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MR in Temporal Lobe Epilepsy: Analysis with Pathologic Confirmation

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PURPOSE: **We evaluated the MR findings in patients with temporal lobe epilepsy to determine the predictive value of MR imaging in assessing patient outcome.**

METHODS: **MR studies from 186 of 274 consecutive patients who underwent temporal lobectomy for intractable epilepsy were reviewed retrospectively. Images were interpreted by an experienced neuroradiologist, who was blinded to the side of seizure activity and to pathologic findings.**

RESULTS: **MR imaging exhibited 93% sensitivity and 83% specificity in detecting hippocampal/amygdalar abnormalities (n = 121), and 97% sensitivity and 97% specificity in detecting abnormalities in the rest of the temporal lobe (n = 60). Abnormal high signal of the hippocampus on T2-weighted images had a sensitivity of 93% and specificity of 74% in predicting mesial temporal sclerosis (n = 115). The presence of hippocampal atrophy on MR correlated with the duration of seizures. Sensitivity and specificity of MR imaging in detecting temporal lobe tumors (n = 42) were 83% and 97%, respectively, based on abnormal signal and mass effect. After surgery, 63% of patients were seizure free and 28% had a significant reduction of seizure frequency at an average of 24 months (range, 12 to 78 months) after surgery. Patients with a single lesion in the anterior temporal lobe or hippocampus/amygdala had a better outcome than patients with multiple lesions (n = 22). Interrater agreement varied from 0.4 to 0.93, with best agreement for tumors or abnormal hippocampal signal on T2-weighted images.**

CONCLUSION: **MR imaging is highly sensitive in detecting and locating abnormalities in the temporal lobe and the hippocampus/amygdala in patients with temporal lobe epilepsy. Hippocampal atrophy appears to correspond to the duration of seizure disorder.**

Numerous studies of patients with temporal lobe epilepsy have demonstrated that magnetic resonance (MR) imaging is a reliable method for locating the origin of temporal lobe epilepsy (1–10). Quantitative (volumetric) MR imaging and T2 relaxometry in addition to conventional inspection are current imaging techniques used in the preoperative assessment of and research into mesial temporal sclerosis. Volumetric measurements can correct for rotation, are reproducible, and are slightly more sensitive than visual inspection in the evaluation of hippocampal sclerosis (10); however, there is still a question of whether the quantitative technique offers additional information over simple visual inspection (11, 12).

Previous studies, though large enough, have not included either pathologically confirmed lesions (13) or combined T2 and volumetric analysis to allow for an assessment of the relationship between signal abnormality on T2-weighted images and atrophic change in the hippocampus (13, 14). Several quantitative studies with a large sample size have demonstrated the relationship between hippocampal volume and duration of seizure disorder, but many of these have lacked pathologic confirmation either in the complete patient group (13) or in part of the patient group (14, 15).

We compared determinants of epileptogenesis and side of temporal resection as assessed visually on MR images with those determined by electroencephalography (EEG) in 186 of 274 consecutive patients, and

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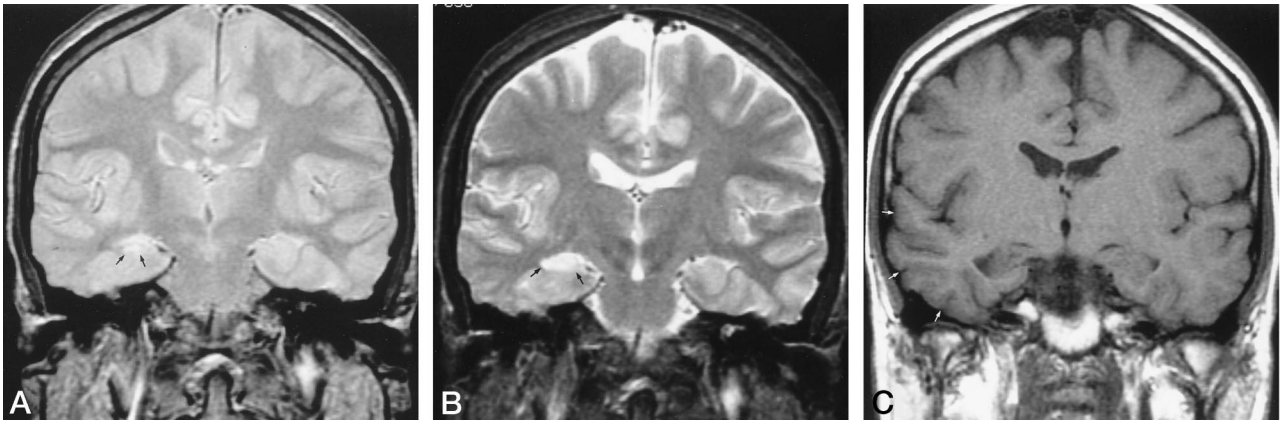

FIG 1. Right mesial temporal sclerosis with MR group 1 manifestations. Coronal proton density–weighted (2800/30/1) (*A*) and T2-weighted (2800/80/1) (*B*) images show increased signal and atrophy in the right hippocampus (*arrows*). Coronal T1-weighted image (400/18/2) (*C*) shows diminished volume of right anterior temporal lobe (*arrows*) as well as diminished volume of the right hippocampus, compared with the left.

compared MR findings with clinical features, histologic findings, and postoperative outcome.

Methods

Patient Population

One hundred eighty-six patients with seizures of temporal lobe origin were included in this study (96 men, 90 women; mean age, 30 ± 12 years). Duration of seizure disorder ranged from 2 months to 44 years (mean duration, 18 ± 10 years). The subjects were derived from 274 consecutive patients. Eighty-eight patients were excluded because of technically inadequate preoperative MR studies (n = 9), a lack of preoperative MR data (n = 30), previous cranial surgery (n = 16), MR examination at another institution (n = 9), or incomplete pathologic studies, usually because an inadequate hippocampal specimen was delivered for examination (n = 24). Of the remaining 186 patients, 99 underwent left temporal lobectomy and 87 right temporal lobectomy for medically intractable temporal lobe epilepsy between January 1, 1987, and November 1, 1993, at our hospital.

Nonradiologic Investigations

Preoperative seizure lateralization was based on seizure description, scalp EEG, video-recorded surface EEG, neuropsychological testing, and intracarotid amobarbital examination in all patients. In addition, in 53 patients, lateralization of epileptogenesis was obtained only with subdural strip EEG recordings.

MR Examination

All MR studies were performed on a 1.5-T system. Sagittal and coronal T1-weighted images (500–600/16–20/1–2 [repetition time/echo time/excitations]) were acquired with a 24-cm field of view, a 3- to 5-mm section thickness with a 1-mm intersection gap, and a 128, 192, or 256 × 256 acquisition matrix. T2-weighted cardiac-gated or flow-compensated coronal and transaxial images (2000–2800/30–35,70–80/1) were acquired with a 3- to 4-mm section thickness with a 1.5-mm intersection gap in the coronal plane and a 5-mm section thickness with a 2.5-mm intersection gap in the axial plane, and a 192 × 256 acquisition matrix. The field of view was 20 cm for the coronal studies and 24 cm for the transaxial studies.

The MR images were interpreted by an experienced neuroradiologist without knowledge of clinical, EEG, or surgical data. MR findings were reported as follows: (*a*) abnormal signal on T2-weighted images in either the hippocampus/amygdala (defined as increased signal of the hippocampus/amygdala relative to other gray matter [Fig 1A and B]) or the temporal lobe (increased signal in gray/white matter relative to other gray/white matter); (*b*) atrophic change in the hippocampus/amygdala or temporal lobe; (*c*) structural or mass deformity, solid or cystic, calcification or hemorrhage (on T1- or T2-weighted images); and (*d*) extratemporal lobe abnormalities.

Criteria for interpretation of atrophy were asymmetry of the hippocampi, amygdalae, or temporal lobes, with the smaller side being designated as atrophic (at least a 20% difference in the size of the hippocampus, amygdala, or temporal lobe relative to the opposite side was required to qualify as atrophic) (Fig 1C).

The MR interpretations were classified overall as either normal or abnormal. If abnormal, an exact description and location of the abnormalities were given, using the criteria outlined above. Abnormalities in the mesial temporal lobe were divided into four groups, depending on the presence or absence of high signal on T2-weighted images and the distribution of any atrophy, as follows: group 1, high signal in the hippocampus/amygdala with ipsilateral hippocampal/amygdalar and temporal lobe atrophy (Fig 1); group 2, high signal in the hippocampus/amygdala with ipsilateral hippocampal/amygdalar atrophy (Fig 2A–C); group 3, high signal in the hippocampus/amygdala only, without appreciable atrophy (Fig 3); and group 4, hippocampal/amygdalar atrophy only, without T2 abnormality.

MR abnormalities in the temporal lobe outside the hippocampus or amygdala were rated on the basis of signal change and mass effect on T1- and T2-weighted images as well as on the nature of tumors (cystic or solid, calcified or hemorrhagic components) if a tumor was seen. After surgery, these overall assessments were compared with pathologic results and clinical outcomes.

To determine the effect of interobserver variation on the findings, all examinations were reviewed by another neuroradiologist and interpreted in the same standardized fashion as above.

Surgery and Pathologic Study

Temporal lobectomy for the patients with presumed mesial temporal sclerosis was performed with a subpial en bloc resection technique, including anterior temporal neocortex, 3 to 4 cm of intact hippocampal formation, most of the basolateral amygdaloid nuclear group and uncus, under neuroleptanesthesia with electrocorticography done before and after the resec-

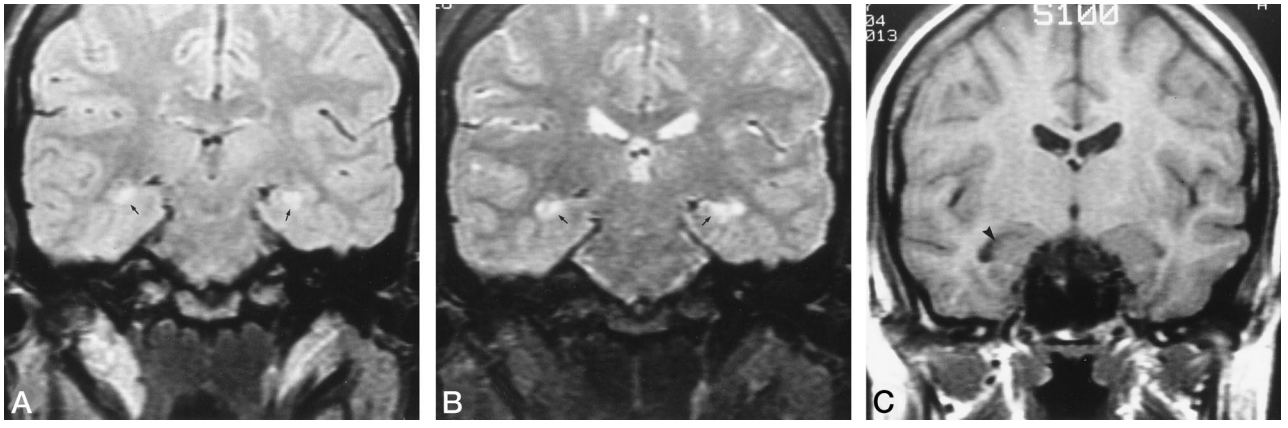

FIG 2. Bilateral mesial temporal sclerosis with MR group 2 manifestations on the right.

A–C, Coronal proton density–weighted (2500/30/2) (*A*), T2-weighted (2500/70/2) (*B*), and T1-weighted (500/20/2) (*C*) images show increased signal in both hippocampi (*arrows*) and diminished size of the right hippocampus (*arrowhead*).

D and *E*, Coronal proton density–weighted (2800/30/1) (*D*) and T2-weighted (2800/80/1) (*E*) images show postoperative change 5 years after standard right temporal lobectomy for intractable seizures (the medial structure is residual posterior parahippocampal gyrus). Hyperintensity in the left hippocampus and seizure frequency have not changed since the surgery.

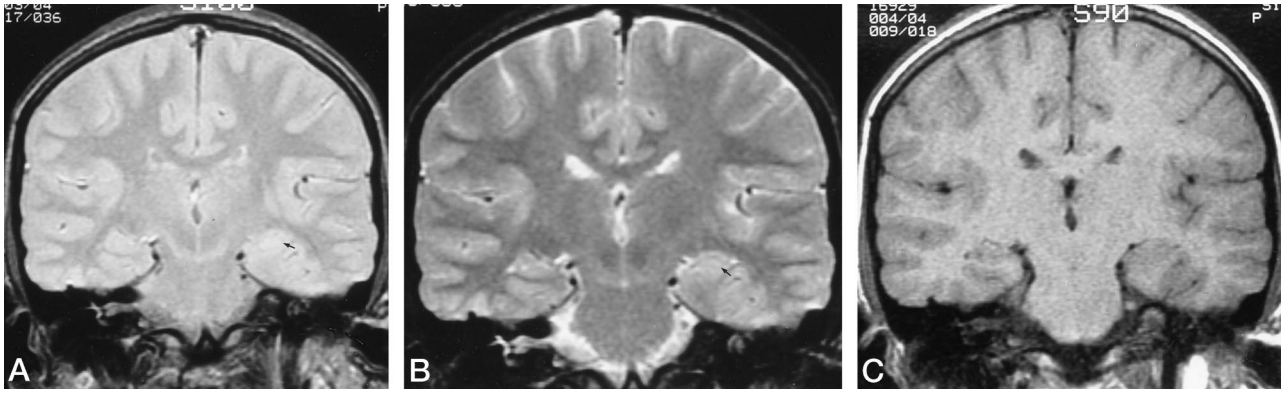

FIG 3. Left mesial temporal sclerosis seen as subtle increased signal intensity, with MR group 3 manifestation. Coronal proton density–weighted (2800/30/1) (*A*), T2-weighted (2800/80/1) (*B*), and T1-weighted (400/18/2) (*C*) images reveal subtle increased signal intensity (*arrows*) in the left hippocampus without ipsilateral hippocampal and temporal lobe atrophy.

tion. Any space-occupying lesions or other focal lesions were removed as radically as possible.

The surgical specimens were assessed by two experienced neuropathologists and divided into four groups: mesial temporal sclerosis; tumors; other lesions; and no, or nonspecific, abnormalities.

Outcome

Outcome after surgery was assessed by standard clinical follow-up. A modified three-point outcome classification rating scale (16) was used to evaluate the surgical outcome for epilepsy: 1, seizure free (no seizures); 2, significant improvement (>75% reduction in seizure frequency); and 3, no significant improvement (<75% reduction in seizure frequency). Only patients who had had at least 12 months' follow-up were included in our outcome analyses.

Statistical Analysis

Multiple paired comparisons were made by using χ^2 analysis to assess the differences between MR detection of hippocam-

pal/amygdalar and temporal lobe abnormalities, between duration of seizures and frequency of hippocampal/temporal atrophy in patients with hippocampal sclerosis, and between MR findings and surgical outcome.

To determine the accuracy of MR imaging in the diagnosis of temporal lobe epilepsy, radiologic interpretation was compared with pathologic findings, and sensitivity and specificity with 95% confidence intervals were calculated. A receiver operating characteristic (ROC) curve was drawn by using the calculated sensitivity and specificity for each of the MR findings in the diagnosis of mesial temporal sclerosis. Interobserver variation was measured by using κ statistics.

TABLE 1: Histologic findings in temporal lobe epilepsy

Histologic Findings	No. (No. Accompanied by Mesial Temporal Sclerosis)	**Total No. (%)**
Mesial temporal sclerosis		**105 (56)**
Hippocampal sclerosis only	90	
Amygdala sclerosis/gliosis	2	
Hippocampal sclerosis plus amygdala sclerosis/gliosis	13	
Tumors		**42 (23)**
Astrocytoma	13	
Oligodendroglioma	8 (1)	
Mixed glioma	3 (1)	
Glioblastoma	1	
Ganglioglioma	10 (2)	
Dysembryoplastic neuroepithelial tumor	1	
Hamartoma	4 (1)	
Meningioangiomatosis	1	
Epidermoid cyst	1	
Other focal lesions		**22 (12)**
Vascular malformation		
Arteriovenous malformation	3	
Cavernoma	3 (1)	
Venous angioma	1	
Trauma	1	
Inflammatory lesions	3 (3)	
Infarct	3 (1)	
Neuronal migration disorder		
Heterotopic gray matter	1	
Cortical dysplasia	4	
Polymicrogyria	1	
Miscellaneous		
Meningeal cyst	1	
Acquired cyst	1	
Nonspecific or normal examination		17 (9)
Total		**186 (100)**

Results

Pathologic Findings (Table 1)

Of the 186 temporal lobectomies performed, 168 provided adequate samples of hippocampus and amygdala. Of these 168, 121 (72%) had abnormalities: 115 had mesial temporal sclerosis, of which 100 had only hippocampal sclerosis; 13 (11%) had both hippocampal and amygdalar sclerosis, and 2 (2%) had amygdalar sclerosis only. Ten (9%) of the 115 with mesial temporal sclerosis had dual abnormalities: five tumors, one cavernoma, one infarct, and three inflammatory diseases (one Rasmussen encephalitis, one cytomegalovirus, and one "viral infection"). In these 10 dual abnormalities, hippocampal sclerosis was the only additional pathologic finding. In the specimens from the six other patients, four contained tumor, one had cortical dysplasia, and one a hamartoma in the amygdala.

The neocortex (including the parahippocampal gyrus) was examined in all 186 resections and was abnormal in 60 cases (32%). Of those, 39 (21%) had tumors and 21 (12%) had other focal lesions.

MR Findings

MR correctly detected 113 of the 121 hippocampal/amygdalar lesions (sensitivity 93%, specificity 83%) and 58 of the 60 lesions in the rest of the temporal lobe (sensitivity 97%, specificity 97%) (Table 2). There was no significant difference in rater ability to detect lesions in the hippocampus/amygdala as compared with the rest of the temporal lobe. The false-positive MR rate for detection of lesions in the hippocampus/amygdala (3 of 47) was not significantly different from that of lesions elsewhere in the temporal lobe (2 of 126) ($P > .05$).

Interobserver agreement ranged from 0.4 to 0.93 for all the MR findings evaluated (Table 3). Interobserver agreement was highest for temporal lobe signal abnormalities (0.93) and mass effect and deformity (0.91), but was also significant for hippocampal signal abnormalities (0.70). Interobserver agreement was lowest for visual assessment of temporal lobe atrophy (0.40).

Twenty-two (12%) of 186 patients had extratemporal lesions, of which seven were extensions from temporal lobe lesions. The remainder were located in frontal, parietal, occipital, or deep white or gray matter. Small, focal, white matter changes less than 5 mm in size on T2-weighted images were seen in eight

TABLE 2: Accuracy of MR imaging in detecting and locating lesions in the hippocampus/amygdala (n = 168) and the temporal lobe (n = 186) in patients with temporal lobe epilepsy

MR Location	Sensitivity (No.) (95% CI)	Specificity (No.) (95% CI)	PPV (95% CI)	NPV (95% CI)
Hippocampus/amygdala	0.93 (113/121) (0.91, 0.95)	0.83 (39/47) (0.80, 0.86)	0.93 (0.87, 0.91)	0.93 (0.70, 0.91)
Temporal lobe	0.97 (58/60) (0.94, 1.00)	0.97 (122/126) (0.92, 0.99)	0.94 (0.84, 0.97)	0.98 (0.94, 1.00)

Note.—CI indicates confidence interval; PPV, positive predictable value; and NPV, negative predictable value.

TABLE 3: Interrater agreement in interpretation of MR images

	Observer Agreement	Chance-Expected Agreement	κ	Standard Error	Critical Ratio
Signal in HC	0.87	0.57	0.70	0.08	8.75
Signal in TL	0.97	0.58	0.93	0.07	13.29
Mass deformity	0.97	0.67	0.91	0.08	11.37
HC atrophy	0.79	0.51	0.56	0.07	8.00
TL atrophy	0.74	0.57	0.40	0.07	5.71

Note.—HC indicates hippocampus; TL, temporal lobe.

cases but were excluded from analysis owing to lack of pathologic confirmation. Thirty-two (17%) of 186 patients had cerebellar atrophy on MR images.

Mesial Temporal Sclerosis.—MR findings in the 115 cases of pathologically determined mesial temporal sclerosis were as follows: abnormal T2 signal in the hippocampus in 107 (93%), visually assessed hippocampal atrophy in 71 (62%), temporal lobe atrophy in 55 (48%), and normal mesial temporal lobe structures in seven (6%). Three patients had abnormal signal in both hippocampi (Fig 2). One patient with abnormal signal and atrophy in the left hippocampus but EEG localization in the right underwent right temporal lobectomy and had mesial temporal sclerosis confirmed pathologically. Four patients had bilateral hippocampal atrophy and three patients had temporal lobe atrophy contralateral to pathologically proved mesial temporal sclerosis.

The extent of hippocampal T2 signal abnormality varied greatly from case to case, from subtle or segmental (Fig 3) to widespread throughout the hippocampus (Fig 1). All these degrees of signal intensity were classified as abnormalities.

Sensitivity in the four groupings of MR findings was as follows: group 1 (abnormal T2 signal in the hippocampus/amygdala with ipsilateral hippocampal/amygdalar and temporal lobe atrophy): 39% (45 of 115 cases); group 2 (abnormal T2 signal in the hippocampus/amygdala with ipsilateral hippocampal/amygdalar atrophy): 61% (70 of 115 cases); group 3 (abnormal T2 signal in the hippocampus/amygdala): 93% (107 of 115 cases); group 4 (hippocampal/amygdalar atrophy without T2 abnormality): no case fell into this category by visual assessment. An ROC curve was constructed (Fig 4) on the basis of the values of true-positive and true-negative readings. Point *C* on the ROC curve, which is closest to the upper left-hand corner, is the best cutoff point in terms of making the fewest mistakes in MR diagnosis of mesial temporal sclerosis. At this point, the positive predictive value was a little lower (0.88) than that of points *A* and *B*, but the negative predictive value was much higher (0.83) than that of points *A* and *B*.

Eight cases of pathologically proved mesial temporal sclerosis were not detected by MR imaging on the basis of increased hippocampal signal on T2-weighted images or hippocampal atrophy (Fig 5). In two cases, imaging results were entirely normal. Of the remaining six, one patient had Sturge-Weber syndrome with lesions in the posterior temporal and occipital regions, with temporal lobe atrophy; one patient had

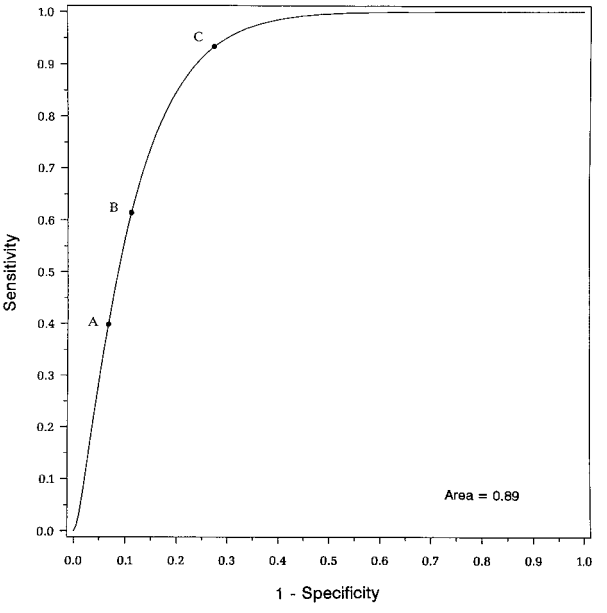

FIG 4. ROC curve compares performance of three diagnostic procedures for mesial temporal sclerosis. The true operating points on this curve are indicated: *A*, abnormal T2 signal in hippocampus with ipsilateral hippocampal and temporal lobe atrophy (sensitivity 40%, specificity 94%); *B*, abnormal T2 signal in hippocampus with ipsilateral hippocampal atrophy (sensitivity 61%, specificity 87%); *C*, abnormal T2 signal in hippocampus only (sensitivity 93%, specificity 74%).

high signal in the nonneocortical temporal lobe (this area showed no pathologic abnormality); three patients had accompanying ipsilateral temporal lobe tumors; and one patient had high signal in the right hippocampus, but a left temporal lobectomy disclosed mesial temporal sclerosis.

A significant relationship was found between the presence of hippocampal atrophy and the duration of seizure disorder ($\chi^2 = 12.09$, $P < .001$) (Table 4 and Fig 6). No significant correlation was found between the duration of seizure disorder and temporal lobe atrophy ($\chi^2 = 6.15$, $P > .05$) (Fig 6). Hippocampal and temporal lobe atrophy did not correlate with the age of the patient.

Temporal Lobe Tumors.—Abnormal T2 signal and mass effect appeared in 35 of the 42 cases with tumors. Sensitivity and specificity of MR imaging for diagnosis of temporal lobe tumors were 83% and 97%, respectively, on these bases. However, two tumors (5%) (one temporal lobe ganglioglioma and one amygdalar hamartoma) had abnormal signal without mass effect. An additional two tumors (5%) (one

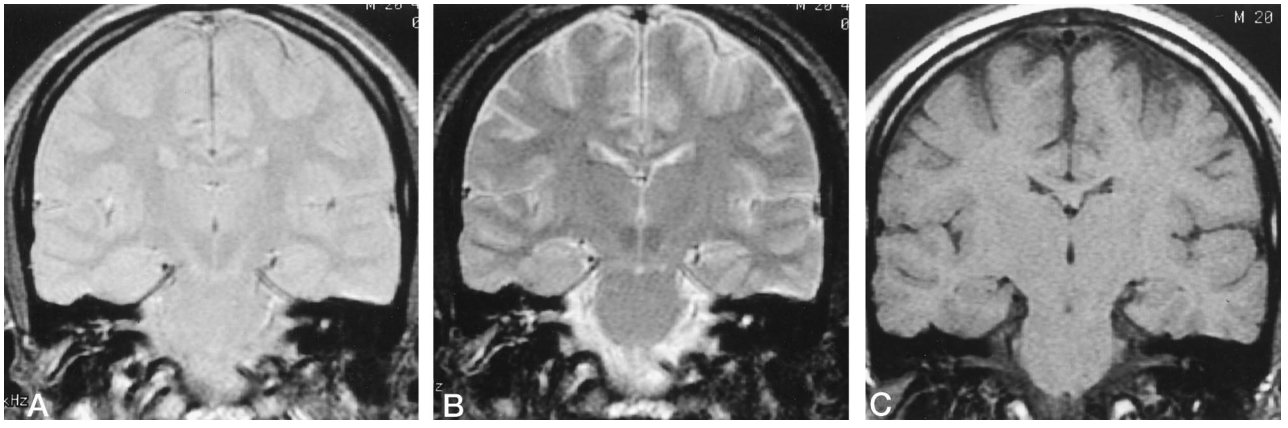

FIG 5. Right mesial temporal sclerosis with unremarkable MR findings. Coronal proton density–weighted (2800/30/1) (*A*), T2-weighted (2800/80/1) (*B*), and T1-weighted (450/16/2) (*C*) images show no evidence of signal or volume abnormality in the right hippocampus. The patient was seizure free at 12-month postsurgical follow-up.

TABLE 4: Hippocampal atrophy and duration of seizures in patients with mesial temporal sclerosis

	Years Since Seizure Onset				
	<11	11–20	21–30	>30	**Total**
Hippocampal atrophy					
Present	8	23	19	17	**67**
Absent	8	18	12	0	**38**
Total	16	41	31	17	105

Note.—The difference between four age groups is significant ($\chi^2 = 12.15$, $P < .01$). The chance of hippocampal atrophy in patients with seizure duration of >30 years is significantly higher than in patients with seizure duration of 11–20, 21–30 ($P < .01$), and <11 years ($P < .001$).

ganglioglioma in the parahippocampal gyrus and one amygdalar hamartoma) had abnormal signal accompanied by atrophy of the surrounding structures.

Three tumors (7%) were not identified on MR images, including one ganglioglioma (2 to 2.5 cm) in the inferior temporal lobe, one mixed glioma (multifocal) in the mesial temporal region, and one hamartoma (small clusters of neurons and oligodendrocytes) throughout the amygdala.

Five tumors (one oligodendroglioma, one mixed glioma, two gangliogliomas, and one hamartoma) were accompanied by hippocampal sclerosis; four of these were located in the mesial temporal structures and one in the temporal pole. However, in three of these cases with hippocampal sclerosis, the MR images were interpreted as only showing tumor.

Other Lesions.—Other focal lesions were seen in 22 of the 186 cases. Most had abnormal signal on T2-weighted images (19 of 22), and they usually had no mass effect. One case of amygdalar inflammatory disease was not detected at MR imaging. Mass effect was seen in one case of cortical dysplasia, one case of polymicrogyria, and one acquired cyst. Of the 22 cases, five were accompanied by hippocampal sclerosis, all of which were detected at MR imaging.

MR Findings and Surgical Outcome

Clinical follow-up data obtained at intervals ranging from 12 to 78 months (average, 24 months) were available for 182 (98%) of the 186 surgical patients. Of these, 114 patients (63%) were free of seizures and auras; 51 (28%) had more than a 75% reduction of seizure frequency; and 17 (9%) had less than a 75% reduction of seizure frequency.

Surgical outcome of patients with localized hippocampal/amygdalar lesions was no different from the surgical outcome of patients with lesions elsewhere in the temporal lobe. However, patients with multiple lesions or temporal lesions with extratemporal involvement were more likely to fall into a non–seizure free category (Fig 2) compared with patients with only temporal lobe lesions ($P < .05$) or hippocampal/amygdalar lesions ($P < .01$) (Table 5).

Of the three patients who had bilateral hippocampal high signal, one was seizure free, one had more than a 75% seizure reduction, and one had no change in seizure frequency (Fig 2). The patient who had

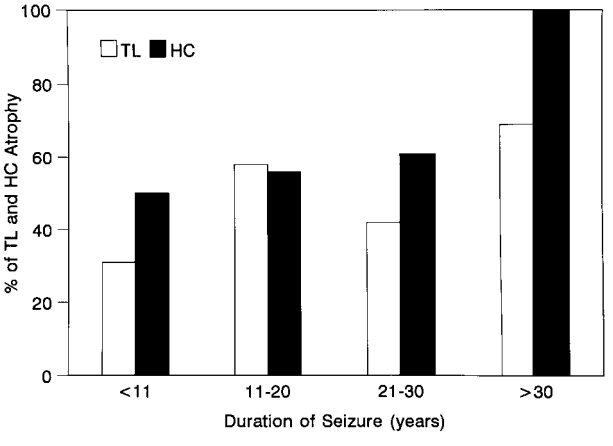

FIG 6. Percentage of ipsilateral hippocampal (*HC*) and temporal lobe (*TL*) atrophy relative to duration of seizures in patients with mesial temporal sclerosis. The percentage of hippocampal atrophy is significantly increased with the duration of seizures ($P < .01$), a correlation that is not significantly present with temporal lobe atrophy ($P > .05$).

TABLE 5: Surgical outcome versus MR findings in patients with temporal lobe epilepsy (n = 182)

MR Findings	Seizure Free, No. (%)	More than 75% Seizure Reduction, No. (%)	Less than 75% Seizure Reduction, No. (%)	**Total**
Hippocampus/amygdala abnormalities	65 (66)	29 (29)	5 (5)	**99**
Temporal lobe abnormalities	32 (69)	9 (20)	5 (11)	**46**
Multiple Lesions*	7 (31)	10 (45)	5 (23)	**22**
Normal	8 (53)	5 (33)	2 (13)	**15**
Total	112	53	17	**182**

* The outcome of multiple lesions depicted on MR images was significantly worse than the outcome of lesions seen only in the temporal lobe ($\chi^2 = 6.84$, $P < .05$) or only in the hippocampus/amygdala ($\chi^2 = 10.24$, $P < .01$).

contralateral hippocampal high signal had more than a 75% seizure reduction.

Discussion

Numerous studies have shown that the preoperative diagnosis of both mesial temporal sclerosis and epileptogenic temporal lobe tumors is best done noninvasively with MR imaging (1–10). Our large series included both mesial temporal sclerosis and other disease entities in a group of patients with medically intractable focal seizures.

Mesial temporal sclerosis is a term coined by Falconer and colleagues (17) to describe a lesion characterized by neuronal loss and gliosis involving principally the hippocampus and amygdala, or both, but occasionally extending to other mesial temporal structures or even throughout the temporal lobe, and leading to generalized atrophy and gliosis. It appears in about 65% of temporal lobectomy specimens resected for intractable epilepsy (18).

In our study, 93% of the cases of mesial temporal sclerosis showed high T2 signal abnormalities localized in the hippocampus and were not associated with mass effect. This 93% detection rate of high T2 signal abnormality of the hippocampus exceeds the 80% to 90% rate reported in other studies (2, 8, 11, 19). Only one other study that had a small number of patients and used T2-weighted images parallel to the long axes of the hippocampi, showed higher sensitivity (14/14) in the detection of hippocampal signal abnormality (20). Heterogeneity of the MR field strength (from 0.15 T to 1.5 T), imaging technique, and image quality most likely account for the considerable variation among studies. The degree and extent of hippocampal gliosis also correlate with the T2 signal in the hippocampus (21). Selection criteria of cases in our series and selection criteria used for surgery could also be responsible for these differences.

Considering the difficulty of visually detecting abnormal or subtle T2-weighted signal intensity in the hippocampus, Jackson et al (8) used quantitative T2 relaxometry to detect hippocampal abnormalities, a technique that objectively measures hippocampal signal intensity; fluid-attenuated inversion recovery (FLAIR) has also been used to show this abnormal signal (22).

The T2-weighted signal abnormalities of mesial temporal sclerosis are due to gliosis in the hippocampus (23), but the causal relationship between seizures and histopathologic findings remains controversial (24, 25). In our series, 10 cases of hippocampal sclerosis were accompanied by another lesion (Table 1). Seven of the 10 temporal lobe lesions were located in the mesial temporal region adjacent or close to the sclerotic hippocampus, one in the temporal pole, one in the insula, and another in the middle cerebral artery distribution (old infarct). These lesions most likely represent the original epileptogenic foci, with hippocampal sclerosis presumably arising as a consequence of the repeated discharges from the adjacent lesion.

A T2-weighted hyperintensity in the hippocampus can also be induced by hippocampal tumor, hamartoma, or an inflammatory process, which produces an appearance similar to that seen in hippocampal sclerosis. Why four of our cases had a definite abnormal T2 signal with a normal hippocampus on microscopic examination is unclear. Some studies suggest that edema caused by seizures (26, 27) or drug effects (28) can induce MR hyperintensity in the hippocampus.

Hippocampal atrophy has been widely studied, particularly since the advent of quantitative MR for measuring hippocampal volume (10), but sensitivity and specificity or relationship to seizures vary among studies. Among our cases, visual hippocampal atrophy was present in 64% of 105 patients with mesial temporal sclerosis (excluding patients with dual abnormalities). Because we used an interhippocampal size difference of less than 20% to establish atrophy, a lesser volume loss would have been considered normal, but it is less likely that false-positive findings would have been identified. Sensitivity of hippocampal volumetric measurements in detecting mesial temporal sclerosis is relatively higher (80% to 100%) than visual analysis (80% to 90%) (11). However, qualitative assessment of hippocampal body atrophy measured segmentally identified 40 of 40 cases of mesial temporal sclerosis (29).

That our visually rated hippocampal atrophy correlated with the duration of seizure disorder corresponds to an earlier finding (30). In this quantitative study of 34 patients with medial temporal lobe seizure onset, the 28 patients with hippocampal atrophy had a longer mean duration of seizure disorder (19 to 21 years) than did the patients without atrophy (12 years). There was a definite association between prolonged febrile convulsions in childhood and seizures

TABLE 6: Sensitivities of different MR techniques in the investigation of mesial temporal sclerosis

Publication	Technique	Sample Size	Sensitivity, % (No.)	Pathologic Confirmation	Postoperative Follow-up
Jack et al (10) 1990	Volumetric	41	76 (31/41)	Yes	Yes
Ashtari et al (36) 1991	Volumetric	28	86 (24/28)	19/28	Yes
Cook et al (9) 1992	Volumetric	20	100 (20/20)	No	No
Cendes et al (40, 41) 1993	Volumetric	31	92 (23/25)	11/31	No
Kuks et al (13) 1993	Volumetric	107	42 (45/107)	No	No
Spencer et al (30) 1993	Volumetric	56	75 (42/56)	Yes	No
Jackson et al (34) 1993	T2 mapping	50	70	14/50	No
Jack et al (22) 1996	Fluid-attenuated inversion recovery	36	97 (35/36)	Yes	No
Bronen et al (35) 1996	Visual	117	98 (47/48)	Yes	Yes
Jackson et al (8) 1990	Visual	81	93 (25/27)	Yes	Yes
Kuzniecky et al (29) 1996	Visual*	47	100 (47/47)	Yes	Yes
Lee et al, Current study	Visual	185	93 (107/115)	Yes	Yes

* The study included only segmental assessment of the hippocampal size.

originating in the mesial temporal lobe (30, 31). The progressive neuronal loss induced by repeated kindled seizures (a laboratory model whereby electrical stimulation via implantation is applied repeatedly to the perforant pathway, amygdala, or olfactory bulb to determine the distribution and time course of neuronal loss induced by seizures in hippocampal, limbic, and neocortical pathways) (32) suggests that as the duration of seizure disorder increases, the hippocampus (and/or amygdala) will atrophy more. Cerebellar atrophy (17%) observed in our patients with temporal lobe epilepsy and in another study (33) may also lend support to the idea that seizures themselves may damage neurons with time.

We observed temporal lobe atrophy in the appropriate lobe in 48% of patients in whom mesial temporal sclerosis was the major pathologic finding. This detection rate does not justify using that finding solely to identify mesial temporal sclerosis in seizures and there was no significant statistical relationship between temporal lobe atrophy and duration of seizure disorder. Temporal atrophy on MR images can, however, increase the specificity of hippocampal hyperintensity for mesial temporal sclerosis. Information revealed from the ROC curve (Fig 4) constructed on the basis of criteria used in this study shows that abnormal hippocampal T2 hyperintensity has the highest diagnostic value (sensitivity 93%, specificity 74%); as more criteria (eg, hippocampal or temporal lobe atrophy) are applied, the diagnosis of mesial temporal sclerosis becomes specific (specificity up to 94%), and can be predicted more confidently. The use of multiple features to evaluate mesial temporal sclerosis has also been emphasized in other reports (11, 34, 35).

In our series, a consistently high positive and negative predictive value for MR imaging was observed with even simple visual assessment (ie, a positive MR finding reliably indicated temporal lobe disease outside the hippocampus and amygdala, and had only a slightly smaller yield for showing disease in the mesial structures). There is, however, a caveat here, in that our material is obviously selected. Other studies, both volumetric (36) and otherwise (37), in which there were control data as well as pathologically confirmed temporal lobe lesions in blindly interpreted MR examinations, have shown that the sensitivity of MR imaging is greater than 90% for depicting pathologic entities, but that specificity drops to between 60% and 80% with this very high sensitivity. Most of the other studies have been selective, with only small numbers of control subjects, or only pathologically confirmed cases that were then compared retrospectively with control data. The only known prospective study using volumetric MR used limited volumetric MR of the mesial temporal lobe structures (sections through only part of the hippocampus) and had pathologic confirmation in a group of patients with seizures that were difficult to localize (30). These authors reported a sensitivity of 75% but a specificity of only 64% for mesial temporal sclerosis.

Most recent MR investigations in mesial temporal sclerosis have focused on either T2 signal abnormality (via T2 mapping and FLAIR) or hippocampal volume (volumetric measurement) or both (visual inspection). The rate of sensitivity for detecting hippocampal T2 signal abnormality via visual inspection in our study and in some other recent studies (22, 35) has been over 90% (Table 6).

As has been reported (16, 38, 39), good or excellent outcomes have been achieved in patients with solitary temporal lobe abnormalities, with 86% to 95% of these showing significant improvement in the seizure disorder. As might be expected, the rate of improvement falls when there are multiple abnormalities or temporal lesions with extratemporal involvement.

Conclusions

MR imaging is highly sensitive in detecting and locating abnormalities in the temporal lobe and the hippocampus/amygdala in patients with temporal lobe epilepsy. Hippocampal T2 signal abnormality is a common presentation in mesial temporal sclerosis; the specificity for and confidence in diagnosing mesial temporal sclerosis on the basis of this finding increase if it is associated with ipsilateral hippocampal and/or temporal lobe atrophy. Finally, visually rated hippocampal atrophy in mesial temporal sclerosis correlates with the duration of seizures. It is likely that further volumetric data will corroborate this finding.

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