	CP, GTC	3/d, intractable	R T	Normal	R abnormal gyration: PH, mOT, lOT; T2 hyperintense	3.5	
6/M	19	10	CP, GTC	4/mo, intractable	L T	Normal	L PH thickened, T2 hyperintense	5	L HF atrophy (tail)
7/F	36	22	CP	4/mo, intractable	L T	Normal	L mOT cleft	2.5	L HF atrophy
8/F	28	25	CP, GTC	Seizure-free under treatment	Bilat T	Normal		1	L subiculum thickened Ammon's horn atrophy
9/F	40	20	CP	12/mo, intractable	L T	Normal		2	L cysternal cyst, L HF atrophy
10/M	27	26	CP, SGTC	Single seizure	R T	Normal		1.5	R cysternal cyst, R HF atrophy
11/M	31	3	CP, GTC	10/mo, intractable	R T + diffuse	Retarded	Thickening of neocortex		Bilat verticalized, globulous HF
12/M	21	14	CP	10/mo, intractable	Bilat T R predom	Normal, memory difficulties			Bilat abnormal HF, fimbria misplaced
13/F	28	2	CP, GTC	6/mo, intractable	R T	Normal	R abnormal gyration: PH, mOT, lOT; heterotopia	6.5	R HF atrophy
14/F	36	35	Nocturnal	Rare seizures	R T	Normal	R abnormal gyration: PH, mOT, lOT; heterotopia	5	R HF atrophy
15/F	28	13	CP, GTC	Seizure-free under treatment	Normal	Normal	R abnormal gyration: PH, mOT, lOT; heterotopia	7	R HF atrophy
16/M	22	1	CP	Seizure-free under treatment	Bilat T	Mildly retarded, school difficulties	Bilat abnormal gyration; PH, uncus	3.8	Subiculum thickened, R HF atrophy (head)

Note.—CP indicates complex partial; SP, simple partial; GTC, generalized tonicoclonic; SGTC, secondarily generalized tonicoclonic; R T, right temporal lobe; L T, left temporal lobe; bilat T, bilateral temporal lobe; predom, predominance; PH, parahippocampal gyrus; mOT, medial occipitotemporal gyrus; lOT, lateral occipitotemporal gyrus; iT, inferior temporal gyrus; and HF, hippocampal formation.

berous sclerosis is difficult and the differentiation between the two may be based on the extent of cytoarchitectural abnormalities. On MR scan, focal cortical dysplasia and the forme fruste of tuberous sclerosis may be similar (7). Pachygyria can have similar radiologic aspects, although the typical four-layered cortex characteristic of true pachygyria was not encountered in the two series of patients reported by Kuzniecki et al (7) and Palmini et al (8). Polymicrogyria may also be the neuropathologic substrate of these areas of thickened cortex (35).

The specificity of the different images visible on MR scans in patients 2 to 6 is an important feature to discuss. Tumors may appear as focal cortical abnormalities with high signal on T2-weighted images. In particular, dysembryoplastic neuroepithelial tumors have been described in association with partial epilepsy in young patients (36). On MR examination, these tumors appeared as focal cortical masses of very low signal on T1-weighted images and high signal on T2-weighted images (37). Calcifications and gadopentetate dimeglumine enhancement are sometimes found. In the present series, many

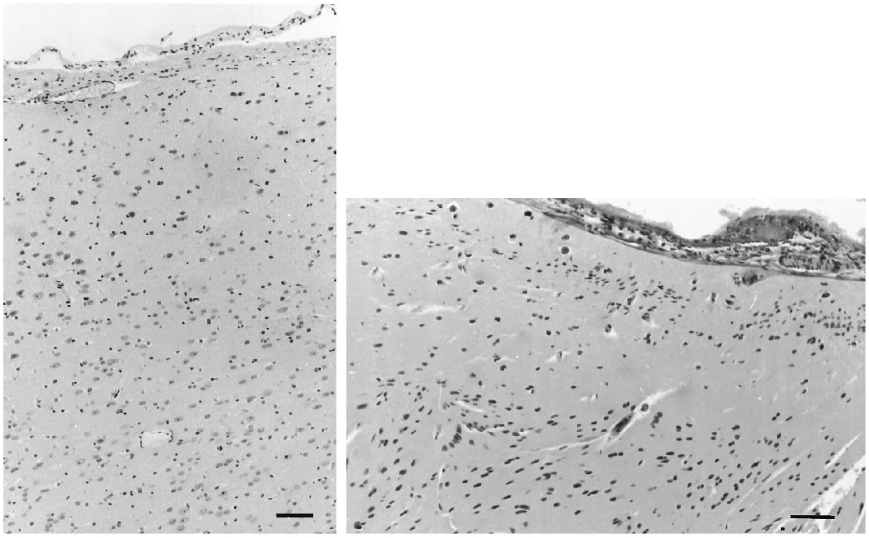

Fig 11. Histologic sections of resected temporal cortex obtained in patients 5 and 13 (hematoxylin-eosin).

A, Histologic section of the temporal cortex in patient 5 showing an aspect of dyslamination throughout all cortical layers, and presence of abnormally numerous neurons in the molecular layer (scale bar = 100 μm).

B, Histologic section in patient 13 showing marked cortical dysplasia in the inferotemporal neocortex with abnormal arrangement of the neurons in layer II and heterotopic neurons beneath the pia matter (scale bar = 100 μm).

features distinguished areas of macrogyric cortex from small tumors. On MR scans, no mass effect, calcification, or gadolinium enhancement was present. On T1-weighted images, areas of macrogyria had the same signal intensity that the rest of the neocortex. Moreover, follow-up of the patients for a period of 2 to 3 years showed no modification in the MR aspects of their lesions. The presence of increased signal intensity on T2-weighted images was the most intriguing feature. This has already been noticed by others and has been related to increased water content in the abnormal cells (7) or gliotic changes (8). Finally, histologic examination was obtained in one patient (patient 5), thereby confirming the diagnosis of focal cortical dysplasia (Fig 11).

Several types of hippocampal abnormalities were found in the present study. These abnormalities either had the typical appearance of malformations, with abnormal morphology of the hippocampus (spontaneous, patients 8 and 11 through 16; or secondary to the presence of a cyst in the choroid fissure, patients 9 and 10) or corresponded to simple atrophy (patients 3 and 7). Three patients presented isolated hippocampal malformations without other temporal abnormality (patients 8, 11, and 12). Patient 8 presented a unilateral malformation of the subiculum, which appeared thickened and protruded into the underlying white matter. This finding, which was not encountered in any other patient with temporal lobe epilepsy, was suggestive of a focal cortical dysgenesis. Two patients demonstrated abnormal morphology of the hippocampal formation (patients 11 and 12). In patients 11, the finding was reminiscent, although to a lesser degree, of the abnormal configuration found in agenesis of the corpus callosum or lissencephaly (38). Thus, patient 11 was considered to have a mild type of lissencephaly. The occurrence of isolated hippocampal malformation, as found in patient 12, was very unusual. A similar morphological pattern has been reported in more widespread brain malformations associated with trisomy 18 (29). The mechanism resulting in this abnormal hippocampus is not known, however. This finding has some similarities to prenatal developmental stages of the human brain (39) and could be secondary to an early interruption in hippocampal and dentate gyrus neuronal migration (38, 40).

The link between the presence of a cyst and epilepsy is a puzzling problem. Cysts, which are probably of developmental origin, are most frequently found in the temporal fossa, the Sylvian fissure, and the choroid fissure (29). In the choroid fissure, cysts may be of neuroepithelial or arachnoid origin (41). These cysts are often discovered fortuitously (29, 41, 42); however, in the two patients in the present series, the cysts were associated with hippocampal abnormalities. The hippocampal formation was atrophic and had an abnormal shape, but was different from hippocampal sclerosis. It seemed that the cyst, perhaps through mass effect, had prevented the hippocampal formation from achieving its normal shape. Moreover, in these patients, the surface encephalographic abnor-

malities were located ipsilateral to the cyst, suggesting a relationship between seizures and hippocampal disease.

Atrophy of the hippocampal formations, with or without other morphological abnormalities, was also found in six of the nine patients with neocortical malformations of the temporal lobe. The association of atrophy of the hippocampal formation and temporal neocortical dysgenesis raises the question of whether the atrophy of the hippocampal formation corresponds to a malformation or to additional disease, such as hippocampal sclerosis. Various degrees of hippocampal cell loss have been reported in epileptic patients operated on for a mass lesion of the temporal lobe. Interestingly, the most severe hippocampal cell loss was found in association with heterotopia of the temporal lobe (1). The relationships between decreased neuronal density in the hippocampal formation, more complex changes that constitute hippocampal sclerosis, and developmental disturbances of the temporal lobe are far from clear. Extrahippocampal malformations may induce some degree of hippocampal cell death through excitotoxicity or deafferentiation mechanisms. Conversely, some features of hippocampal sclerosis, such as dispersion of the granule cells of the dentate gyrus or heterotopic clusters of cells in the hilus, have been interpreted as neuronal migration disorders (43). These findings have suggested that some abnormal developmental mechanisms play a role in the pathogenesis of hippocampal sclerosis (43).

The incidence of temporal lobe malformations was evaluated at 7.2% of our 222 cases. Comparison with previous studies is difficult because they were based on pathologic material obtained in patients with refractory seizures and used different terminology. However, in these series, the incidence of malformations of the temporal lobe has been estimated at 5.2% (2), which is close to the present value. In the present study, medial temporal lobe malformations generally were not associated with cognitive deficit, except in one patient who had a mild type of lissencephaly. The severity of the disease was apparently not related to a specific type of malformation, as similar malformations were either associated with intractable epilepsy or mild form of the disease (for example, patients 8, 9, 13, and 14). Patients with focal cortical dysgenesis tended to be more severely epileptic, however, as four of these five patients had intractable epilepsy.

To what extent does the malformation represent the epileptogenic tissue? Electroencephalography, either with surface or depth electrodes, provided interesting data. Unilateral malformations were associated with ipsilateral surface encephalographic abnormalities in 10 of the 12 patients and with normal encephalographic or bilateral abnormalities in 2 patients. Bilateral malformations were associated with bilateral surface encephalographic abnormalities (n = 4), although in 3 of these 4 patients, surface encephalographic abnormalities were predominant on one side despite no clear structural asymmetry of the malformations on MR scans. Thus, the interictal surface encephalographic recordings were concordant with the MR location of the malformations. However, a higher degree of correlation between the site of the seizure onset and the MR abnormalities is needed when surgery is considered, because the postoperative outcome has been reported to be correlated to the extent of dysplastic tissue removal (44). This is particularly important in large malformations, in which resections including the whole malformation may not be possible (as in patients 13 and 15, for example). In this regard, MR guided the placement of subdural and intracerebral electrodes in patient 13 by showing the presence of associated hippocampal disease, which corresponded to the epileptogenic tissue. Thus, MR assessment of the malformation and hippocampal formation allowed a better evaluation of the preoperative prognosis and of the extent of the resection.

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