Inter-modality comparisons of seizure focus lateralization in complex partial seizures

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Abstract. Anterior temporal lobectomy offers a high chance of seizure-free outcome in patients suffering from drug-refractory complex partial seizure (CPS) originating from the temporal lobe. Other than EEG, several functional and morphologic imaging methods are used to define the spatial seizure origin. The present study was undertaken to compare the merits of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET), magnetic resonance imaging (MRI) and single-voxel proton MR spectroscopy (MRS) for the lateralization of temporal lobe seizure foci. The clinical charts and imaging data of 43 consecutive CPS patients were reviewed. Based on surface EEG, 31 patients were classified with temporal lobe epilepsy (TLE; 25 lateralized, 6 not lateralized) and 12 with non-temporal lobe epilepsy. All were examined by FDG-PET, MRS and MRI within 6 weeks. FDG-PET and MRI were interpreted visually, while the *N*-acetyl-aspartate to creatine ratio was used for MRS interpretation. One FDG-PET scan was invalid due to seizure activity post injection. The MR spectra could not be evaluated in five cases bilaterally and three cases unilaterally for technical reasons. A total of 15 patients underwent anterior temporal lobectomy. All showed a beneficial postoperative outcome. When the proportions of agreement between FDG-PET (0.77), MRI (0.58) and MRS (0.56) and surface EEG in TLE cases were compared, there were no significant differences ($P>0.10$). However, FDG-PET showed a significantly higher agreement (0.93) than MRI (0.60; $P=0.03$) with the side of successful temporal lobectomy. The concordance of MRS with the side of successful temporal lobectomy was intermediate (0.75). When the results of functional and morphologic imaging were combined, no significant differences were found between the rates of agreement of FDG-PET/MRI and MRS/MRI with EEG (0.80 vs 0.68; $P=0.50$) and with the side of successful temporal lobectomy (0.87 vs 0.92; $P=0.50$) in TLE cases. However, MRS/MRI showed significantly more lateralized temporal lobe abnormalities in non-temporal lobe epilepsy cases than FDG-PET/MRI (0.90 vs. 0.17; $P<0.01$). Although FDG-PET seems to be the most reliable and stable method for this purpose, we conclude that in TLE cases it may be justified to perform MRS, which is less expensive, faster and has no radiation exposure, in combination with MRI before FDG-PET, since FDG-PET offers little additional diagnostic information if MRS and MRI indicate the same seizure focus lateralization.

Keywords: Complex partial seizure – Temporal lobe epilepsy – Positron emission tomography – Magnetic resonance imaging – Proton magnetic resonance spectroscopy

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Introduction

The seizure disorder of approximately 5%–10% of all new epilepsy patients will become medically intractable within the time course of disease. The majority of these patients suffer from complex partial seizures (CPS) originating in the temporal lobe [1]. Mesial temporal sclerosis (MTS) is the predominant histologic change found in surgical specimens of these patients [2]. Once the location of the focal onset of the seizure disorder has been

established, a resection of the epileptogenic zone (most often as a temporal lobectomy) offers a high chance of a seizure-free outcome (70%–90%) [1]. The determination of the site of seizure origin, therefore, remains the crucial factor for the success of this surgical approach. While noninvasive electroencephalographic examinations (EEG) are necessary to define the epileptogenic nature of the disorder, they offer only limited information about underlying structural and/or functional changes and their spatial location and extension. Structural and functional imaging modalities, like magnetic resonance imaging (MRI), proton magnetic resonance spectroscopy (MRS) and positron emission tomography with fluorine-18 fluorodeoxyglucose (FDG-PET), provide this valuable information and diminish the need for invasive EEG procedures.

MRI is not only useful to diagnose neoplastic, infectious, or vascular lesions, and gross anatomic alterations underlying epilepsy, but is also capable of detecting subtle signal and/or structural abnormalities caused by cortical malformations and MTS. Several studies report a high accuracy of MRI for the determination of temporal lobe seizure onset lateralization [3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14]. Some studies have employed quantitative measurements of temporal lobe or hippocampal volumes, showing decreased volumes on the affected side [4, 5, 7, 8, 9, 13, 14, 15, 16, 17, 18, 19] as a correlate to neuronal cell loss [4, 9]. Other groups have used quantitative measurements of T2 relaxation times, which are found to be prolonged in cases of MTS [6, 11, 13, 16]. A visual description of such features has also proved to be valuable: increased signal intensity on coronal T2-weighted or fluid-attenuated inversion recovery (FLAIR) images [10] in the mesial temporal lobe, hippocampal/temporal lobe atrophy, and structural disruption of the hippocampus [3, 12]. Although some investigators question a relationship between the degree of abnormalities and the duration of disease or frequency of seizures [7, 18] and age of onset [17], several other studies have found significant correlations with some or all of these parameters [11, 12, 15, 16, 17, 18], especially with the prevalence of febrile seizures in early childhood [7, 15, 17, 19]. The MRI features have also been shown to be of prognostic value [3, 5, 13, 19].

In MRS studies of focal seizure disorders, the concentration of *N*-acetyl-aspartate (NAA) has been consistently shown to be diminished at or in proximity to the site of seizure origin [13, 14, 18, 20, 21, 22, 23, 24, 25]. Although several other metabolites have been investigated [creatine (Cr), choline (Cho), lactate, amino acids, etc.], their value for seizure focus localization is uncertain. However, the semi-quantitative assessment of NAA/Cr, NAA/[Cr+Cho], or NAA/Cho ratios was found to be reliable and clinically useful [21, 23, 24]. Since NAA is exclusively found within neurons [26], it was assumed to represent a measure of neuronal intactness. Recent reports showing transsynaptic effects [27, 28] and reversible decreases [29, 30] challenge this. The definite physiologic role of NAA remains unclear. MRS results seem to correlate with seizure duration [18] and surgical outcome [23].

Seizure foci and adjacent cortical areas demonstrate hypometabolism on interictal FDG-PET scans and, less frequently, hypermetabolism if captured ictally [13, 19, 31, 32, 33, 34, 35, 36, 37]. The cause of the interictal hypometabolism is still unknown, but it seems to be more due to a dysfunction in conjunction with a decreased hexokinase function [38] than due to simple structural changes. Earlier studies found a correlation between the degree of hypometabolism and the extent of neuronal cell loss and histopathological changes [31]. The degree of hypometabolism was also shown to correlate with atrophy seen on volumetric MRI [36, 39]. However, these findings could not be reproduced in more recent studies [34, 40, 41, 42]. The degree of FDG uptake abnormality correlates with the duration of the disorder [43] and the postoperative outcome [19, 33, 34, 37].

According to the 1998 neuroimaging guidelines for patients with uncontrolled epilepsy from the International League Against Epilepsy [44], MRI is considered to be essential for presurgical evaluation while MRS in its current state is regarded as a research technique rather a routine clinical tool. Although its availability is still restricted, FDG-PET for the assessment of interictal cerebral glucose metabolism is regarded as clinically useful for the delineation of epileptogenic regions. However, the rapid development of MRS, providing clinically orientated, reliable, and easy-to-implement software packages like the one used in the present study [45], and the quickly growing availability of FDG-PET make a direct comparison of these imaging techniques desirable to define their roles. Such a comparison will be mandatory to establish cost- and time-effective diagnostic algorithms. This retrospective study was therefore undertaken to evaluate the relative contributions of these three imaging modalities (separately and in conjunction) for seizure focus lateralization in patients suffering from CPS and considered for temporal lobectomy in a routine clinical setting.

Materials and methods

Patient selection. All patients included in this study were evaluated for surgical treatment of drug-refractory CPS at the Seizure Center of the Department of Neurology of the Hospital of the University of Pennsylvania between January 1998 and December 1999. Only those patients undergoing imaging by FDG-PET, MRI and MRS within a maximal period of 6 weeks (mean ± SD =12.0±13.1 days) were included. The clinical charts and imaging data of 43 consecutive patients who met the criteria mentioned above were reviewed retrospectively. The sample consisted of 18 males and 25 females. Their age at the time of the FDG-PET study ranged from 15.7 to 61.8 years; the mean (±SD) age was 34.6 (±11.6) years.

Neurological examination and EEG. All patients underwent a comprehensive neurological and neuropsychological examination. All patients showed symptoms typical for CPS. Fifty-five percent (*n*=23) of all patients had also experienced tonic-clonic generalizations. Risk factors could be identified by chart review in 42% (*n*=18) of all cases, including prolonged febrile seizure in childhood (*n*=7), severe head trauma (*n*=5), central nervous system infections (*n*=3), complicated or premature delivery (*n*=2), and hydrocephalus (*n*=1). The mean (±SD) age at the time of first seizure was 16.0 (±13.8) years. The mean (±SD) seizure duration at the date of FDG-PET scanning was approximately 18.0 (±12.7) years.

All patients were hospitalized for prolonged video-EEG monitoring (mean±SD duration =7.4±3.4 days) under withdrawal of their usual medications. In general, at least three ictal events were captured. For the EEG examination, a full array of electrodes was placed according to the International 10–20 Placement System. Infrequently, sphenoidal EEG electrodes were also used. EEG recordings were interpreted by experienced board-certified electroencephalographers as part of the routine evaluation. Based on ictal and interictal EEG recordings, the seizure disorder was classified into the group of temporal lobe epilepsy (TLE; *n*=31) and the more heterogeneous group of non-temporal lobe epilepsies (*n*=12). The seizure origin of TLE patients was categorized as lateralized or not lateralized as shown by ictal recordings. In a few cases in which less than three ictal events were recorded or in which overlying artifacts complicated the interpretation, the seizure disorder was also assumed to be lateralized if the vast majority of interictal EEG abnormalities arose from the same side as the ictal changes. In total, 14 patients showed right temporal lobe seizure onset, and 11 patients a left temporal lobe onset. In the remaining TLE cases, the interictal and ictal EEG changes occurred bilaterally without a predominant lateralization (*n*=6 not-lateralized TLE). Of the 12 patients with non-temporal lobe epilepsy, six showed predominantly frontal lobe (in two of these more right than left sided) and one showed bilateral occipital ictal and interictal EEG changes. Four patients presented primarily with generalized EEG changes, and in one of these cases, the EEG changes occurred predominantly over the right hemisphere (right hemimegalocephaly). Finally, one patient was diagnosed to suffer from complicated migraine worsened by antiepileptic medication. The frequency of primary or secondary generalized tonic-clonic seizures (9 of 12 cases, 75%) in this group was considerably higher than in the group of all patients (55%).

FDG-PET procedure. FDG-PET imaging was performed on a UGM PENN PET 240H scanner (*n*=8) and the UGM HEAD PET scanner (*n*=35) (UGM, Philadelphia, Pa.). Until September 1998 the PENN PET scanner was used in most cases; thereafter the dedicated brain HEAD PET scanner was used exclusively. The scanners have been described in detail elsewhere [46, 47]. Both scanners use NaI(Tl) crystals for photon detection. After three-dimensional image reconstruction of 126 transaxial planes of 2 mm slice thickness, the HEAD PET scanner yields a spatial resolution of approximately 3.5 mm (full-width at half-maximum, FWHM) in all directions. Image acquisition lasting 30 min was started approximately 45 min after intravenous injection of 0.037 mCi/kg FDG (total range =1.46–5.19 mCi, mean±SD =2.66±0.87 mCi). The PENN PET 240H scanner provides a spatial resolution of approximately 5.5 mm FWHM in all directions after 3D image reconstruction (126 transaxial planes, 2 mm slice thickness). Image acquisition (30 min) was started approximately 45 min after intravenous injection of 0.117 mCi/kg FDG (total range =6.11–11.5 mCi, mean±SD =8.16±1.84 mCi). Scans acquired by both cameras were fully corrected for scatter and randoms. A calculated attenuation correction was used employing a skull compensation factor of 1.1 cm^{-1} and soft tissue compensation factor of 0.095 cm^{-1}. During the radiotracer distribution time, the patients remained in a resting condition in a light-dimmed room at reduced ambient noise. The FDG-PET protocol requested a minimum seizure-free time period before injection of at least 12 h. The patients were interviewed for seizure and/or aura occurrence.

The fully corrected images were read by at least two experienced board-certified nuclear medicine physicians for temporal and extratemporal radiotracer distribution abnormalities during daily conferences. All interpretations were made in consensus. By reviewing the reports, in cases of temporal lobe abnormalities, the findings were categorized as *lateralized* to the abnormal side if the finding consisted of a marked one-sided hypometabolism. The scan was called *possibly lateralized* if the finding was mild or if a bilateral hypometabolism was observed with one side being more pronounced than the other. If no abnormality or an equally bilateral abnormality was present, the scan was called *not lateralized*.

To evaluate the appropriateness of this categorization, we calculated an asymmetry index of the temporal lobe FDG uptake. Using PETView software (UGM Medical Systems), one blinded observer (P.T.M.), who did not participate in the initial reading of the PET scans, placed a set of predefined temporal lobe gray matter regions of interest (five lateral, three basal, five mesial ROIs per side) onto eight transaxial slices (one slice gap). After manual adjustment of the ROI positions and only minimal correction of the ROI size if necessary, average counts rates per pixel were assessed for the total volume of each of the temporal lobe regions. Asymmetry indices were calculated as follows: AI (%) = [(right ROI–left ROI)/(right ROI + left ROI)] × 200. Thus, positive and negative values indicate a relatively decreased FDG uptake on the left and right side, respectively. The mean AI of the three temporal lobe regions was used for comparison with the results of the visual readings, referred to as AI-PET. (The results of the ROI analyses will be addressed in a separate report in detail.)

MRI procedure. All patients were imaged according to the seizure evaluation MRI protocol implemented at our institution using a Signa 1.5-T MRI scanner (General Electric Medical Systems, Milwaukee, Wis.) and a standard head coil. Whole brain imaging was done by a sagittal T1-weighted spin echo [TR =600 ms, TE =17 ms, slice thickness (ST) =5 mm, matrix =192×256], an axial T2-weighted fast spin echo (TR =4,000 ms, TE =85 ms, ST =5 mm, matrix =192×256), and an axial multiplanar gradient echo (*susceptibility*; TR =750 ms, TE =40 ms, α =10°, ST =5 mm, matrix =128×256) sequence. Coronal images perpendicular to the long axis of the temporal lobe were acquired using a T1-weighted 3D spoiled gradient echo (TR =35 ms, TE =5 ms, α =45°, ST =1.5 mm, matrix =192×256), a T2-weighted fast spin echo (TR =4,000 ms, TE =85 ms, ST =3 mm, matrix =512×256), and a FLAIR (TR =10,000 ms, TE =133 ms, TI =2,200 ms, ST =4 mm, 2 mm gap, matrix =256×192) sequence. In cases of questionable structural abnormalities, additional gadolinium contrast-enhanced axial T1-weighted spin echo (TR =550 ms, TE =20 ms, ST =5 mm, matrix =256×192) images were acquired after MRS. All scan interpretations were made in consensus by at least two experienced board-certified neuroradiologists during daily conferences.

The presence of temporal and extratemporal lesions and alterations were assessed. The following criteria were used to determine the lateralization of the seizure origin: increased hippocampal signal intensity on T2-weighted images, hippocampal/temporal lobe atrophy, structural disruption of the amygdala/hippocampus (all

three considered as evidence of MTS), cortical/subcortical signal abnormalities or thickening (considered as evidence of cortical dysplasia or heterotopia), and other structural lesions. By reviewing the reports, the seizure disorder was assumed to be lateralized (left/right) to the side of the abnormality if a marked unilateral abnormality was present. If the detected abnormality was only mild or if a bilateral abnormality was observed with one side being more affected than the other, the origin was regarded as possibly lateralized. If no abnormality or an equally bilateral abnormality was present, the scan was called not lateralized.

MRS procedure. The MRS of the temporal lobes was usually performed in conjunction with the MRI using the same 1.5-T MRI scanner. A fully automatic, single-voxel proton spectroscopy package [proton brain examination (PROBE-p), PRESS localization] provided by the scanner manufacturer was used. The package has been described in detail elsewhere [45]. A single voxel including the anterior part of the hippocampus was selected using graphic prescription for each hemisphere from an axial image. Acquisition parameters were TR =2,000 ms, TE =35 ms, 64–128 averages in a 256×128 matrix. The voxel size ranged from 3.4 to 9 cm^3 [mean (±SD) =6.8 (±1.8) cm^3]. The peak area ratio of *N*-acetyl-aspartate (at 2 ppm) to creatine (at 3 ppm) was assessed. No absolute quantification of metabolite concentrations was pursued.

An NAA/Cr ratio was considered to be markedly abnormal if it was less than 1.3, which is equivalent to the institutional normal value (1.7) minus 2 standard deviations (±0.2). A one-sided markedly abnormal result was therefore considered as lateralized (left/right). If the NAA/Cr ratio was less than 1.4 (institutional normal value minus 1.5 SD), it was considered as a mild abnormal result. If a mild abnormal NAA/Cr ratio was found on one side only, then the result was classified as possibly lateralized. If the NAA/Cr was abnormal on both sides, with the decrease on one side being approximately 0.1 units (~7%) greater than on the other side, the result was also regarded as possibly lateralized. If no abnormality or an equally bilateral abnormality was present, the scan was called not lateralized. In addition to this analysis, asymmetry indices of the NAA/Cr ratios, referred to as AI-MRS, were calculated by means of the formula mentioned above.

Surgery. Fifteen TLE patients underwent anterior temporal lobectomy (n=5 left, n=10 right) of the temporal lobe harboring the seizure origin based on surface EEG, intracranial EEG, clinical examination and imaging data. (The remaining ten patients with lateralized TLE EEG foci are either scheduled for surgery, have dropped out or are not considered for TLE for other reasons.) After a follow-up period of 7.6–35.7 months (mean±SD=20.1±7.7 months; only two patients with follow-up less than 12 months, 7.6 and 7.7 months, respectively), a seizure-free status was achieved in 13 patients. Of the remaining two patients, one patient was seizure-free for 10 months after experiencing a few seizures immediately after surgery and the other was seizure-free for 15 months before seizures at a greatly reduced frequency started to occur again in both cases. One patient continued to experience rare occasional auras. However, in all cases, surgery could be regarded as successful.

Statistics. Kappa values (κ) were calculated to assess the inter-modality agreement. Cochran's Q test was used (1) to compare the agreement of the three imaging modalities with the scalp EEG results in TLE cases, (2) to compare the proportions of agreement of the three imaging modalities and the actual seizure focus lateralization as determined by successful surgery, and (3) to compare the proportions of lateralized temporal abnormalities in non-temporal lobe epilepsy cases. Subsequently, pairwise inter-modality comparisons were made using a McNemar test if (a) the Q test yielded a significant result or (b) if more pairs of valid results were available for the two imaging modalities to be compared for pairwise testing than were actually considered for the Q test. Focus lateralization based on combined morphofunctional imaging was assessed by combining the results of FDG-PET with MRI and MRS with MRI. Again, the proportions of agreement with surface EEG, with the side of successful temporal lobectomy and with lateralized temporal abnormalities in non-temporal lobe epilepsy cases were compared using a McNemar test. Because of the overall limited number of not-agreeing decisions (which are only considered in these tests), we did not use an approximation by the χ^2 distribution but calculated the actual cumulative binomial likelihood for the McNemar test.

Statistical comparisons involving the AI-PET and AI-MRS, respectively, were done by the Kruskal-Wallis one-way analysis of variance and subsequent pairwise comparisons by the Mann-Whitney U test with correction for multiple comparisons.

Results

The results of the imaging procedures and the corresponding seizure focus lateralizations given by EEG are summarized in Table 1. Five of the total 43 MRS performed could not be evaluated due to technical difficulties including susceptibility artifacts, insufficient water signal suppression, and questionable voxel misplacement. In additional nine cases, the automatic quantitative spectroscopy analyses of the NAA/Cr ratio technically failed on one side. However, in six of these, the obtained spectra could be evaluated manually in comparison to the other side. In the other three cases, the spectroscopy of the contralateral side appeared normal in two cases and showed a minor reduction of the NAA/Cr ratio in one case. Thus a total number of 35 spectra pairs from both anterior hippocampal regions were available. All but one of the FDG-PET scans could be used for diagnostic purposes. In one case a clinically manifest seizure occurred approximately 20 min after FDG injection. Figure 1 shows an example of a TLE case unanimously lateralized by FDG-PET, MRS, and MRI.

The mean AI-PET (±SD) of scans classified as left lateralized, possibly left lateralized, not lateralized, possibly right lateralized and right lateralized were 8.8%±3.7%, 4.7%±2.4%, –1.6%±3.3%, –9.1%±10.9%, and –11.8%±7.4%, respectively (Kruskal-Wallis test: P<0.0001). Post hoc comparisons (U test, corrected α=0.005) showed that the mean AI-PET of the lateralized groups were significantly different from each other (P=0.0001), from the not lateralized group (left: P=0.0002; right: P=0.0003), and from the possibly lateralized group of the opposite side (left: P=0.002; right: P=0.001). The AI-PET of possibly lateralized groups were marginally significant different from each other (P=0.006), but not significantly different from the lateralized group of the same side (on left side: P=0.06; on

Table 1. EEG and imaging findings in the enrolled patients

No.	EEG	FDG-PET findings	MRI findings	Lt. NAA/Cr	Rt. NAA/Cr	MRS focus
1	*Lt. TLE*	Mild lt. temp. hypomet.	Lt.>rt. temp. atrophy	1.18	1.23	Not lateral.
2	*Lt. TLE*	Lt.>rt. temp. hypomet.	Lt. hippoc. atrophy and increased T2 signal	1.07	1.18	Pos. lt.
3	*Lt. TLE*	Lt. temp. hypomet.	Lt. hippoc. atrophy and increased T2 signal	1.26	1.46	Lt.
4	*Lt. TLE*	Lt. temp. hypomet.	Unremarkable	Decreased	1.09	Pos. lt.
5	*Lt. TLE*	Lt. temp. hypomet.	Lt. hippoc. atrophy and increased T2 signal	1.35	1.35	Not lateral.
6	Lt. TLE	Bilat. temp. hypomet.	Lt. temp. atrophy	1.19	1.29	Pos. lt.
7	Lt. TLE	Lt. temp. hypomet.	Unremarkable. Small rt. sphenoid wing meningioma	1.56	Invalid	
8	Lt. TLE	Lt.>rt. temp. hypomet.	Lt.>rt. increased hippoc. T2 signal	1.15	1.11	Not lateral.
9	Lt. TLE	Lt.>rt. temp. hypomet.	Lt.>rt. temp. atrophy and increased T2 signal	Invalid	Invalid	
10	Lt. TLE	Lt. temp. hypomet.	Unremarkable	1.39	1.6	Pos. lt.
11	Lt. TLE	Lt. temp. hypomet.	Mild lt. temp. cortical thickening	Decreased	1.24	Pos. lt.
12	*Rt. TLE*	Rt. temp. hypomet.	Unremarkable	1.2	1.1	Pos. rt.
13	*Rt. TLE*	Rt. temp. hypomet.	Mild rt. temp. atrophy	1.6	1.22	Rt.
14	*Rt. TLE*	Rt. temp. hypomet.	Mild rt. hippoc. atrophy	1.51	1.24	Rt.
15	*Rt. TLE*	Rt. temp. hypomet.	Rt.>lt. temp. atrophy	Invalid	Invalid	
16	*Rt. TLE*	Bilat. temp. hypomet.	Bilat. hippoc. atrophy and increased T2 signal	1.08	1.25	Pos. lt.
17	*Rt. TLE*	Rt.>lt. temp. hypomet.	Unremarkable	1.46	1.29	Rt.
18	*Rt. TLE*	Rt.>lt. temp. hypomet.	Mild rt. temp. atrophy	1.23	1.12	Pos. rt.
19	*Rt. TLE*	Rt. temp. hypomet.	Questionable rt.-sided cortical dysplasia	Invalid	1.31	
20	*Rt. TLE*	Rt. temp. hypomet.	Unremarkable	1.47	Invalid	
21	*Rt. TLE*	Rt. temp. hypomet.	Unremarkable	1.4	Decreased	Pos. rt.
22	Rt. TLE	Invalid due to seizure activity p.i.	Unremarkable	1.21	1.3	Pos. lt.
23	Rt. TLE	Rt. temp. hypomet.	Unremarkable	1.26	1.26	Not lateral.
24	Rt. TLE	Rt. temp. hypomet.	Rt.>lt. hippoc. atrophy	1.15	1.07	Pos. rt.
25	Rt. TLE	Mild rt. temp. hypomet.	Unremarkable	1.38	1.32	Not lateral.
26	Not lateral. TLE	Lt. temp. hypomet.	Mild thickening of lt. temp. cortex	1.1	1.6	Lt.
27	Not lateral. TLE	Mild rt. temp. hypomet.	Unremarkable	1.18	1.28	Pos. lt.
28	Not lateral. TLE	Lt. temp. hypomet.	Questionable lt. mesial temp. cortical dysplasia	1.24	1.63	Lt.
29	Not lateral. TLE	Rt. temp. hypomet.	Unremarkable	1.26	1.16	Pos. rt.
30	Not lateral. TLE	Bilat. temp. hypomet.	Unremarkable	1.08	1.06	Not lateral.
31	Not lateral. TLE	Lt.>rt. temp. hypomet.	Unremarkable	Invalid	Invalid	
32	N-TLE[a]	Mild rt. temp. hypomet.	Lt. hippoc. atrophy and increased T2 signal	1.41	Normal	Not lateral.
33	N-TLE	Bilat. temp. hypomet.	Unremarkable	Decreased	1.47	Pos. lt.
34	N-TLE	Lt. temp. hypomet.	Mild rt. temp. atrophy	Invalid	Invalid	
35	N-TLE	Unremarkable	Unremarkable	Invalid	Invalid	
36	N-TLE[a]	Bilat. temp. + rt. hemispheric hypomet.	Rostrum/corpus callosum agenesis. bilat. temp. atrophy	0.93	0.94	Not lateral.
37	N-TLE	Bilat. temp. hypomet.	Mild lt. temp. atrophy	1.08	1.34	Pos. lt.
38	N-TLE[b]	Rt. hemispheric hypomet., especially temp.	Rt. hemimegalocephaly, rt. increased temp. T2 signal	Normal	1.03	Rt.
39	N-TLE	Lt.>rt. temp. hypomet.	Lt.>rt. increased hippoc. T2 signal and temp. atrophy	0.95	1.07	Pos. lt.
40	N-TLE	Unremarkable	Unremarkable	1.27	1.49	Lt.
41	N-TLE	Unremarkable	Unremarkable	1.59	1.24	Rt.
42	N-TLE	Unremarkable	Unremarkable	1.15	1.23	Pos. lt.
43	N-TLE	Bilat. temp. hypomet.	Lt.>rt. hippoc. atrophy and increased T2 signal	0.97	1.63	Lt.

The EEG findings of the patients who underwent an anterior temporal lobectomy are in italics

lt., Left; rt., right; temp., temporal; hypomet., hypometabolism; pos., possibly; lateral., lateralized; hippoc., hippocampal; (N-) TLE, (non-)temporal lobe epilepsy)

[a] Predominantly right frontal EEG changes

[b] Predominatly right hemispheric EEG changes

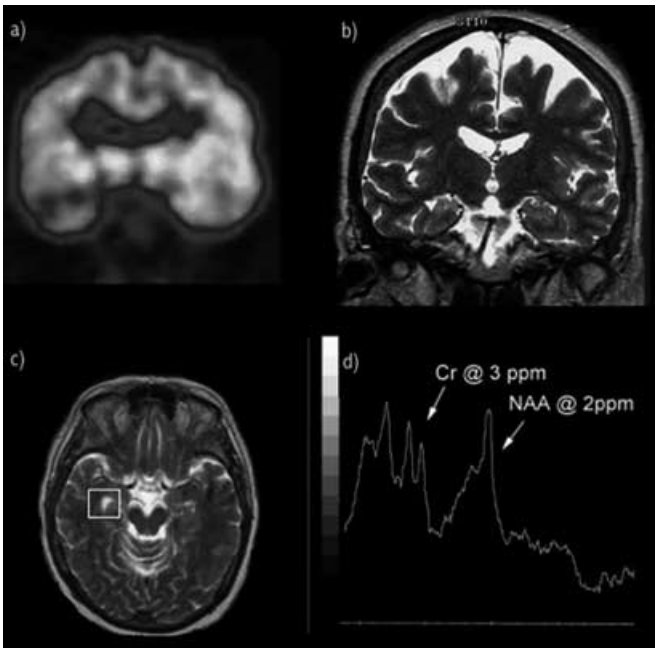

Fig. 1. FDG-PET (**a**), MRI (**b**, T2-weighted fast spin echo), and MRS (**c**, right-sided voxel placement; **d**, proton MR spectrum with peaks of creatine at 3 ppm and *N*-acetyl-aspartate at 2 ppm) of a 57-year-old female suffering from CPS for approximately 30 years. The patient presented interictal right sphenoidal spikes and a right temporal seizure onset on EEG. Note the decreased FDG uptake of the right mesial and lateral temporal lobe on the FDG-PET scan and the mildly increased hippocampal T2 signal intensity and dilatation of the anterior horn of the right lateral ventricle. The NAA/Cr ratio on the right side was 1.22, and on the left side 1.72 (not shown). Successful anterior temporal lobectomy was performed

right side: P=0.23). While the AI-PET of the possibly left lateralized group was significantly different from the AI-PET of the not lateralized group (P=0.0013), this was not true for the possibly right lateralized group (P=0.13). The group of possibly right lateralized PET scans (n=5) contained a patient with a right-sided hemimegalocephaly (bilateral temporal hypometabolism, right<left). The AI-PET of this patient (–29%) was the lowest of all. Exclusion of this patient would considerably reduce the group variance (to mean±SD =–5.1%±5.6%). In only one case did the AI-PET (AI-PET =2.6%) indicate a weak lateralization to the opposite side than that indicated by visual FDG-PET interpretation (possibly right lateralized) and EEG (right TLE). The visual interpretation presumably depended on a small right mesial hypometabolic area (AI mesial =–0.2), which contrasted with the overall slightly higher right temporal uptake. There was no effect of the scanner used on the results (ANOVA P>0.05).

Inter-modality comparisons

If only lateralization decisions of high confidence (i.e., the lateralized category) were considered to indicate actual lateralization, overall agreement between the imaging modalities was low. The agreement between functional modalities (FDG-PET and MRS, κ=0.21) was higher than between functional and morphologic modalities (FDG-PET and MRI, κ=0.09; MRS and MRI, κ=0.01). If possibly lateralized findings were also considered to indicate actual lateralization, the agreement between FDG-PET and MRI was highest (κ=0.41), while the concordance between FDG-PET and MRS (κ=0.34) was still higher than that between MRI and MRS (κ=0.27). However, the overall agreement was still low to moderate.

The comparison of the imaging modalities with surface EEG in TLE cases is summarized in Table 2. While FDG-PET and MRI never lateralized to the opposite of the side demonstrated by surface EEG, the MRS results of two cases did indicate an opposite lateralization to EEG with low confidence (possibly lateralized). Never-

Table 2. Lateralizations given by the imaging modalities in comparison to the focus lateralization shown by EEG (n=11 left, n=14 right, n=6 not lateralized) and to the side of successful temporal lobectomy (n=5 left side, n=10 right side) in TLE cases

	Lateralization (n)			Agreement with surface EEG		Agreement with the side of successful temporal lobectomy	
	Left	Right	Not lat.	Agreeing	Not agreeing	Agreeing	Not agreeing
PET (h.c.)	8	10	12	18 (60%)	12 (40%)	10 (67%)	5 (33%)
MRI (h.c.)	4	1	26	11 (35%)	20 (65%)	4 (27%)	11 (73%)
MRS (h.c.)	3	3	19	7 (28%)	18 (72%)	4 (33%)	8 (67%)
PET (l.c.)	13	14	3	23 (77%)	7 (23%)	14 (93%)	1 (7%)
MRI (l.c.)	10	6	15	18 (58%)	13 (42%)	9 (60%)	6 (40%)
MRS (l.c.)	11	8	6	14 (56%)	11[a] (44%)	9 (75%)	3[a] (25%)

PET (h.c.), MRI (h.c.), and MRS (h.c.) show lateralizations when only decisions of high confidence (i.e., lateralized) were considered to indicate lateralization. PET (l.c.), MRI (l.c.), and MRS (l.c.) show lateralizations when decisions of lower confidence (i.e., possibly lateralized) were also considered to indicate lateralization

[a] MRS showed a lateralization to the opposite side than EEG and the side of successful temporal lobectomy in two and one cases, respectively

theless, the agreement between imaging modalities and surface EEG was maximal when possibly lateralized abnormalities were also considered to indicate a lateralization.

Subsequently, possibly lateralized findings were regarded as indicative of an actual lateralization. When the proportions of agreement between imaging modalities and surface EEG were compared statistically including the 24 cases in which all modalities yielded valid results, there were no significant differences (*Q* test: $P>0.25$). Pairwise comparisons including also the additionally available pairs of valid results ($n=30$ FDG-PET vs MRI, $n=25$ MRI vs MRS) confirmed this result: The proportions of agreement of FDG-PET (0.77), MRI (0.58), and MRS (0.56) with surface EEG were not significantly different (McNemar test, FDG-PET vs MRI: $P=0.13$, MRI vs MRS: $P>0.5$). The PET scanner used had no influence on these results (χ^2 test: $P>0.15$). The mean AI-PET of the patient groups with left, right, and not lateralized EEG foci were 6.8%±4.6%, –9.4%±7.9%, and –0.9%± 7.9%, respectively (Kruskal-Wallis test: $P=0.0001$). There was a considerable overlap between the AI-PET values of the groups with lateralized and the group with not lateralized EEG changes (*U* test, corrected $\alpha=0.0167$; left/right lateralized vs not lateralized: $P=0.06$/$P=0.03$, respectively). The mean AI-PET values of the groups with lateralized EEG foci were significantly different ($P<0.0001$; only one data point overlap, see above). The AI-MRS of the groups with left, right, and not lateralized EEG foci were 6.7±6.9, –6.7±12.1, and 12.4±19.2, respectively, with a considerable overlap between all groups (Kruskal-Wallis test: $P=0.028$). The difference in mean AI-MRS values of the groups with left- and right-sided EEG foci were only marginally significant (*U* test, corrected $\alpha=0.0167$; $P=0.0167$).

Fifteen patients underwent a successful temporal lobectomy. Cochran's *Q* test comparing the proportions of agreement between the imaging modalities and the side of successful temporal lobectomy (see Table 2) showed no significant differences ($n=12$ with valid results in all three modalities; $P=0.13$). However, when additional patients with valid results in only two of the three modalities ($n=15$ in total) were also taken into consideration, the comparison between FDG-PET and MRI showed that the proportions of agreement of FDG-PET (0.93) and MRI (0.60) with the side of successful temporal lobectomy were significantly different ($P=0.03$). The concordance of MRS with the side of successful temporal lobectomy was intermediate (0.75). In one case, MRS indicated a lateralization to the opposite side of the actual lateralization demonstrated by successful temporal lobectomy (AI-MRS =14.6%). The mean AI-PET of the patients with successful left and right temporal lobectomy were 9.9%±3.2% and –9.5%±8.5%, respectively (*U* test: $P=0.002$). The respective AI-MRS values were 7.2%±6.4% for left sided and –10.4%±14.1% for right-sided temporal lobectomy ($P=0.055$).

The seizure disorders of 12 patients were diagnosed to be of nontemporal origin by surface EEG. In eight cases (67%), FDG-PET showed no lateralized temporal lobe hypometabolism, while possibly lateralized and lateralized findings were reported in one and three cases, respectively. No lateralized abnormality was found in half of these patients on MRI (50%). The MRI scans were read to show a lateralization in one and a possible lateralization in five cases. In two cases, MRS was not lateralized (20%), while it showed a lateralized and a possibly lateralized decrease in the NAA/Cr ratio in four cases each (two MRS examinations not valid). Although these proportions of lateralized findings varied to a considerable extent, the differences did not reach a statistically significant level (comparing $n=10$ patients with valid results in all three modalities, *Q* test: $P=0.07$). The difference between the proportions of lateralized findings in FDG-PET and MRS was marginally significant (McNemar test: $P=0.06$). The mean AI-PET and AI-MRS (range) were –1.75%±9.4% (–29%–11.2%) and 9.44%±17.1% (–22.2%–31.2%), respectively.

Finally, both FDG-PET and MRS were analysed in combination with MRI. This was done by combining the results of functional (FDG-PET and MRS) and morphologic imaging (MRI) in a separate manner for each of the two combinations, minimizing the number of discordant decisions when compared to surface EEG in TLE cases. For the combination FDG-PET/MRI, a possibly lateralized finding must have been shown by both modalities or a lateralized abnormality by at least one modality. For MRS/MRI, at least a possibly lateralized result must have been given by one of the two modalities. In cases where the modalities to be combined yielded lateralizations to the opposite sides, the combined result was not lateralized regardless of the level of confidence.

When the proportions of agreeing results of FDG-PET/MRI (80%) and MRS/MRI (68%) with surface EEG in TLE patients were compared (Table 3), no significant difference was found ($P=0.50$, McNemar test for 24 cases with valid results). Likewise, the proportions of agreement of FDG-PET/MRI (87%) and MRS/MRI (92%) with the side of successful temporal lobectomy were not significantly different ($P=0.50$, McNemar test for 12 cases with valid results). As in MRS alone, the combination MRS/MRI showed a lateralization to the opposite side when compared to the side of successful temporal lobectomy in one case. The combination of FDG-PET/MRI (17%) yielded significantly fewer lateralized temporal lobe findings in non-temporal lobe epilepsy cases than did MRS/MRI (90%) ($P<0.01$).

The agreement of FDG-PET/MRI (80%) and MRS/MRI (68%) with surface EEG in TLE patients was considerably higher than the agreement of MRI alone with EEG (58%). In 11 patients with lateralized TLE foci based on EEG, MRI showed not lateralized results. In this group of patients, nine of ten valid FDG-PET scans concurred with EEG (one FDG-PET scan also not lateralized). Fur-

Table 3. Rates of agreement of the combined results of FDG-PET and MRI (FDG-PET/MRI) and MRS and MRI (MRS/MRI) with EEG and the side of successful temporal lobectomy in TLE cases

	Lateralization (*n*)			Agreement with EEG		Agreement with the side of successful temporal lobectomy		Lateralized findings in N-TLE
	Left	Right	Not lat.	Agreeing	Not agreeing	Agreeing	Not agreeing	
PET/MRI	14	12	16	24 (80%)	6 (20%)	13 (87%)	2 (13%)	2 (17%)
MRS/MRI	21	10	4	17 (68%)	8[a] (32%)	11 (92%)	1[a] (8%)	9 (90%)

[a] MRS/MRI showed a lateralization to the opposite side than EEG and the side of successful temporal lobectomy in two and one cases, respectively

ther, MRS concurred with EEG in five of nine valid examinations (in two cases MRS was not lateralized and possibly lateralized to the opposite side than EEG, respectively). Nevertheless, FDG-PET and MRS offered no diagnostic benefit in cases with lateralized TLE EEG foci in which MRI showed a corresponding marked (lateralized) abnormality (5 of 25 cases). In the remaining nine cases with lateralized TLE EEG foci, in which MRI showed possibly lateralized findings, FDG-PET and MRS confirmed the MRI lateralization in all cases with valid examinations. As can be appreciated in Table 1, the diagnostic information regarding the seizure focus lateralization contributed by FDG-PET was negligible when MRS and MRI yielded the same result, especially when they lateralized to the same side in TLE cases. In 13 of the total 25 TLE (52%) cases with valid MRS scans, MRS and MRI gave the same result. In ten of these cases (77%), FDG-PET indicated the same lateralization. In one case, FDG-PET was not lateralized where EEG showed the same lateralized seizure origin as MRS and MRI. In the remaining two cases, FDG-PET was possibly lateralized and lateralized, respectively, in agreement with surface EEG, while MRS and MRI showed a not lateralized result.

Discussion

The present study was undertaken to compare the merits of FDG-PET, MRI, and MRS for the lateralization of temporal lobe seizure foci. Since MRI is an essential part of neuroimaging protocols for seizure evaluation, the comparison of the functional imaging modalities FDG-PET and MRS alone and in combination with MRI is most interesting. Other functional imaging techniques like receptor single-photon emission tomography (SPET) and PET or continuous arterial spin labeled perfusion MRI were not part of this investigation, since they are still rather experimental or logistically more difficult to implement into a routine environment. However, it has to be emphasized that ictal perfusion SPET might represent a method equally as accurate as FDG-PET, although results are conflicting [48, 49]. In particular, the technically more demanding ictal-interictal perfusion SPET difference image technique appears to be very promising [50].

We found no significant proportional differences in the agreement of the separate imaging modalities with surface EEG in TLE cases. The frequencies of detected lateralized temporal lobe abnormalities in non-temporal lobe epilepsy cases were not significantly different. While earlier studies [13, 14, 19, 22, 23, 39, 49] reported superior results for the functional imaging modalities, FDG-PET and MRS, compared with MRI, we were not able to find convincing statistical support for this claim. The fact that the differences among the agreement of the imaging modalities with surface EEG did not reach a significant level despite considerably diverging results could be mainly due to the limited number of cases. However, the rate of agreement with the side of successful temporal lobectomy was significantly higher for FDG-PET (0.93) than for MRI (0.60) with no significant difference between MRS (0.75) and MRI. Nevertheless, it has to be kept in mind that we did not contemplate temporal lobe MRI volumetry or T2 relaxation time measurements, which are likely to be more sensitive than qualitative readings but which are also more difficult to implement into clinical routine.

A significant bias due to the fact that the observers might have been aware of the results of other modalities has to be excluded. Particularly for the visually interpreted FDG-PET and MRI examinations, this is of crucial importance. Although the retrospective nature of this study precludes the possibility of ruling out any bias completely, we are confident that this study is reliable for several reasons: In 37 cases, the imaging studies were performed before or during the video-EEG monitoring. Thus, the interpreting physicians could not have been aware of the EEG results in these cases, although we cannot completely rule out this possibility in the remaining six cases. The MRI and PET scans were read during separate sessions by different teams of physicians. The order of imaging examinations was approximately counterbalanced (in 23 of 43 cases PET was performed first). Thus, the interpreting physicians could not have been aware of the results of the other modality in at

least half of the cases. For the remaining cases, it must be emphasized that the scans were usually interpreted without explicit correlation to other modalities. Since MRI and MRS were performed in conjunction, the knowledge of the NAA/Cr ratios could have biased the MRI readings. However, the fact that MRI and MRS showed the lowest inter-modality agreement argues against a strong bias.

The major aim of this study was to assess the value of the included modalities in day-to-day clinical routine. We therefore intentionally did not re-read the scans. Thus, it should be noted that this study reflects "real life" performance in a given clinical environment. Consequently, we cannot exactly enumerate reading reproducibility of the MRI and FDG-PET readings. However, the retrospectively assessed AI-PET strongly supports the reliability of the initial PET readings and underlines the appropriateness of the visual reading categorization. The MRS studies were carefully reviewed for artifacts by an experienced chemist and the voxel position was verified by an experienced physician. The method itself is known to be highly reproducible [45].

Despite lack of statistical significance (except the higher agreement of FDG-PET as compared to MRI with the side of successful lobectomy), the authors' overall impression is that FDG-PET is the most reliable method for seizure focus lateralization among the investigated methods. On the one hand, FDG-PET consistently yielded the highest rates of agreement in our comparisons (77% agreement with surface EEG in TLE and 93% with the side of successful temporal lobectomy). Unlike MRS, the visually read FDG-PET never lateralized to the side opposite to EEG or successful temporal lobectomy in our sample. Additionally, the calculated asymmetry index, AI-PET, showed considerably less overlap between the different groups of foci lateralization than AI-MRS. On the other hand, FDG-PET showed the lowest number of lateralized temporal lobe abnormalities in non-temporal lobe epilepsy cases. Although it may be possible that lateralized changes occur in the temporal lobes in non-temporal lobe epilepsy owing to repeated injuries by generalized seizures and epileptic statuses [8, 16, 18, 51] or other influences, the detection of these potential changes is obviously a confusing situation when a mixed population (TLE and non-TLE) is examined with the aim of focus lateralization. Additionally, FDG-PET seems to provide a higher degree of decision confidence. The frequency of detection of possible lateralizations was lowest, allowing correct statements of high confidence in most cases. However, this only favors FDG-PET for the current clinical goal, since the present study and earlier investigations [24] showed that MRS is capable of detecting subtle pathologic changes that are not appreciated by FDG-PET. Finally, FDG-PET seems to be a more stable method than MRS. While FDG-PET was only invalid in one case owing to seizure activity post injection, five MRS studies failed totally and nine additional studies failed on one side owing to technical difficulties. If MRS examinations are monitored online by an attending physician it would be possible to control these problems more effectively and to repeat invalid measurements. However, such time-demanding monitoring is not always feasible in clinical routine.

The employed single-voxel MRS method was chosen because of its simple implementation and application. The fully automated package proved to give results of lower variance than single-voxel methods employing manual adjustments and processing [45]. Nevertheless, it should be noted that two-dimensional chemical shift imaging (CSI) is becoming more and more available while yielding excellent results [13, 14, 20, 21, 23]. Although CSI can be complicated and distorted by water and lipid contamination in areas of the temporal lobes close to the skull and sinuses, which favors the single-voxel approach [20, 21, 52], the interpretation of entire metabolite maps provided by CSI may be more valid and reliable [21].

MRI is the accepted means of neuroimaging for the evaluation of patients considered for temporal lobectomy [44]. In nonsymptomatic epilepsy cases, where structural imaging is often inconclusive, functional imaging modalities can provide significant contributions to the seizure focus localization/lateralization. Thus a combination of the two imaging approaches seems to be ideal. Previously, the roles of MRS and FDG-PET appeared to be complementary, since it was assumed that the decline in the NAA/Cr ratio reflects the degree of neuronal cell loss while FDG-PET measures decreased glucose metabolism due to an unclear neuronal dysfunction. However, the complementary roles of MRS and FDG-PET appear challenged since a correlation between FDG uptake and the NAA/(Cr+Cho) ratio in TLE patients has been described (r=0.54; [25]). (Because of different MRS voxel and FDG-PET ROI placements in the present study, we did not examine a possible correlation between the NAA/Cr ratio and the FDG uptake.) Like the partially reversible decreased FDG uptake [53], the decline in NAA is also reversible to some extent postoperatively [29, 30] and occurs even transsynaptically [27, 28], which is not compatible with neuronal cell loss. Possible explanations of these observations could be that the oxidative metabolism of both glucose and NAA is impaired on a mitochondrial level (as proposed for NAA [30, 51]) or that a synaptic dysfunction (e.g., synapse density changes) leads to decreased FDG uptake and a lowered NAA concentration [25]. To avoid possibly redundant information and unnecessary costs, it appears justified to select only one of the methods as the first step for seizure patient evaluation after MRI. We compared the combinations MRS/MRI and FDG-PET/MRI and found no significant differences in the agreement with surface EEG and the side of successful temporal lobectomy. However, the combination MRS/MRI showed significantly more lateralized findings in non-temporal lobe epilepsy cases,

which may be diagnostically confusing. Nevertheless, the diagnostic contribution of FDG-PET appeared negligible when MRS and MRI showed the same result, especially when they lateralized unanimously to the same side in TLE cases.

Based on the results of this preliminary study, the fact that an MRS examination is less time demanding (in conjunction with MRI it only takes a few minutes) and less expensive than FDG-PET, and the absence of exposure of the patient to ionizing radiation with MRS, the following sequential use of MRS and FDG-PET in patients considered for temporal lobectomy may be proposed for further evaluation: After EEG confirms the epileptogenic nature of the seizure disorder and shows convincing evidence of temporal seizure origin, the usual MRI examination will be performed (1st step). If MRI (qualitative readings, or preferably volumetry) detects a marked lateralized temporal lobe abnormality in correspondence with the lateralization by surface EEG, a lateralized temporal lobe seizure focus seems to be likely. To gain additional diagnostic confidence, and in cases where MRI and EEG do not concur or where MRI shows only a mild or a bilateral abnormality, an additional MRS examination should be performed (2nd step). If the results of MRS and MRI agree with each other and lateralize to the same side as EEG, a lateralized temporal lobe seizure focus can be assumed. In cases where MRS and MRI do not agree, an FDG-PET scan may provide additional valuable diagnostic information (3rd step). If the FDG-PET scan indicates the same lateralization as EEG and one of the other imaging modalities, a lateralized temporal lobe seizure focus seems to be most likely. If the results are still conflicting, an intracranial EEG recording may be indicated. In cases where MRS and MRI give the same results (i.e., lateralized or not lateralized) but do not agree with EEG, an intracranial EEG recording seems to be more promising than FDG-PET (4th step).

The first three of the four steps are strongly supported by our own investigation. The fourth point, however, is based on the assumption that it is very likely that FDG-PET will yield the same result as MRS and MRI if MRS and MRI have already both shown the same lateralization. This was the case in 10 of 13 of our TLE patients (in one of the remaining three cases FDG-PET showed a different lateralization than EEG and in two cases, the same lateralization as EEG). Although it is known that FDG-PET can indicate the correct lateralization when EEG is inconclusive or incorrect [32, 33, 35, 37], the decision confidence would probably not be high enough to initiate a surgical treatment. Therefore an intracranial EEG recording might be indicated to gain highest diagnostic reliability.

If the proposed algorithm had been performed in our sample of 25 TLE patients in whom valid MRS scans were acquired, four FDG-PET scans and four MRS examinations could have been avoided on the basis of the above-mentioned first step (lateralized EEG and marked abnormal MRI). An additional five FDG-PET examinations could have been avoided on the basis of the above-mentioned second step (same lateralization shown by MRI, MRS and EEG). Finally, in four more cases, the FDG-PET scan might have been replaced by an intracranial EEG recording, in accordance with the fourth step. In the remaining cases, where MRI and MRS could not unanimously lateralize the seizure focus, FDG-PET was very helpful. One might argue that even more FDG-PET and MRS examinations could be avoided if, in addition, MRI lateralizations of low confidence (i.e., asymmetric or mild abnormalities) in conjunction with an agreeing EEG are regarded to be sufficient for positive lateralization. As described earlier, FDG-PET and MRS only play a confirmatory role in this situation. However, the authors believe that the diagnostic confidence given by a mildly abnormal visually read MRI scan in conjunction with surface EEG is not high enough to initiate a surgical treatment.

Conclusion

This retrospective study confirms that three brain imaging modalities, FDG-PET, MRS, and MRI, are capable of lateralizing the seizure focus in patients suffering from temporal lobe epilepsy. FDG-PET seems to be the most reliable and stable method on its own. When the functional imaging modalities, FDG-PET and MRS, are compared in conjunction with the standard structural imaging modality, MRI, the combinations FDG-PET/MRI and MRS/MRI appear to be equivalent. Based on our results, we conclude that it may be justified to perform MRS, which is less expensive, faster, and entails no radiation exposure, in combination with MRI before FDG-PET in TLE cases, since FDG-PET offers only minor additional diagnostic information if MRS and MRI indicate the same seizure focus lateralization.

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