

Is Ictal Recording Mandatory in Temporal Lobe Epilepsy?

Not When the Interictal Electroencephalogram and Hippocampal Atrophy Coincide

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Objective: To investigate the concordance between scalp electroencephalogram (EEG) lateralization and side of hippocampal atrophy in patients with temporal lobe epilepsy (TLE).

Methods: We studied 184 consecutive patients with TLE without lesions other than those compatible with mesial temporal sclerosis. In this study, we studied specifically hippocampal atrophy and the results of scalp EEG investigation. Patients were classified according to the localization of interictal epileptiform discharges as unilateral, bilateral asymmetric, and bilateral symmetric. The EEG seizure onsets were also classified separately as unilateral, bilateral asymmetric, and bilateral symmetric. The hippocampal atrophy was determined by volumetric measurements using high-resolution magnetic resonance imaging (MRIVol).

Results: Only 3% of patients had discordance between the ictal and interictal EEG lateralizations; however, none of these had unilateral interictal EEG abnormalities. Interictal EEGs were considered unilateral in 62.0% of patients, bilateral asymmetric in 31.5%, and bilateral symmetric in 6.5%. Ictal EEGs were considered unilateral in

63.5% of patients, bilateral asymmetric in 30.0%, and bilateral symmetric in 6.5%. The MRIVol showed unilateral hippocampal atrophy in 60.9% of patients, bilateral asymmetric hippocampal atrophy in 19.0%, symmetric hippocampal atrophy in 3.8%, and normal volumes in 16.3%. There was a significant concordance between MRIVol lateralization and both interictal and ictal EEG lateralization ($P < .001$). All patients with unilateral hippocampal atrophy had concordant interictal and ictal EEG lateralization. Six (18.2%) of the 33 patients with bilateral asymmetric hippocampal atrophy had MRI lateralization discordant with EEG lateralization.

Conclusions: We found a strong concordance between EEG and MRIVol lateralization in patients with TLE. Unilateral hippocampal atrophy predicted ipsilateral interictal epileptiform abnormalities and ipsilateral seizure onsets with no false lateralization. Previous studies in addition to the present series support that a concordant outpatient EEG evaluation in patients with TLE and unilateral hippocampal atrophy would obviate the need for inpatient EEG monitoring.

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HIGH-RESOLUTION magnetic resonance imaging (MRI) has had a major impact on the evaluation of patients with refractory epilepsy, because MRI can detect many underlying lesions that previously could not be identified in vivo. The most common example of this is mesial temporal atrophy associated with neuronal loss and gliosis on histopathologic examination, a condition known as mesial temporal sclerosis or hippocampal sclerosis.^{1,2} The demonstration by MRI of obvious atrophy or altered signal intensity of mesial temporal structures suggestive of mesial temporal sclerosis has greatly streamlined the presurgical evaluation of patients with temporal lobe epilepsy (TLE) in whom these abnormalities are

present.³⁻⁸ However, there are still uncertainties about the predictive value of hippocampal atrophy for electroencephalogram (EEG) lateralization and how often discrepancies between MRI and EEG are to be expected in the evaluation of patients with TLE.

We performed this study to investigate the concordance between scalp EEG lateralization, defined by ictal and interictal abnormalities separately, and the side of hippocampal atrophy in patients with medically refractory TLE. Traditionally, the ictal EEG recordings are considered the most important information for surgical decision, and although interictal EEG abnormalities play an important role in the presurgical investigation for TLE, there is no consensus about its weight in the decision-making process. We wanted to

PATIENTS AND METHODS

We studied 184 consecutive patients (mean \pm SD age, 34 \pm 11 years; 82 males) with a clinical diagnosis of TLE without lesions other than those compatible with mesial temporal sclerosis. In this study, we specifically investigated hippocampal atrophy and the results of scalp EEG investigation.

We diagnosed TLE if the seizure symptoms⁹ and other clinical and EEG features were consistent with this diagnosis according to the *International Classification of Epileptic Syndromes*¹⁰ and there were no findings suggesting an extratemporal partial epilepsy. The following criteria were met: (1) the clinical manifestations were compatible with TLE, including stereotyped simple partial seizures with déjà vu or epigastric sensation, associated or not with fear and other autonomic symptoms, followed by a complex partial seizure consisting of staring and lip smacking or masticatory automatisms or both, accompanied or not by upper extremity automatisms and contralateral arm dystonia⁹; (2) the EEGs during wakefulness showed no clear-cut epileptiform abnormalities elsewhere; and (3) there were epileptiform EEG abnormalities over temporal regions, consistent intermittent slow-wave abnormalities localized over temporal areas on interictal EEGs, or both.

The EEGs were reported independently of the MRI diagnosis and before the final presurgical decision was made. The EEG interpreters were unaware of the imaging results. Prolonged and routine EEG recordings using the International 10-20 System, including sphenoidal electrodes, and long-term video EEG monitoring were performed for all patients. A minimum of 5 routine EEG recordings and 4 days of video EEG monitoring were obtained for all patients. Twenty-one patients underwent intracranial EEG recordings with stereotaxically implanted depth electrodes for several reasons, most often because of discrepancies between ictal and interictal EEG findings and bitemporal scalp EEG seizure onsets or to rule out extratemporal seizure onsets. For the present study, we used only the information obtained from the scalp EEG investigation. All EEG data presented herein do not include results from the intracranial recordings. Some of the patients investigated with intracranial EEG have been described previously.¹¹

We analyzed separately interictal EEG abnormalities and ictal EEG recordings. For the analysis of interictal abnormalities, we used the routine EEG recordings and

samples from the spike detection program obtained during daytime video EEG monitoring. Spikes that were localized over the temporal lobe regions, ie, anterior, mid, or inferomedial (sphenoidal electrodes), were taken into account together. Patients were classified according to the localization of interictal epileptiform discharges as unilateral left (L) or right (R) if more than 90% of interictal abnormalities were unilateral or clearly lateralized to the left or right side, respectively; bilateral asymmetric (L>R or R>L) if more than 70% of abnormalities were lateralized to the left or right side; and bilateral symmetric (L = R) if less than 70% of EEG abnormalities were lateralized.

Patients were also classified according to ictal EEG onsets as unilateral (>90% of seizures localized to one temporal lobe), bilateral asymmetric (>70% of seizures clearly lateralized), and bilateral symmetric (<70% of seizures lateralized).

The above classification of EEG abnormalities was not part of the standard presurgical investigation and was performed for the purpose of this study.

The MRIVol were performed using 1- or 3-mm-thick contiguous T1-weighted coronal slices perpendicular to the plane of the long axis of the hippocampi. The images were transferred to a computer workstation, and the regions of interest were outlined using a locally developed interactive software program.^{4,12,13} We analyzed the absolute volume of the hippocampal formation and the asymmetry between sides. The anatomical guidelines used for identification and segmentation of medial temporal structures have been described by Watson et al.¹³ Volumes and asymmetry index 2 SDs below the mean of the 52 age-matched healthy volunteers were considered abnormal. Volumes were corrected for the variation of total brain volume that allowed us to determine unilateral hippocampal atrophy and bilateral symmetrical or asymmetrical atrophy.^{4,12}

Informed consent was obtained from all subjects. This study is part of a research project approved by the Ethics Review Committee of the Montreal Neurological Institute and Hospital, Montreal, Quebec.

We used χ^2 tests and Cohen κ statistic to determine significance and the strength of the association between EEG and MRIVol lateralization.

We performed analyses of variance to compare the hippocampal volume z scores (standardized scores that express the number of SDs away from the mean of the control group) for the different groups according to the EEG classification.

clarify how often there was concordance between the ictal and interictal EEG abnormalities and between each of these abnormalities and results of MRI volumetric measurements (MRIVol). Should high concordance exist, presurgical evaluation could be streamlined, and ideal surgical candidates could be identified. This could be done without need for prolonged and/or invasive studies to record seizures, thus reducing morbidity and cost.

RESULTS

We could not include analysis of ictal EEG onsets in 14 patients, either because they did not have seizures dur-

ing the video EEG investigation or because the seizures recorded were completely obscured by artifacts. For the remaining 170 patients, there was a strong concordance between ictal and interictal EEG classification as described herein (χ^2 , $P < .001$; $\kappa = 0.94$). Only 5 (2.9%) of 170 patients had discordant ictal and interictal EEG lateralizations; however, none of them were classified as having unilateral interictal EEG abnormalities. In 9 (5.3%) of 170 patients, ictal and interictal EEG findings agreed in terms of lateralization but were discrepant, because ictal EEG was classified as unilateral and the interictal EEG as bilateral (in 8 patients) or the opposite in 1 patient. In the remaining 156 patients (91.8%), the ictal and

Magnetic Resonance Imaging Volumetric Results According to the Electroencephalogram (EEG) Findings*

EEG Classification	Unilateral Hippocampal Atrophy		Bilateral Hippocampal Atrophy			Normal Volumes	No. of Patients
	R	L	R>L	L>R	L = R		
Unilateral R							
Interictal	22 (61)	0	6 (17)	0	1 (3)	7 (19)	36 (19.6)
Ictal	22 (64.7)	0	5 (14.7)	0	1 (3)	6 (17.6)	34 (20.0)
Unilateral L							
Interictal	0	60 (77)	0	6 (8)	0	12 (15)	78 (42.4)
Ictal	0	57 (77)	0	6 (8)	0	11 (15)	74 (43.5)
Bilateral R>L							
Interictal	9 (47.5)	0	4 (21)	2 (10.5)	2 (10.5)	2 (10.5)	19 (10.3)
Ictal	7 (39)	0	5 (28)	2 (11)	2 (11)	2 (11)	18 (10.6)
Bilateral L>R							
Interictal	0	18 (46)	4 (10.5)	8 (20.5)	2 (5)	7 (18)	39 (21.2)
Ictal	0	14 (42.5)	4 (12)	7 (21.3)	2 (6)	6 (18.2)	33 (33.0)
Bilateral L = R							
Interictal	1 (8.2)	2 (16.7)	3 (25)	2 (16.7)	2 (16.7)	2 (16.7)	12 (6.5)
Ictal	1 (9)	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)	11 (6.5)
Total							
Interictal	32 (17.5)	80 (43.5)	17 (9)	18 (10)	7 (4)	30 (16)	184 (100)
Ictal	30 (17)	73 (43)	16 (10)	17 (10)	7 (4)	27 (16)	170 (100)

*Data are presented as number (percentage). R indicates unilateral right; L, unilateral left; R > L, bilateral with right-sided predominance; L > R, bilateral with left-sided predominance; and L = R, bilateral with no lateralization.

interictal EEG lateralizations were concordant. We did not consider bilateral symmetric and bilateral asymmetric as discordant.

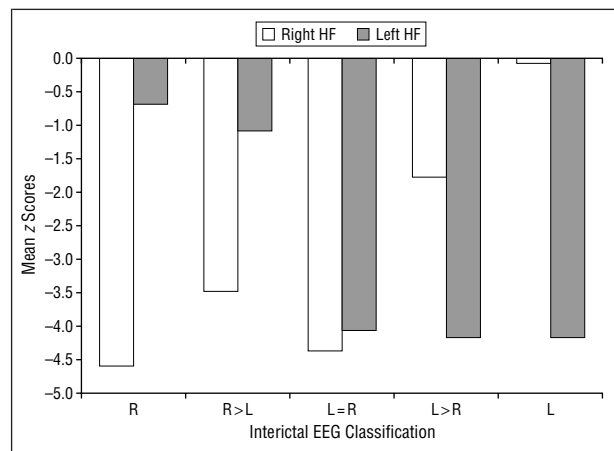
Ictal EEGs were considered unilateral in 108 (63.5%) of 170 patients (74 L), bilateral asymmetric in 51 patients (30.0%) (33 L>R and 18 R>L), and bilateral in 11 patients (6.5%) (L = R).

Interictal EEGs were considered unilateral in 114 (62.0%) of 184 patients (78 L), bilateral asymmetric in 58 (31.5%) patients (39 L>R and 19 R>L), and bilateral in 12 (6.5%) patients (L = R).

The MRIVol showed unilateral hippocampal atrophy in 112 (60.9%) of 184 patients (80 L), bilateral asymmetric hippocampal atrophy in 35 patients (19.0%) (18 L>R and 17 R>L), symmetric hippocampal atrophy in 7 patients (3.8%), and normal volumes in 30 patients (16.3%). The **Table** summarizes the MRIVol results according to the EEG classification.

There was a significant association between EEG and MRIVol lateralization (χ^2 , $P < .001$). The lateralization MRIVol to either left or right showed a strong agreement with lateralization given by interictal and ictal EEG ($\kappa = 0.90$). Moreover, all patients with unilateral hippocampal atrophy had concordant EEG lateralization. Six (18%) of the 33 patients with bilateral asymmetric hippocampal atrophy had discordant EEG lateralization. The majority of patients with unilateral interictal EEGs (82/114; 71.9%) and unilateral ictal EEGs (79/108; 73.1%) had unilateral hippocampal atrophy, and most of those with bilateral (L = R) interictal or ictal EEGs had bilateral hippocampal atrophy (Table).

Patients with unilateral EEGs had significantly more pronounced ipsilateral hippocampal atrophy than those with bilateral EEG abnormalities ($P < .001$). The **Figure** shows the mean hippocampal volume z scores from all the EEG groups.



Each bar represents the mean z score for the volumes of right and left hippocampal formation (HF) for each group of patients defined by the interictal electroencephalogram (EEG) results: unilateral right (R), bilateral with right-sided predominance (R>L), bilateral symmetric (L = R), bilateral with left-sided predominance (L>R), and unilateral left (L). Mean hippocampal z scores for the ictal EEG groups were similar, and analysis of variance showed a significant difference among groups with $P < .001$.

COMMENT

Visual discrimination of a normal from an abnormal hippocampus is straightforward when one is clearly normal and the other is grossly abnormal, but the visual binary paradigm breaks down in the presence of symmetric bilateral disease or mild unilateral disease.^{12,14,15} Therefore, to accurately determine the presence and severity of hippocampal atrophy in both hippocampi, absolute quantitative measurements are necessary.¹² The published results indicate that the presence and severity of hippocampal sclerosis in both hippocampi may provide useful prognostic information about both postoperative

seizure control and memory outcome.^{12,15-19} Since the initial publication on the utility of MRIVol of the hippocampus in patients with TLE,⁵ many studies^{4,5,7,12-14,16,20,21} have illustrated the correlation between the EEG lateralization of the epileptogenic region in TLE and the presence of significantly reduced hippocampal volumes. However, most recent studies consider only or mainly ictal recordings for defining EEG lateralization. Interictal EEG data are considered to have less localizing value and therefore are either disregarded or considered as additional and perhaps nonessential information. In the present study, we decided to analyze each of these 2 sets of data separately to determine if interictal EEG findings could be sufficiently reliable for defining EEG lateralization in patients with a clinical diagnosis of TLE in whom high-resolution MRI shows hippocampal atrophy.

We found a strong agreement between ictal and interictal scalp EEG lateralization and also between each of these 2 sets of EEG data and MRI lateralization in 184 consecutive patients with TLE without foreign tissue lesions. This is the largest series reported so far, and our findings agree with those of another large study²¹ of 159 patients with TLE; in that study, patients with unilateral hippocampal atrophy always had concordant lateralization by long-term EEG monitoring and routine EEG examinations.

The crucial practical clinical question during pre-surgical evaluation of patients with TLE that previous MRI studies have not yet fully answered is when is it still necessary to record seizures in patients with TLE who have clear-cut hippocampal atrophy. The results of this large series help clarify this issue. We demonstrated that in patients with a history and ictal symptoms suggestive of mesial TLE, interictal epileptiform discharges recorded during serial routine EEGs can reliably lateralize the seizure focus if they are consistently lateralized to one temporal lobe and are concordant with MRI-identified unilateral and ipsilateral hippocampal atrophy. Long-term EEG monitoring for recording seizures is still mandatory in patients without or with scarce interictal epileptiform discharges and bitemporal interictal EEG abnormalities and in patients with normal MRI results, bilateral hippocampal atrophy, or extrahippocampal lesions.

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