An MR Protocol for Presurgical Evaluation of Patients with Complex Partial Seizures of Temporal Lobe Origin

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PURPOSE: To find an optimal diagnostic protocol for the presurgical MR evaluation of patients with temporal lobe epilepsy. **METHODS:** MR imaging in 14 healthy subjects and 25 consecutive patients with temporal lobe epilepsy was performed in paracoronal sections perpendicular to the hippocampi with T1-weighted inversion recovery and T2 weighting. Volume measurements of the hippocampus/amygdala complex were performed and a multiecho sequence yielded T2-calculated images. **RESULTS:** Hippocampal disease was seen in 22 of 25 temporal lobe epilepsy patients on paracoronal T1-weighted inversion recovery images. Four had bilateral abnormalities. Characteristic for hippocampal disease were features such as volume loss, decreased signal, and loss of internal morphology. Only 17 of 25 patients demonstrated hippocampal pathology on T2-weighted images, and in one patient this was bilateral. Patients with only minimal structural loss on T1-weighted inversion recovery had normal T2-weighted images. T2 calculation was no more sensitive than visual assessment on the T2-weighted images. Volume measurements were normal in one patient and misleading in two patients. Lateralization, as compared with clinical and electroencephalographic findings, was most confidently done with paracoronal T1-weighted inversion recovery images and volume measurements. **CONCLUSIONS:** An optimum MR protocol for temporal lobe epilepsy patients is proposed. Its essential feature is that the hippocampus be evaluated by paracoronal T1-weighted inversion recovery images and volume measurements. T2-weighted imaging can be omitted.

Index terms: Sclerosis, hippocampal; Brain, magnetic resonance; Brain, temporal lobe; Seizures, complex partial

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Patients with medically uncontrolled partial seizures of temporal lobe origin are possible candidates for surgery. To locate the seizure focus correctly, they are evaluated with scalp and video electroencephalography, neuropsychological examination, and morphological (magnetic resonance [MR]) and metabolic (positron emission tomography, single-photon emission computed tomography) imaging (1–3). MR has become the most important imaging modality to evaluate patients with temporal lobe epilepsy (TLE) (2, 4, 5), because morphologic abnormalities can be easily detected and their extent defined. Recent estimates indicate that as many as 70% to 90% of patients with chronic focal epilepsy present with some kind of structural abnormality, be it a foreign tissue lesion or scarring and/or atrophy of the hippocampus or the temporal neocortex (2). Foreign tissue lesions are readily detected and characterized with computed tomography (CT) and standard MR imaging, including gadolinium-enhanced T1-weighted imaging (6). Hippocampal damage has been diagnosed qualitatively with T2-weighted paracoronal imaging, increased signal and volume loss being the landmarks of hippocampal sclerosis (1, 2, 7–9). An asymmetric decrease in the calculated hippocampal volume has been found highly sensitive for hippocampal sclerosis by some authors (7, 10–13), but others found clear exceptions (14). Jackson et

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TABLE 1: Hippocampal disease detected on paracoronal T1-weighted inversion recovery images compared with electroencephalography findings

Electroencephalography	Hippocampal disease		
	None	Unilateral	Bilateral
Unilateral	3*	16	2†
Nonlateral	0	2‡	2

* Two patients with a neuronal migration disorder, one with a foreign tissue lesion.

† Severe damage on the side of the electroencephalography abnormality, minimal structural loss on the other side.

‡ One side minimal structural loss only.

al (15) did an extensive qualitative visual evaluation of four parameters from paraxial T1-weighted inversion recovery and paracoronal T2-weighted and T1-weighted inversion recovery images. Paracoronal T1-weighted inversion recovery images were most sensitive and specific in depicting hippocampal disease. Only 39% of their patients with hippocampal sclerosis demonstrated all the features considered characteristic. These authors also advocate that calculating the T2 of the hippocampi could help identify subjects with bilateral disease (16). We compared different MR sequences in their ability to identify structural hippocampal and temporal neocortical damage in relation to clinical and electrophysiologic data.

Materials and Methods

Fourteen healthy subjects with a mean age of 23 years (range, 20 to 37 years) and 25 consecutive patients with an established diagnosis (clinical and electroencephalographic) of TLE refractory to medical treatment were selected for preoperative evaluation. The mean age of the patients was 34.5 years (range, 14 to 53 years) and the mean age of seizure onset was 10 years, 2 months (range, 3 months to 28 years). All patients underwent a clinical neurologic examination, neuropsychological testing, and prolonged video-electroencephalographic monitoring. At least two habitual complex partial seizures were recorded. Clinical features and electroencephalographic findings were analyzed by two experienced neurologists (P.B. and J.D.R.) to locate the seizure focus. These results then were compared with the MR findings (Table 1).

MR imaging of the temporal lobes was performed on a 1.5-T MR system (Siemens [Erlangen, Germany] Magnetom 1.5-T SP4000). An axial long-repetition-time/long-echo-time spin-echo sequence was used to screen for extratemporal pathology. In patients with a history of trauma, an axial gradient-echo T2*-weighted sequence ruled out small hemosiderin deposits. After biplane location, using a midline sagittal T1-weighted sequence followed by a turbo inversion recovery T1-weighted paraxial sequence along the axis of the hippocampus, imaging of the temporal lobes was performed in 4-mm-thick paracoronal sections perpendicular to the hippocampi with an inplane resolution of 0.9 mm (256^2) (Fig 1). Images were acquired first with a T1-weighted inversion recovery sequence (3500/20/1; inversion time, 300) in 10 sections with an intersection gap of 2 mm (Fig 2A), second with a T2-weighted, spin-echo sequence (2370/80/1; flip angle, 75°) in 20 sections with an intersection gap of 0.4 mm (Fig 2B), and third with a multiecho sequence (Carr-Purcell-Meiboom-Gill) with 8 echos yielding T2 calculated images (2000/20–160/1) in 10 sections with an intersection gap of 2 mm (Fig 2C). Last, the head was then scanned with a three-dimensional magnetization preparation rapid-acquisition gradient-echo sequence (11/5/1; inversion time, 200; flip angle, 8°; 192 sections; 128 partitions) that provided 1.5-mm-thick contiguous paracoronal T1-weighted images with the same tilt as the two-dimensional paracoronal images (Fig 2D). The total scan time for this protocol was approximately 45 minutes.

Qualitative evaluation was performed by two experienced observers (E.A. and P.B.). In cases of disagreement, a consensus was reached. Section-by-section visual as-

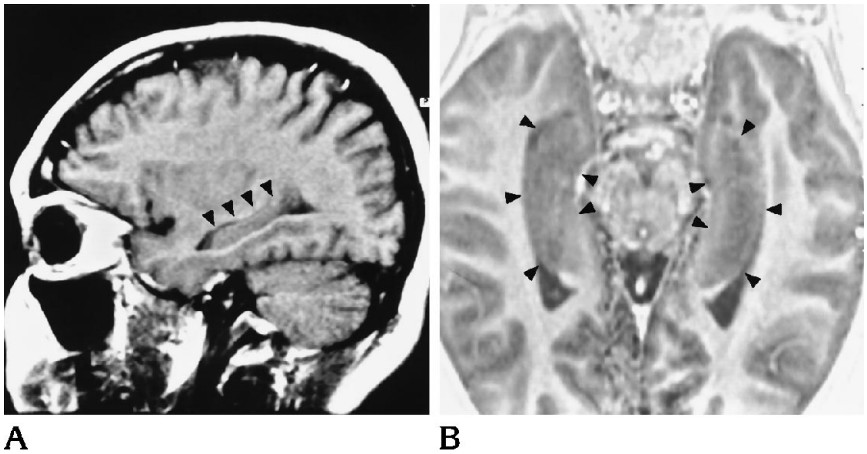


Fig 1. Locating the hippocampus. *A*, Parasagittal T1-weighted image (500/15/1 [repetition time/echo time/excitations]) shows the hippocampus (*arrowheads*) and is used to position the paraxial turbo inversion recovery locater (2500/19/1; inversion time, 300).

B, In such a way, the plane for symmetric paracoronal hippocampal imaging is defined.

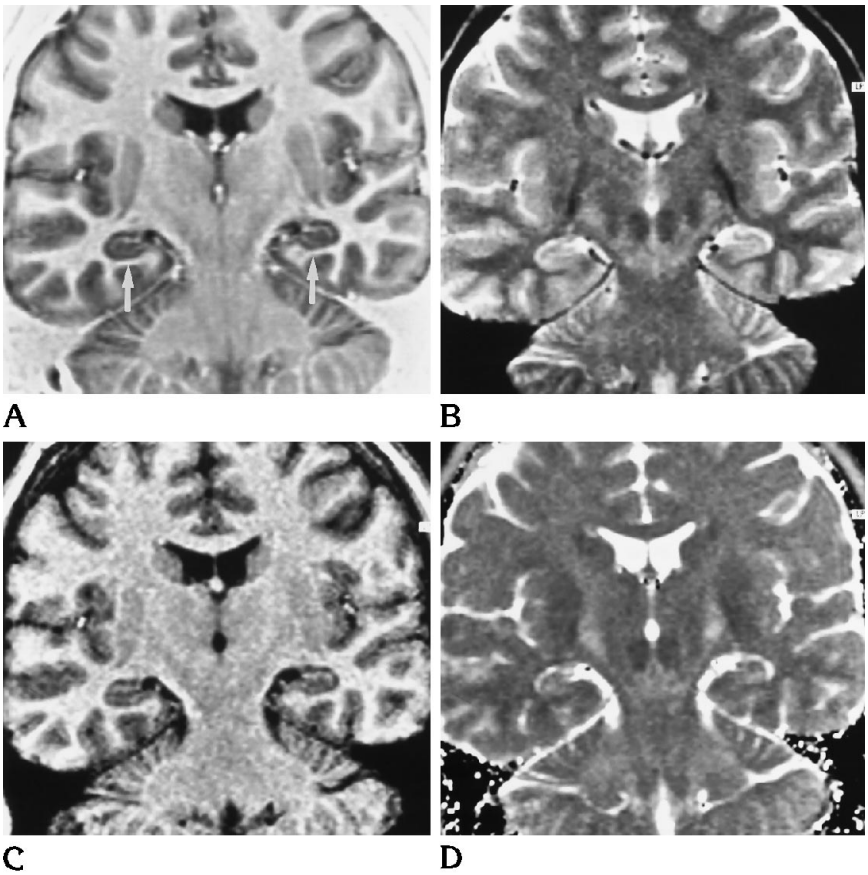


Fig 2. Imaging the hippocampus. Images acquired from a healthy subject.

A, Paracoronal T1-weighted inversion recovery image (3500/20/1; inversion time, 300). Note the symmetry and the excellent detail on the internal morphology of the hippocampus (*white arrows*; see Fig 3).

B, Paracoronal T2-weighted image (2370/80/1). The hippocampi have signal comparable to gray matter, and no internal structure is visible as on the T1-weighted inversion recovery image.

C, Section from the three-dimensional magnetization preparation rapid-acquisition gradient-echo (see text). The hippocampal volume was measured by manual contouring (see Fig 4).

D, T2-calculated image. The T2 values were measured in a circular region of interest positioned over the hippocampus and the temporal white matter.

sessment of the signal and the volume of the hippocampus and the temporal lobe was performed on the T2-weighted images. Signal increase and/or a clear decrease in volume as compared with the contralateral side were considered a sign of disease (1, 8, 9). On the T1-weighted inversion recovery images, on the other hand, a loss of gray matter volume and/or a decreased signal in the hippocampus and/or the temporal white matter and/or a loss of the normal internal structure of the hippocampus were considered proof of disease (15, 17).

The volume of the hippocampus/amygdala (12) complex was measured on the individual 3-D magnetization preparation rapid-acquisition gradient-echo images by manual contouring on a DEC5033 workstation (Digital, Maynard, Mass) with a homemade software routine. The images were viewed in a posteroanterior direction, and the volume measurements started on the first section where the thalamus was clearly visible. The last section was always at the level where the middle cerebral arteries were visible. Hippocampal volume measurement was assessed as an absolute parameter and as a comparative parameter by calculating the interhippocampal volume difference δV_{HC} as:

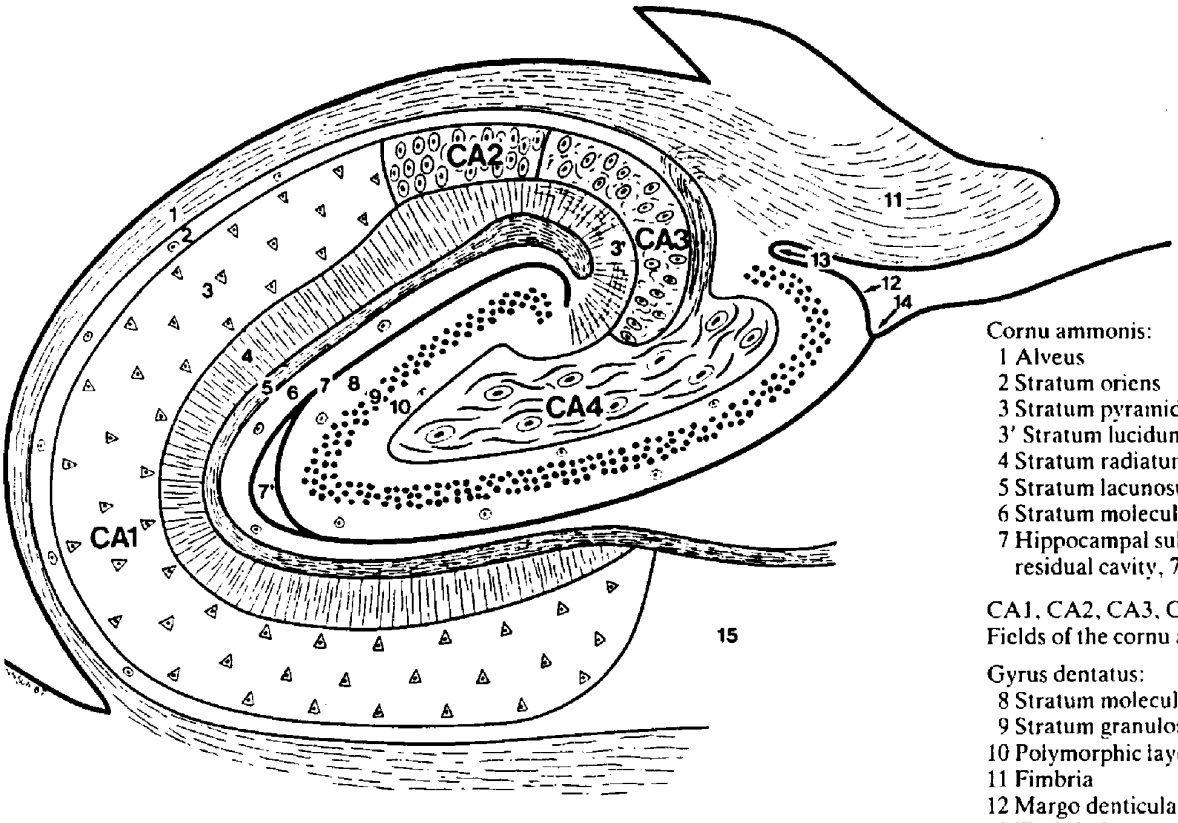
$$\delta V_{HC} = |200*(V_L - V_R)/(V_L + V_R)|,$$

where V_L was the volume of the left hippocampus and V_R, the volume on the right. A pixel-per-pixel monoexponential fit on the original Carr-Purcell-Meiboom-Gill images (standard SP-software, Siemens) yielded T2-calculated images (Fig 2C). The mean T2 values of the hippocampus and anterior temporal white matter were calculated from 4 or 5 sections using a simple circular region of interest.

Results

Healthy Subjects

None of the 14 healthy subjects had any abnormality on the axial T2-weighted images in any part of the brain. On visual inspection, the hippocampus and temporal lobes were of equal size on paracoronal inversion recovery T1-weighted and T2-weighted images. On the T2-weighted images, the signal of the normal hippocampus was comparable to that of cortical gray matter, and no signal asymmetries could be detected. On the T1-weighted inversion recovery images, a symmetric three-layered architecture was seen (Fig 2A). The signal of the inner and outer layers was equal to the signal of gray matter, whereas the middle layer had signal comparable to white matter (Fig 3). Although an internal architecture was sometimes



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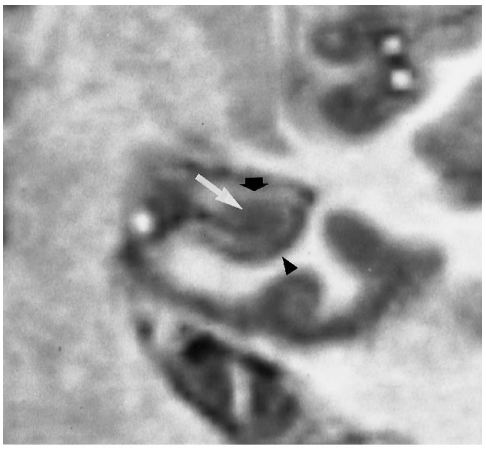

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Fig 3. Hippocampal morphology and cytoarchitecture. *A*, Diagram of a transverse section of the hippocampal body (from Duvernoy [18]). *B*, The inferolateral gray matter zone (*black arrowhead*) seen in the hippocampus on paracoronal T1-weighted inversion recovery images results mainly from two fields of the cornu ammonis, CA-1 and CA-2. The gray matter–like center (*white arrow*) is composed by CA-4 of the cornu ammonis and the stratum granulosum of the gyrus dentatus. Between these two, white matter tracts in the stratum radiatum of the cornu ammonis are responsible for the intermediate zone of higher signal, more like white matter. The small very white flat structure on top of the hippocampus (*black arrow*) is formed by the fimbria and the alveus.

seen in the hippocampi of healthy subjects on T2-weighted paracoronal images, its presence was inconsistent. Therefore, no attempt has been made to evaluate hippocampi of TLE patients on the paracoronal T2-weighted images with this parameter. The signal of the anterior white matter was symmetric and homogeneous on inversion recovery T1-weighted and T2-weighted images. When compared, there was no difference with the white matter in other parts of the brain.

The average measured volume of the hippocampus/amygdala complex was 5.14 ± 0.39 mL (mean ± SD, n = 28, minimum = 4.43 mL, maximum = 5.72 mL). The value of δV_{HC} was between 0.45% and 5.17%, with a mean of

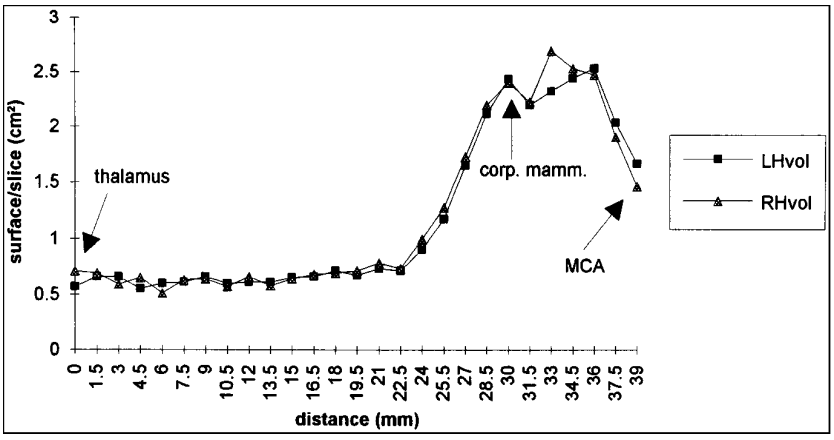

Fig 4. Volume curves from a healthy subject. Manual contouring of the three-dimensional magnetization preparation rapid-acquisition gradient-echo sections from thalamus to middle cerebral artery resulted always in symmetric, superimposable volume curves. The contribution of the amygdala starts from the moment the corpora mammillaria are encountered. *LHvol* indicates left hippocampal volume and *RHvol*, right hippocampal volume.

1.89%. From the plots of the hippocampal volume curves, no local volume variations of importance could be detected (Fig 4).

In 28 hippocampi, 134 T2 values were calculated with a simple circular region of interest. A mean value of 93.9 milliseconds with a rather high standard deviation of 4.62 milliseconds resulted. We never measured more than 105 milliseconds in more than two consecutive sections, and the left-right difference was never more than 4 milliseconds. T2 values for the anterior temporal white matter ranged between 66.6 and 79.9 milliseconds (mean ± SD = 73.9 ± 1.95).

To determine the side of seizure focus on the basis of our quantitative MR parameters, the following values were considered signs of disease: (*a*) a hippocampal volume of less than 4.4 mL or more than 5.8 mL, (*b*) an interhippocampal volume difference, δV_{HC}, of more than 6%, (*c*) hippocampal T2-calculated values of more than 105 milliseconds or a clear asymmetry of more than 5 milliseconds, both in at least two sections, and (*d*) a T2-calculated value of more than 81 milliseconds in the anterior temporal white matter.

Subjects with TLE

All 25 patients were typified as having complex partial seizure of temporal lobe origin, and all were refractory to drug therapy. Two had a neuronal migration disorder with ectopic gray matter confined to the right occipital and temporal paraventricular white matter (Fig 5). These subjects had normal hippocampi on all imaging sequences.

Five of 25 patients had foreign tissue lesions in the medial-temporal region; 3 of these with the lesion located outside the hippocampus had associated hippocampal damage on the same side (Fig 6). Another had a low-grade astrocytoma in the right hippocampus and amygdala. Still another patient with a foreign tissue lesion had a porencephalic cyst in the anterior temporal neocortex with a normal hippocampus on all sequences.

The remaining 18 patients had cryptogenic temporal lobe epilepsy: of these, 14 had lateral TLE (8 right-sided, 6 left-sided); in 4 the side of seizure focus could not be determined during the noninvasive electroencephalographic monitoring (hereafter this state is referred to as "nonlateralized" temporal lobe epilepsy).

Two patients had a history of head trauma, but axial T2*-weighted gradient-echo images

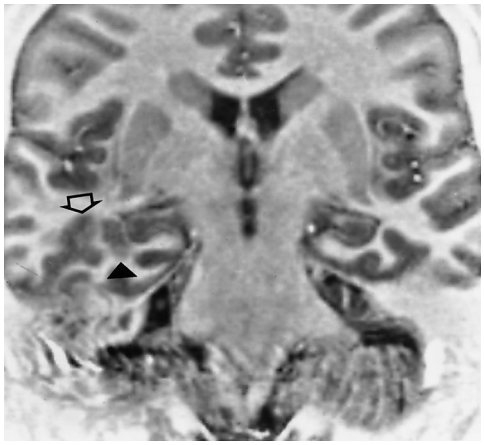

Fig 5. Neuronal migration disorder. Paracoronal T1-weighted inversion recovery image (3500/20/1; inversion time, 300) of a patient with a neuronal migration disorder confined to the right temporal lobe. An abnormal gyrus (*arrow*) and patchy zones of aberrant gray matter are seen (*arrowhead*). Note the normal internal structure in both hippocampi.

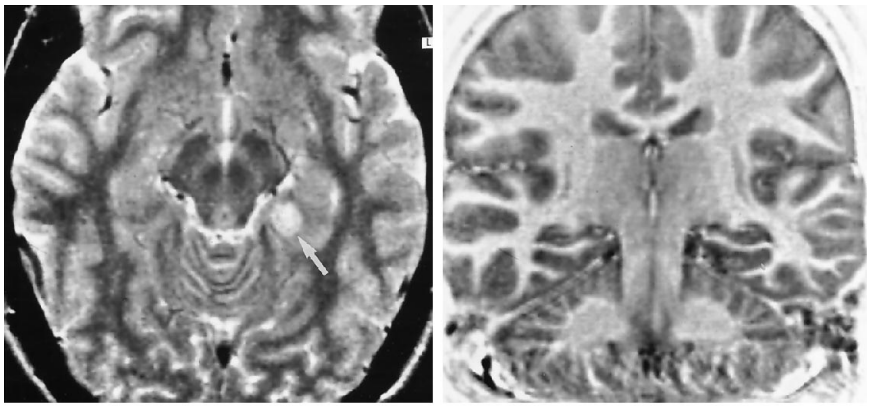

Fig 6. Foreign tissue lesion. *A*, On the left is an axial T2-weighted (2370/80) image of a patient with lateral TLE. A small hyperintense nodule (*arrow*) is seen in the posterior part of the left parahippocampal gyrus.

B, A paracoronal T1-weighted inversion recovery image (3500/20; inversion time, 300) shows a clear loss of internal morphology of the hippocampus on the left side, whereas the right hippocampus is normal. This subject underwent surgery, and a gliotic nodule was removed. The hippocampus was left in place. The patient remains seizure-free for more than 1 year.

could not reveal any hemosiderin deposits. No attempts have been made to evaluate medial-temporal structures using the axial T2-weighted images, but these images revealed small focal extratemporal white matter lesions in two patients and a slight atrophy in one patient. These findings were not considered important with regard to their temporal lobe epilepsy.

Qualitative Evaluation of the Hippocampus

On paracoronal T1-weighted inversion recovery images, hippocampal disease was considered present in 26 hippocampi of 22 patients. Hippocampal damage was suspected when one or more of the following features were present: (*a*) a decrease in signal (global or central), (*b*) a loss of volume, or (*c*) a loss of the

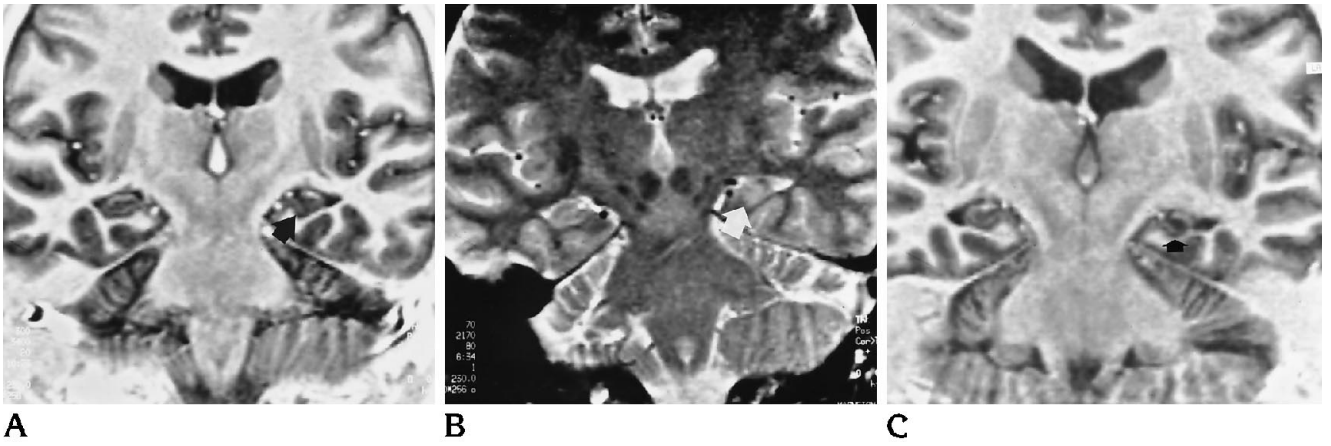

Fig 7. Different stages of hippocampal damage. The images of two patients with cryptogenic lateral TLE and unilateral hippocampal damage are shown.

A, One subject has only minimal structural loss on the left side (*black arrow*) on T1-weighted inversion recovery images (3500/20; inversion time, 300) and *B*, a normal (*white arrow*) T2-weighted study (2370/80). This corresponds to minimal hippocampal damage.

C, The T1-weighted inversion recovery images (3500/20; inversion time, 300) of the other patient show a combination of structure loss, a decreased signal, and a diminished volume (*arrow*) on the left side and *D*, an increased signal and diminished volume (*white arrow*) on T2-weighted images (2370/80). This corresponds to moderate to severe hippocampal damage. The right-sided hippocampi are normal in both cases.

TABLE 2: Absolute value hippocampal volume measurements compared with paracoronal T1-weighted inversion recovery images

T1-weighted inversion recovery findings	Absolute Hippocampal Volume Measurements*	
	Normal	Pathologic†
Normal	23	1‡
Minimal structural loss	7§	1‡
Severe damage	2§	15

* One hippocampus invaded by a foreign tissue lesion and not measured.

† All were decreased in volume.

‡ Side correctly determined with δV_{HC}.

§ One patient had regional increased volume.

internal structure (Fig 7), visible on at least two consecutive sections in the same hippocampus (11, 13). When two or more signs were present in any combination, hippocampal damage was considered moderate to severe (17 of 26 pathologic hippocampi). The presence of only minimal structure loss in 8 hippocampi was considered a sign of minimal hippocampal damage. In one patient, 1 hippocampus appeared somewhat smaller than the other, with a normal internal morphology; we classified this mild atrophy only.

Three patients had entirely normal hippocampi on both sides (Table 2). Eighteen (69%) subjects showed unilateral hippocampal damage; 14 of these had moderate to severe hippocampal damage, 1 had mild atrophy, and 3 only had minimal structural loss, 1 being a patient with a foreign tissue lesion. Four patients had bilateral hippocampal abnormalities, 2 with asymmetric damage (eg, severe to moderate hippocampal damage on one side and minimal structural loss on the other side [Fig 8]), and 2 with symmetric abnormalities.

Of the patients with temporal foreign tissue lesions, two had signs of severe hippocampal damage on T1-weighted inversion recovery images ipsilateral to the side of the foreign tissue lesion, one of whom also had minimal structural loss on the other side. Another patient with a foreign tissue lesion had minimal structural loss ipsilateral to a small parahippocampal gliotic nodule.

On T2-weighted images, an increase in signal as a sign of hippocampal damage (1, 19, 24) was present in all but one hippocampus, with signs of moderate to severe damage on T1-weighted inversion recovery image (Fig 7). In the remaining case, no signal abnormality could be found, but a clear volume loss was seen in association with an ipsilateral foreign tissue lesion. The eight hippocampi with only minimal structural loss on T1-weighted inversion recovery showed no abnormalities on the paracoronal T2-weighted images (Fig 7). Therefore, with T2-weighted paracoronal imaging alone, 2 (14%) of 14 patients with lateralized cryptogenic TLE would have had negative imaging results. In addition, 2 of 4 patients with nonlateralized TLE and 1 of 5 patients with a foreign tissue lesion also would have had a normal hippocampus using T2-weighted paracoronal imaging alone. We could not detect any hippocampi in which disease was suspected on T2-weighted images and there were normal T1-weighted inversion recovery findings.

Quantitative Evaluation of the Hippocampus (Tables 3 and 4)

A normal volume was measured in 23 of 24 hippocampi with a normal appearance on T1-weighted inversion recovery images. In one ap-

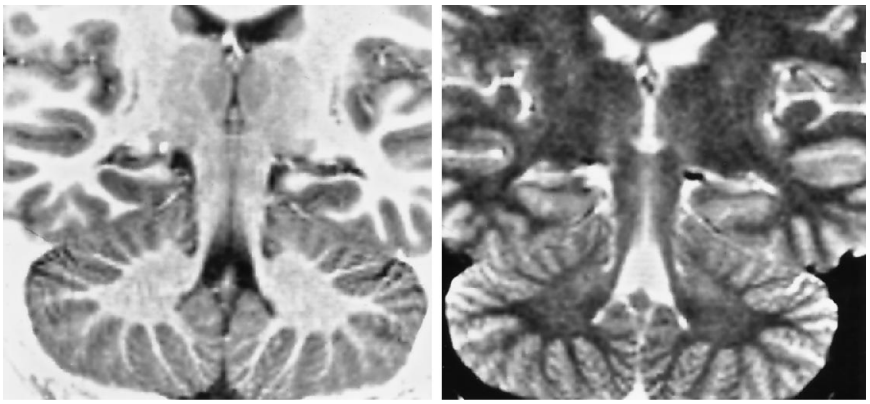

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Fig 8. Images of a patient with nonlateral TLE (see text).

A, The paracoronal T1-weighted inversion recovery image (3500/20; inversion time, 300) depicts bilateral moderate to severe hippocampal damage with a loss of internal structure, a decreased signal, and a low volume in both hippocampi.

B, The corresponding T2-weighted image (2370/80) shows an increased signal in both hippocampi compared with that in the surrounding gray matter and volume loss.

TABLE 3: Interhippocampal volume difference (δV_{HC})

TLE Subjects	Relative Hippocampal Volume Measurements	
	Normal δV_{HC}	Lateral δV_{HC}
Foreign tissue lesion*	2	2
Lateral cryptogenic TLE	2	12
Nonlateral TLE	3†	1

* Only 4 of 5 patients with a foreign tissue lesion are included; the patient with a hippocampal glioma was excluded. All had lateral cryptogenic TLE.

† One patient with bilateral diminished hippocampal volumes, one with normal hippocampal volumes on both sides.

parently normal hippocampus, the volume was too low (4.12 mL), suggesting mild atrophy, but the other hippocampus depicted severe damage on paracoronal T1-weighted inversion recovery and T2-weighted images with an even lower volume of 3.68 mL. Two of 12 hippocampi with moderate to severe hippocampal damage diagnosed on T1-weighted inversion recovery images in patients with lateral cryptogenic TLE had normal volumes. Hippocampi presenting with minimal structural loss had a normal volume in 7 of 8 cases.

The interhippocampal volume difference δV_{HC} was greater than 6% in 14 patients. One patient with unilateral moderate to severe hippocampal damage and 2 with unilateral minimal structural loss had a normal δV_{HC} (Table 5). While inspecting the volume curves, we found that 2 of these patients (1 with minimal structural loss) had a regional hippocampal volume increase where the T1-weighted inversion recovery images showed disease (Fig 9, Table 2). The absolute volumes were normal.

In all but two patients in whom T2-weighted paracoronal imaging showed an increased hippocampal signal, an increased T2 value was measured. The two exceptions presented with lateral cryptogenic TLE and had normal T2 calculated values, although a slight increase in sig-

TABLE 4: Determination of side with MR compared with electroencephalography and clinical data

Electroencephalography Findings	MR Findings				
	Migration Disorder	Foreign Tissue Lesion		Cryptogenic	
		Unilateral	Bilateral	Unilateral	Bilateral
Lateral TLE	2	4	1*	13	1*
Nonlateral TLE	0	0	0	2	2

* Subjects with bilateral disease demonstrated on MR and unilateral TLE had major disease in the hippocampus and, in one case, a foreign tissue lesion on the side predicted by the electroencephalography, and minimal structural loss in the other hippocampus. Two subjects with nonlateral TLE had only unilateral abnormalities on MR.

TABLE 5: Comparison of different MR parameters in relation to clinical and electroencephalography findings

Patients*		Hippocampal Pathology Compared with Electroencephalography				
		T1-weighted inversion recovery	T2-weighted	Volume	δV_{HC}	T2 calculation
Foreign tissue lesions with lateral TLE	Ipsilateral‡	4	3	2†	2†	3
	Contralateral§	1	0	0	0	0
Cryptogenic and lateral TLE	Ipsilateral‡	14	12	11	12	9
	Contralateral§	1	0	1	0	0
Nonlateral cryptogenic TLE	Unilateral‖	2	1	1	1	0
	Bilateral¶	2	1	0	0	1

* Two patients with a neuronal migration disorder and one with a foreign tissue lesion with normal hippocampi on all sequences are not included.

† One patient with a foreign tissue lesion had no volume measurement on one side.

‡ Disease detected on same side as predicted by electroencephalograph.

§ Disease detected on the other side as predicted by electroencephalography. The disease detected on this side was always less severe than on the side that corresponded with electroencephalographic abnormalities.

‖ Unilateral disease detected.

¶ Bilateral disease detected.

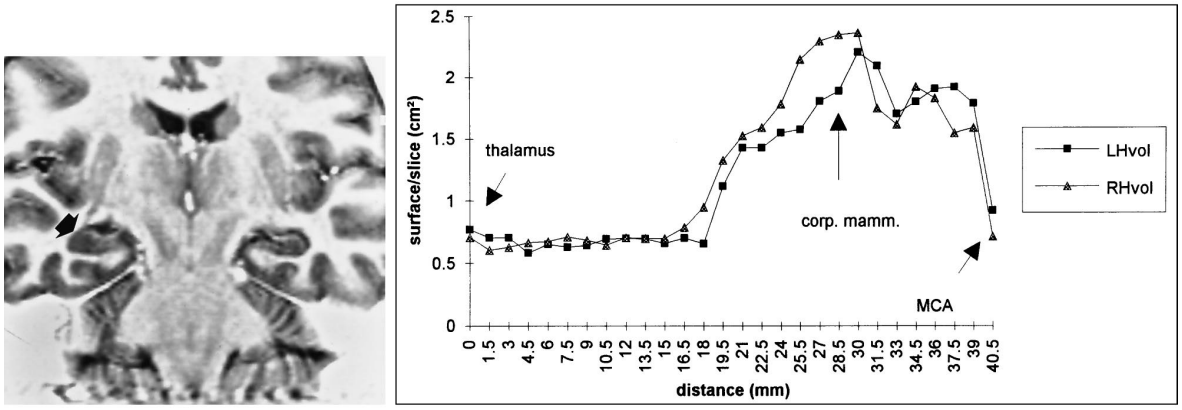

Fig 9. Misleading volume study. *A*, Paracoronal T1-weighted inversion recovery image (3500/20/1; inversion time, 300) of a subject with cryptogenic right-sided TLE. A clear loss of internal structure is seen in the right hippocampus (*arrow*).

B, The corresponding volume curves show a locally increased volume in the anterior part of the hippocampus. Because of the local character of this volume change, δV_{HC} and the absolute volumes were within normal limits. *LHvol* indicates left hippocampal volume and *RHvol*, right hippocampal volume.

nal was present on T2-weighted images in the moderately to severely damaged hippocampi. We never measured an increase in T2 values when visual inspection of the paracoronal T2-weighted images proved normal. One patient had a seizure during the Carr-Purcell-Meiboom-Gill sequence, and no T2 values could be calculated attributable to movement artifacts.

Evaluation of the Temporal Lobe

In 5 of 14 patients with lateral cryptogenic TLE, temporal white matter or neocortical damage was suspected ipsilateral to moderate or severe hippocampal damage. In all these cases, elevated T2 values, increased signal on T2-weighted images and decreased signal on the inversion recovery T1-weighted images were found in the anterior temporal white matter.

Lateral Temporal Lobe Epilepsy: MR Compared with Clinical and Noninvasive Electroencephalography Findings (Table 5)

The patients with a neuronal migration disorder had clinically determined lateral TLE, and MR showed imaging abnormalities ipsilateral to the epileptic activity on electroencephalogram. In the five patients with foreign tissue lesions, the side of the lesion was also correctly determined.

Agreement with the electroencephalogram-determined side of focus was possible with paracoronal T1-weighted inversion recovery images in all 14 patients with lateral cryptogenic TLE. Of the 4 patients with nonlateral TLE, 2 had bilateral abnormal hippocampi, and 2 had lateral hippocampal damage with the other hippocampus normal. One subject needed additional volume measurements to confirm a slight volume asymmetry that was seen on paracoronal T1-weighted inversion recovery images. When an asymmetric increased signal was seen on T2-weighted paracoronal images, the side was correctly determined in 12 of 14 cases of lateral cryptogenic TLE. With a δV_{HC} of more than 6%, also in 12 of 14 subjects with lateral cryptogenic TLE the side was correctly determined. Three of these had normal absolute volumes. In one patient with cryptogenic TLE the side could not be determined with volume measurements, and another even showed a local increased volume at the uncus-hippocampi where the T1-weighted inversion recovery images showed minimal structural loss (Fig 9). Correct determination of side with absolute volume was possible in only 9 of 14 patients with lateral cryptogenic TLE.

Two patients with severe hippocampal disease on the same side as the electroencephalographic abnormalities, one with a foreign tissue lesion, had additional mild disease suspected on the contralateral hippocampus on T1-weighted inversion recovery images only. This was depicted as minimal structural loss. Both have been operated on and had the hippocampus removed on the side of the electroencephalographic abnormalities. They remain seizure-

free. One patient with a foreign tissue lesion had a gliotic nodule in the parahippocampal gyrus on the side of the electroencephalographic abnormalities with minimal structural loss in the ipsilateral hippocampus on T1-weighted inversion recovery. No abnormalities were present in the other hippocampus. The lesion was surgically removed, leaving the hippocampus intact, and the patient remains seizure free after more than 1 year.

Discussion

Many MR procedures have been proposed and tested in the evaluation of the hippocampus and temporal lobe for patients with TLE (1, 4, 7–16, 18, 19). In this study, hippocampal disease was thought to be present in 22 of 25 consecutive patients with proved TLE referred for presurgical evaluation. Paracoronal T1-weighted inversion recovery images were more sensitive for detecting this hippocampal disease than T2-weighted paracoronal imaging, volume measurements, and T2 values. Only 11 (52%) of 21 patients with lateral TLE showed corresponding unilateral hippocampal disease on all sequences on the side ipsilateral with the electroencephalographic findings. This is somewhat better than what Jackson found (39%) in a recent study using a multiparameter qualitative approach with T1-weighted inversion recovery and T2-weighted images (15). In 3 patients, both hippocampi were completely normal on all sequences, 2 with neuronal migration disorder, and one with a foreign tissue lesion.

The association of extrahippocampal foreign tissue lesions with signs of ipsilateral hippocampal damage in four of these cases is a phenomenon that has previously been reported (14). Two of these patients had moderate to severe hippocampal damage associated with an extrahippocampal but medial-temporal foreign tissue lesion, and one had minimal structural loss in the hippocampus ipsilateral to a parahippocampal gliotic nodule. The mechanism involved in damaging these hippocampi possibly relates to the longstanding or severe epileptic activity (20). These patients have been operated on and when moderate to severe hippocampal damage was suspected on MR, the hippocampus was removed as well. In the case of only minimal structural loss, the hippocampus was left untouched. All these patients are seizure-free for more than 1 year after surgery.

The high signal-to-noise ratio and the excellent contrast between gray and white matter provided by the inversion recovery images provide good visibility of the microanatomy of the hippocampus, which will be obscured in the presence of gliosis (15). This normal internal morphologic structure of the hippocampus (Fig 3) is produced by the alveus, the molecular cell layer of the gyrus dentatus, and the pyramidal cell layer of the cornu ammonis (21–25). The high sensitivity of paracoronal T1-weighted inversion recovery images to detect hippocampal disease was proved by Jackson (15). In our study, T1-weighted inversion recovery images revealed a total of 26 pathologic hippocampi. Disruption of the internal morphology of the hippocampus on paracoronal T1-weighted inversion recovery images was the only qualitative abnormality found in 4 of our patients. One had bilateral abnormalities and was classified as nonlateral TLE. Another is the subject with minimal structural loss associated with a parahippocampal hamartoma on the ipsilateral side who remains seizure-free after tumor removal. Of the other two patients whose side of focus was consistently determined with minimal structural loss as the only abnormality, one has been operated on and remains seizure-free. The other is scheduled for depth electrode placement. Structure loss also was present in the nonepileptic hippocampus of 2 patients with lateral TLE, one with a foreign tissue lesion. In these, all imaging sequences demonstrated more severe disease in the hippocampus on the side of epileptic activity where they had undergone surgery. They remain seizure-free. All this suggests that minimal structural loss seen on T1-weighted inversion recovery images is a very sensitive marker for hippocampal gliosis, but that minimal gliosis does not always lead to seizures. We also believe that in some subjects hippocampal scarring could have developed (ipsilateral and/or contralateral; eg, gliosis) as a result of longstanding epilepsy. It remains to be proved whether this is related to the frequency of secondary generalized seizures (20). We do agree with the statement of Jackson (15) that a hippocampus that is normal on T1-weighted inversion recovery images is most probably free of disease, but we would add that a normal measured volume probably is an essential control (vide infra).

Semiquantitative grading of hippocampal damage was possible by looking for the pres-

ence or absence of features such as minimal structural loss, volume loss, and decreased signal. These imaging abnormalities correspond to histopathologic features of hippocampal sclerosis (21–24). A large gradation of abnormalities can be pathologically described in hippocampal specimens of TLE patients who had surgery, ranging from minor end-folium gliosis to extensive gliosis and cell loss (23). Structural loss without any other abnormality, such as volume loss or decreased signal, presumably corresponds to minimal hippocampal gliosis. The presence of volume loss and/or decreased signal was considered suggestive of more severe damage. In this respect, in our TLE patients, 36% of the evaluated hippocampi presumably had moderate to severe damage with extensive gliosis and volume loss, whereas 16% had minimal damage. The remaining 48% were considered normal.

Only 16 of 26 hippocampi with abnormalities on paracoronal T1-weighted inversion recovery also had a high signal on T2-weighted images, and 1 of 26 had only visible volume asymmetry. The reason for this is the high number of hippocampi in which only structural abnormalities could be detected on the T1-weighted inversion recovery images (8 of 26). In these, no abnormalities could be detected visually with any of the other sequences. In early studies, Bronen (8) found a high sensitivity using paracoronal T2-weighted images. Jackson (15) found that this parameter was less sensitive. In only 77% of the patients in his study was the side determined with paracoronal T2-weighted imaging alone. Our results indicate that in 12 of 14 patients with lateral cryptogenic TLE could the side be determined with paracoronal T2-weighted images alone, indicating a sensitivity of 86%. We could not detect any hippocampus in which the T2-weighted images showed an increase in signal, and T1-weighted inversion recovery images were normal. On the other hand, when the T2-weighted signal was increased in one hippocampus, the electroencephalographic determination was always of that same side.

In still another study, Jackson (16) used a single-section technique to calculate the T2 values, positioned at the level of the middle of the hippocampus and used 16 echos. The high sensitivity claimed in that study could not be reproduced with the eight-echo multisection Carr-Purcell-Meiboom-Gill that was used in this work. No elevated T2 values were found when T2-weighted images did not reveal a high signal. This indicates that T2 calculation had no additional value in determining the side in our TLE patients over the qualitative signal increase of the T2-weighted images. An explanation could be that multisection techniques give less reproducible results than single-section techniques (26). We were inspired to use a multisection technique, because we did not want to miss focal hippocampal disease.

Volume measurements are considered sensitive and specific for the detection of hippocampal sclerosis or damage (10, 11, 25). In this study, volume measurements correctly predicted the epileptogenic side for 12 (86%) of 14 patients with cryptogenic TLE. This is somewhat less than the 93% found by Cendes (12, 13) using volume measurements of both hippocampus and amygdala. On the other hand, 2 subjects in whom side was correctly determined with cryptogenic TLE, one with minimal structural loss only, had a local volume increase in the pathologic uncus-hippocampi (Fig 9). Another patient had no volume asymmetry, but side was correctly determined with T1-weighted inversion recovery images where minimal hippocampal damage was suspected. One case with nonlateral TLE and damage demonstrated with T1-weighted inversion recovery images in both hippocampi had normal volumes and a normal δV_{HC}. We believe that volume measurements remain important for quantitative control. When only slight atrophy is suspected with an intact hippocampal structure, a clear pathologic volume measurement increases the likelihood that the hippocampus is damaged. This was the case in one of our patients, and the volume loss was indeed qualitatively verified. A normal appearing hippocampus should have a normal volume. In subjects in whom minimal structural loss is found as the only hippocampal abnormality, one should rely less on volume measurements because the volume can be pathologically increased (Fig 9). From this study we can conclude that structural hippocampal abnormalities as seen on paracoronal T1-weighted inversion recovery images are a stronger argument for disease than an altered (local) volume.

In view of this work, we propose an "optimum MR protocol" for patients with TLE (Fig 10). To rule out extratemporal gross pathology and to detect foreign tissue lesions, an axial T2-

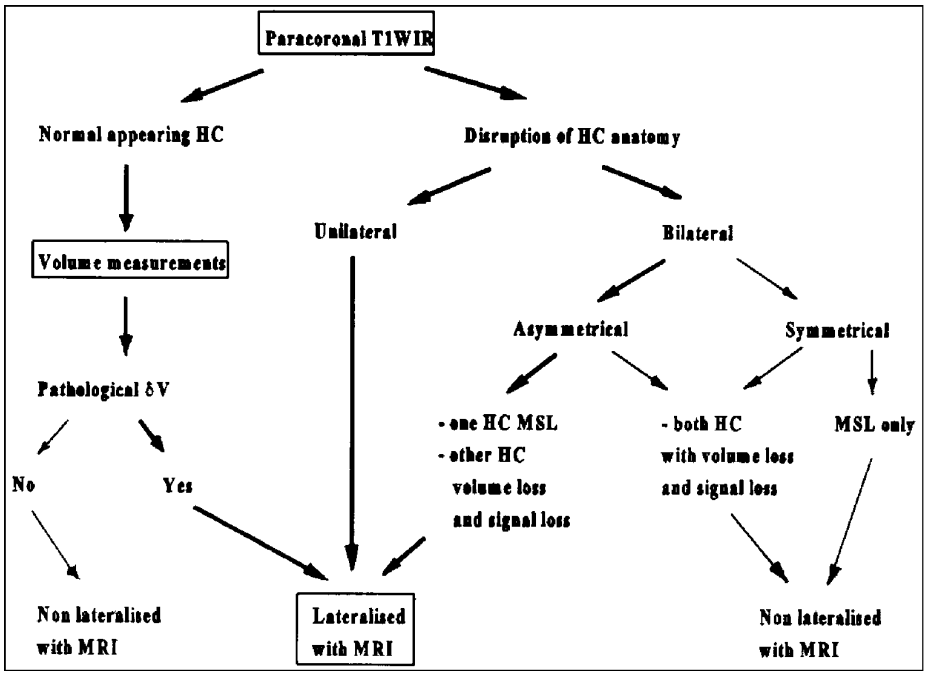

Fig 10. Current optimum MR imaging (*MRI*) for TLE patients. Flow chart for decision making in the preoperative screening of patients with cryptogenic TLE. Paracoronal T1-weighted inversion recovery (*T1WIR*) imaging plays the key role, and volume measurements are necessary only if normal hippocampal (*HC*) anatomy is seen on the T1-weighted inversion recovery images. *MSL* indicates minimal structural loss.

weighted spin-echo sequence is used to screen the brain. After biplane localization, the hippocampus and temporal lobes are evaluated using paracoronal T1-weighted inversion recovery imaging. In the absence of hippocampal structure loss, volume measurements have to be performed to depict possible neuronal loss in the hippocampus without gliotic changes, in which case the seizures can be lateral. If a structural abnormality is seen in one hippocampus, the side of seizures is determined with MR on the side of the abnormality and a gradation can be given. If bilateral abnormalities are seen on paracoronal T1-weighted inversion recovery images, a distinction must be made between symmetric qualitative abnormalities on T1-weighted inversion recovery images where no determination of side is possible and asymmetric ones (eg, one hippocampus has moderate to severe damage and the other one minimal structural loss only, in which cases determination of side with MR is possible). Axial gradient-echo T2*-weighted images are used to rule out hemosiderin deposits in posttraumatic epilepsy. Because MR is evolving quickly, techniques used today may be obsolete tomorrow. We believe that paracoronal T2-weighted images are not needed in the evaluation of TLE patients.

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