Clinical Role of Subtraction Ictal SPECT Coregistered to MR Imaging and ^{18}F-FDG PET in Pediatric Epilepsy

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A precise assessment of the drug-resistant epileptic pediatric population for surgical candidacy is often challenging, and to date there are no evidence-based guidelines for presurgical identification of the epileptogenic zone. To evaluate the usefulness of radionuclide imaging techniques for presurgical evaluation of epileptic pediatric patients, we compared the results of video-electroencephalography (EEG), brain MR imaging, interictal SPECT, ictal SPECT, subtraction ictal SPECT coregistered to MR imaging (SISCOM), and interictal PET with ^{18}F-FDG. **Methods:** Fifty-four children with drug-resistant epilepsy who had undergone video-EEG monitoring, brain MR imaging, interictal and ictal brain perfusion SPECT, SISCOM, and ^{18}F-FDG PET were included in this study. All abnormal findings revealed by these neuroimaging techniques were compared with the presumed location of the epileptogenic zone (PEZ) as determined by video-EEG and clinical data. The proportion of localizing studies for each technique was statistically compared. In the 18 patients who underwent resective brain surgery, neuroimaging results were compared with histopathology results and surgical outcome. **Results:** SISCOM and ^{18}F-FDG PET concordance with the PEZ was significantly higher than MR imaging ($P < 0.05$). MR imaging showed localizing results in 21 of 54 cases (39%), SISCOM in 36 of 54 cases (67%), and ^{18}F-FDG PET in 31 of 54 cases (57%). If we consider SISCOM and ^{18}F-FDG PET results together, nuclear medicine imaging techniques showed coinciding video-EEG results in 76% of patients (41/54). In those cases in which MR imaging failed to identify any epileptogenic lesion (61% [33/54]), SISCOM or ^{18}F-FDG PET findings matched PEZ in 67% (22/33) of cases. **Conclusion:** SISCOM and ^{18}F-FDG PET provide complementary presurgical information that matched video-EEG results and clinical data in three fourths of our sample. SISCOM was particularly useful in those cases in which MR imaging findings were abnormal but no epileptogenic lesion was identified. Radionuclide imaging techniques are both useful and reliable, extending the possibility of surgical treatment to patients who may have been discouraged without a nuclear medicine approach.

Key Words: epilepsy; children; SPECT; SISCOM; PET

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Children with drug-resistant epilepsy usually respond more readily to surgery than adult patients mainly due to the greater plasticity of the immature brain (*1*). In the presurgical evaluation of these patients, the limits of the epileptogenic brain area, referred to as the epileptogenic zone (EZ), need to be precisely determined. EZ is defined in theory as "the minimum amount of cortex that must be resected to produce seizure freedom" (*2*). However, in practice, the EZ is a theoretic concept; only if seizure freedom is achieved after surgery can it be concluded that the EZ must have been included in the resected cortex (*3*).

Although an intracranial electroencephalogram (iEEG) with correctly placed electrodes remains the gold standard procedure in the delimitation of a focal EZ, the invasiveness of this technique limits its use to only those patients with ambiguous findings (*4*).

Patients usually begin their assessment with a video-electroencephalogram (EEG) and preidentification of the presumed epileptogenic brain lesion by MR imaging. Nonetheless, in some cases MR imaging shows multifocal structural abnormalities or fails to show any lesion at all (*5*) despite localizing features on seizure semiology and EEG. In the pediatric population, this situation is often due to a poor differentiation between gray and white matter and a higher frequency of cortical dysplasia (*6*), a type of lesion that often shows negative on MR imaging scans (*7*).

Complex drug-resistant epilepsy cases, and the pediatric population in particular, can benefit from the use of nuclear medicine imaging techniques such as interictal and ictal brain perfusion SPECT, subtraction ictal SPECT coregistered to MR imaging (SISCOM), and interictal PET with ^{18}F-FDG (*8,9*). Radionuclide imaging techniques can offer a complementary function in the localization of the epileptogenic focus (*5,10–15*). However, most studies refer to an adult population, analyzing the contribution of these techniques independently. Few have directly contrasted multiple neuroimaging methods in children (*8,16–19*).

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The aim of this work was to evaluate the usefulness of SISCOM and ^{18}F-FDG PET in the process of presurgical EZ identification in drug-resistant epileptic pediatric patients by comparing these techniques with conventional diagnostic procedures.

MATERIALS AND METHODS

Patients

Patient evaluation was performed as part of the clinical work-up judged necessary to optimally localize the EZ using clinical and neuropsychologic examination, EEG surveillance, and anatomic and functional neuroimaging studies. SISCOM or ^{18}F-FDG PET studies are requested after MR imaging in patients who are candidates for surgery, especially in cases of unclear or diffuse video-EEG results; normal MR imaging, multiple MR imaging lesions, or MR imaging findings discordant to video-EEG; for the evaluation of potential secondary epileptic foci; for iEEG placement guidance; to better define the limits of the brain area to be resected; and for evaluating the functional integrity of the rest of the brain (*9*).

We retrospectively reviewed 122 children with medically intractable epilepsy who underwent video-EEG and MR imaging evaluation for presurgical assessment between 2006 and 2012. The inclusion criteria for this analysis were that all patients had undergone video-EEG monitoring, brain MR imaging, SISCOM, and ^{18}F-FDG PET studies. Radionuclide imaging was not performed in 33 cases because it was judged not necessary in cases of multifocal epilepsy, nonepileptic paroxysmal events, and MR imaging lesions in eloquent areas that excluded surgical treatment or when MR imaging showed a structural lesion that was clearly concordant with video-EEG. In 25 occasions, ictal SPECT was requested but not achievable because of the short duration of or lack of seizures on the injection day. In 10 patients, ^{18}F-FDG PET was not requested in view of MR imaging and SISCOM findings. Finally, 54 children (29 male, 25 female) with an age range of 1–22 y (mean, 8 y) were included for study. Informed written consent was obtained from all patients or their parents or legal guardians, and all procedures were approved by the hospital Ethics Committee.

Scalp-EEG Recording and Video-EEG Monitoring

Video-EEG monitoring was performed in the epilepsy unit for 5 d, and antiepileptic drugs were reduced when necessary to facilitate seizure occurrence. Video-EEG monitoring was performed using Deltamed equipment (Natus Medical Inc.) and was interpreted by an epileptologist who had experience with pediatric EEG.

MR Imaging

MR imaging was performed using a 1.5-T unit (Signa Exite; GE Healthcare) with a specific epilepsy protocol. Sedation was used in selected cases. All MR imaging studies were interpreted visually by an expert neuroradiologist.

SPECT and SISCOM

Ictal SPECT was performed as part of patient admission for video-EEG monitoring at the epilepsy unit of our center. Seizure onset was defined as the time of earliest indication of auras or the beginning of the rhythmic ictal discharges detected by video-EEG continuous monitoring. The radiotracer was administered intravenously at seizure onset by an experienced nurse trained to inject radioactive material and waiting in the EEG technician's room on the day of the ictal study. Interictal SPECT was performed within the following week. Ictal and interictal SPECT studies were performed with ^{99m}Tc-ethyl cysteinate dimer or ^{99m}Tc-hexamethylpropyleneamine-oxime. SPECT studies were acquired within 2 h of radioisotope injection and following the same protocol using a dual-head SPECT imaging system (Infinia Hawkeye 4; GE Healthcare) with a specific epilepsy protocol

Abnormal findings were defined purely on visual assessment as a hypoperfused area in interictal SPECT and a hyperperfused area in ictal SPECT. SISCOM images were obtained by a subtraction of the interictal study from the ictal SPECT and coregistered to an MR image. Abnormal findings were defined by the visual evaluation of brain areas greater than 2 SDs above mean activity of the subtraction image considering all voxels.

^{18}F-FDG PET Imaging

^{18}F-FDG PET images were acquired in 3-dimensional mode using PET/CT equipment (Biograph; Siemens) with a specific epilepsy protocol. Sedation was used in selected cases and a portable EEG was used to detect possible ictal discharges during the study. ^{18}F-FDG PET studies were registered with MR imaging using registration algorithms in FocusDET, with a multiresolution rigid registration scheme. Fusion images were interpreted exclusively by visual evaluation with a transparency of ^{18}F-FDG PET over the MR images that could be adjusted to any degree of fusion: from displaying only ^{18}F-FDG PET images to only MR images. Abnormal findings were defined as hypometabolic brain areas shown in ^{18}F-FDG PET.

Dose administration, software description, and acquisition parameters for video-EEG, MR imaging, SPECT, SISCOM, and ^{18}F-FDG PET are set out in the supplemental data (available at http://jnm.snmjournals.org).

Image Interpretation and Statistical Analysis

All neuroimaging modalities were prospectively evaluated by specialists masked from clinical data and other study results. We retrospectively reviewed the neuroimaging results of all 54 patients included in this study.

SPECT, SISCOM, and ^{18}F-FDG PET image interpretations were performed conjunctly by 2 nuclear medicine physicians. The location of the presumed epileptogenic zone (PEZ) was determined by consensus during patient management meetings in the epilepsy unit, taking into account video-EEG monitoring data as well as clinical and neuropsychologic data. The following concepts were used to classify neuroimaging results. The classification localizing study was used when the location of the abnormal finding revealed by any of the neuroimaging techniques was concordant with the brain location of PEZ. When the abnormal finding was localized in the same hemisphere but not exactly concordant with the brain location of PEZ, the classification was lateralizing study. The not-localizing-study category was used for cases in which abnormal findings were visualized but could not be correlated to PEZ (malacic changes related to ischemic or traumatic lesions, multiple tubers, hippocampus sclerosis, or hemispheric atrophy). When the location of the abnormal findings was discordant with the brain location of PEZ, the study was considered discordant, and in the absence of abnormal findings, the study was considered normal.

The proportion of localizing studies found by MR imaging, SISCOM, and ^{18}F-FDG PET was reported with its 95% confidence interval (CI). The proportions obtained using each technique were compared by means of the McNemar test, with a P value of less than 0.05 considered significant. A κ statistic of concordance was also calculated where relevant. Statistical procedures were performed using SPSS (version 17.0; SPSS Inc.).

Surgical Treatment and Follow-up

On the basis of the standard evaluation protocol of the epilepsy unit, taking into consideration all clinical, electrophysiologic, and neuroimaging data, patient surgical candidacy was settled. Lobar or multilobar selective cortical resection was performed by neurosurgeons from the epilepsy unit. In selected cases, iEEG was used to better delimit the focal epileptogenic region. All resected brain tissue was sent to the anatomopathology department for histopathologic analysis.

The postoperative seizure outcome 6 and 12 mo after final surgery was analyzed. Surgical outcome was classified according to Engel's

classification scheme: Engel class I (completely seizure-free, auras only, or atypical early postoperative seizures only), Engel class II (≥90% seizure reduction or nocturnal seizures only), Engel class III (≥50% seizure reduction), and Engel class IV (<50% seizure reduction). Patients who were operated on were divided into 2 subgroups: favorable outcome (Engel class I and II) and nonfavorable outcome (Engel class III and IV).

RESULTS

Seizure Focus Localization

When clinical data and video-EEG were combined, the epilepsy unit at our center was able to define the PEZ in 47 of 54 patients (87%). In the remaining 7 patients, video-EEG showed lateralizing results in 5, 1 case of multifocal activity, and in the remaining case video-EEG failed to record seizures.

MR imaging findings were abnormal in 28 of 54 (52%) patients: in 21 of 54 cases (39%; 95% CI, 27%–52%), MR imaging showed a lesion concordant with PEZ (localizing study), and in 6 of 54 (11%) studies, it was not possible to correlate the findings with PEZ (not-localizing study). This latter group consisted of 2 cases of multiple cortical tubers, 2 large ischemic lesions, and 2 cases of encephalomalacia. In the remaining case (patient 34), MR imaging showed a cavernous malformation that did not match video-EEG results and was classified as discordant. No abnormalities were found in 26 of 54 (48%) MR imaging studies, and these cases were considered normal.

Interictal SPECT findings were abnormal in 26 of 54 (48%) patients: 17 of 54 (31%) of these cases were classified as localizing study, and the remaining 9 of 54 abnormal (17%) studies comprised 4 lateralizing-study cases, 1 discordant-study case, and 4 not-localizing-study cases. Interictal SPECT studies were classified as normal in 28 of 54 (52%) cases.

Ictal SPECT study findings were abnormal in 35 of 54 (65%) patients: 27 of 54 (50%) were classified as localizing study, and there were 4 lateralizing-study, 2 discordant-study, and 2 not-localizing-study cases. Ictal SPECT studies were classified as normal in 19 of 54 (35%) cases. The average duration of seizures was 56 s (range, 2–234 s), and the average time from seizure onset to radiotracer injection was 17 s (range, 2–69 s).

SISCOM results were abnormal in 41 of 54 (76%) patients: 36 of 54 (67%; 95% CI, 53%–78%) cases were classified as localizing study, with 2 of 54 (4%) lateralizing-study cases and 3 of 54 (6%) discordant-study cases. SISCOM studies were classified as normal in 13 of 54 (24%) cases.

^{18}F-FDG PET results were abnormal in 41 of 54 (76%) patients: 31 of 54 (57%; 95% CI, 44%–70%) cases were classified as localizing study, and there were 2 lateralizing-study, 2 discordant-study, and 6 not-localizing-study cases. ^{18}F-FDG PET studies were classified as normal in 13 of 54 (24%) cases.

MR Imaging, SISCOM, and ^{18}F-FDG PET Comparison

A significant difference was found when comparing the proportion of SISCOM localizing study with MR imaging (67% vs. 39%, $P = 0.001$) and ictal SPECT (67% vs. 50%, $P = 0.004$). Also the proportion of ^{18}F-FDG PET localizing study was significantly higher than MR imaging (57% vs. 39%, $P = 0.03$). If we group SISCOM and ^{18}F-FDG PET results together, nuclear medicine imaging techniques showed localizing study in 41 of 54 (76%) of cases (Fig. 1).

MR imaging failed to show an epileptogenic lesion that matched PEZ (normal + not-localizing + discordant study) in 33 of 54 (61%) patients (Fig. 2). Within this group, SISCOM or ^{18}F-FDG PET

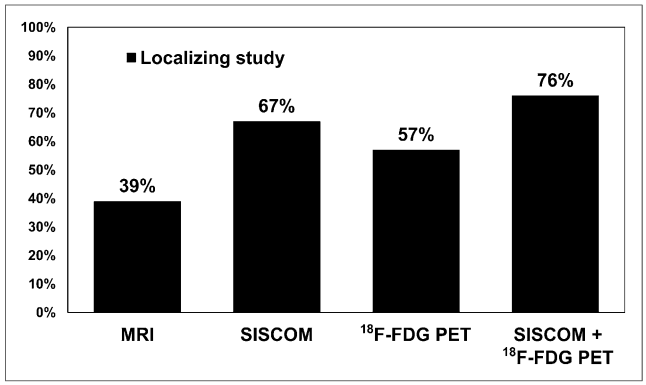

FIGURE 1. MR imaging, SISCOM, and ^{18}F-FDG PET rate of localizing study.

successfully presented localizing-study results on 22 of 33 (67%) occasions (in 8 cases exclusively by SISCOM [patients 8, 13, 14, 25, 27, 48, 52, and 54], in 3 cases exclusively by ^{18}F-FDG PET [patients 11, 15, and 21], and in 11 cases both). From all 6 of 54 (11%) not-localizing-study MR imaging cases, positive SISCOM findings matched the PEZ in 5 of 6 (83%) of the patients and were therefore classified as localizing study. ^{18}F-FDG PET showed not-localizing hypometabolism in all 6 cases. In the remaining case (patient 34), ^{18}F-FDG PET showed a hypometabolic right temporal lobe area that matched video-EEG– and SISCOM-positive findings when MR imaging showed a discordant left temporal cavernous malformation. Because the unclear nature of the neuroimaging results, this patient was not considered for surgery.

The difference between the proportion of SISCOM and PET localizing study was not significant ($P = 0.3$). SISCOM and ^{18}F-FDG PET showed coinciding localizing-study results in 26 of 54 (48%) patients, classified as moderate concordance (κ statistic of concordance, 0.42).

All imaging results are shown in Table 1, and localizing-study concordance of results among MR imaging, SISCOM, and ^{18}F-FDG PET is shown in Figure 3.

Surgical Results and Follow-up

On the basis of the decision of the epilepsy unit, 18 of 54 (33%) patients underwent resective surgical treatment. Four of those resections needed the use of iEEG to confirm the location and extent of EZ for resection. Of all 18 resected brain tissues analyzed, histopathologic examination revealed 14 cases of focal cortical

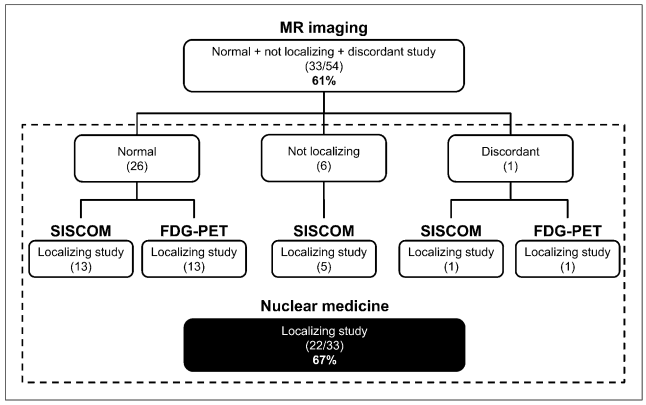

FIGURE 2. SISCOM and ^{18}F-FDG PET in MR imaging normal, not-localizing, and discordant cases.

TABLE 1
Imaging Results of All 54 Patients

Neuroimaging technique	Normal	Localizing study	Lateralizing study	Not-localizing study	Discordant study
MR imaging	26	21	0	6	1
Interictal SPECT	28	17	4	4	1
Ictal SPECT	19	27	4	2	2
SISCOM	13	36	2	0	3
PET	13	31	2	6	2

dysplasia, 1 case of low-grade glial tumor associated with cortical dysplasia, 1 case of chronic herpes encephalitis, 1 case of a low-grade astrocytoma, and 1 case of cortical tubers.

Up to the end of the study, 12-mo postoperative seizure outcome evaluation was performed for 14 patients. For the remaining 4 cases, only 6-mo postoperative evaluation was possible. Twelve of 18 patients (67%) had favorable Engel outcomes (class I and II) and 6 of 18 unfavorable Engel outcomes (class III and IV). Vagus nerve stimulation was used in 5 of 54 patients, all of whom presented an unfavorable Engel outcome.

Unfavorable clinical outcome was attributed to incomplete epileptic zone resection in 5 interventions: 3 cases of affected margins were found after histopathologic analysis, and complete resection was not achieved because of carotid artery involvement in one patient with a right temporal low-grade astrocytoma and eloquent cortex area involvement in another patient. The remaining case was a patient with multiple cortical tubers in whom a right parietal cortical tuber was identified as the EZ and was surgically removed. But shortly after, epileptic seizures restarted because of new epileptogenic activity from a previously silent cortical tuber.

Of the group of 18 patients who underwent resective surgery, MR imaging successfully localized PEZ in 13 of 18 cases (72%), whereas both SISCOM and ^{18}F-FDG PET independently showed 15 of 18 cases (83%) each. If we combine SISCOM and ^{18}F-FDG PET results, nuclear medicine imaging techniques successfully identified PEZ in all 18 of 18 patients (100%).

Data relating to the abnormal-finding brain location of each test, use of iEEG, histopathologic study, and surgical outcome are listed in Table 2. A sample case can be seen in Figure 4.

DISCUSSION

A careful assessment of drug-resistant epileptic pediatric population for surgical candidacy is often challenging and, although multimodal neuroimaging techniques can play a key role, to date there are no evidence-based guidelines for the EZ identification process. Our work aimed to bring additional information on the role that SISCOM and ^{18}F-FDG PET could play in this pathology.

In this presurgical neuroimaging study, we found that together SISCOM or ^{18}F-FDG PET findings matched the brain location of PEZ in 76% (41/54) of cases, with a significantly higher proportion of localizing-study results for SISCOM (67% [36/54]) and ^{18}F-FDG PET (57% [31/54]) than for MR imaging (39% [21/54]).

Localizing-study ratios in our group of patients are lower than the results of other similar studies in children (*8,16,19*) in which rates for localizing epileptogenic lesions ranged from 62% to 88% for MR imaging, 76% to 89% for SISCOM, and 67% to 83% for ^{18}F-FDG PET. But all 3 studies consider only a population of surgically intervened pediatric patients; consequently, all complex nonsurgical cases were consciously excluded from the study from the outset. Although this may provide the most reliable gold standard, it could lead to an overestimating bias in neuroimaging sensitivity rates. If within our studied population we consider only the group of patients who had undergone surgery (18 patients), localizing-study rates would rise to 72% for MR imaging and 83% for SISCOM and ^{18}F-FDG PET. All our surgically intervened patients had a SISCOM or ^{18}F-FDG PET study classified as localizing study (100%).

The SISCOM proportion of localizing study was significantly superior ($P = 0.004$) to an unsubstracted ictal SPECT study (50% vs. 67% of localizing study). The use of SISCOM via dedicated software offers improved sensitivity by avoiding possible errors related to the visual analysis of ictal SPECT alone. In the light of our results and a large body of other concordant published studies (*8,16,17,20,21*), we highly encourage the regular use of SISCOM in the SPECT evaluation of pediatric drug-resistant epileptic patients.

Of the cases for which MR imaging showed a not-localizing study, SISCOM findings matched the PEZ in 83% (5/6) of patients. Therefore, SISCOM proved particularly useful in the assessment of those patients with abnormal MR imaging findings that did not fully explain the presence of epileptic seizures such as malacic changes related to ischemic or traumatic lesions, multiple tubers, hippocampus sclerosis or hemispheric atrophy, or even the reevaluation of an already surgically intervened brain area. In such cases, ^{18}F-FDG PET studies did not provide helpful information

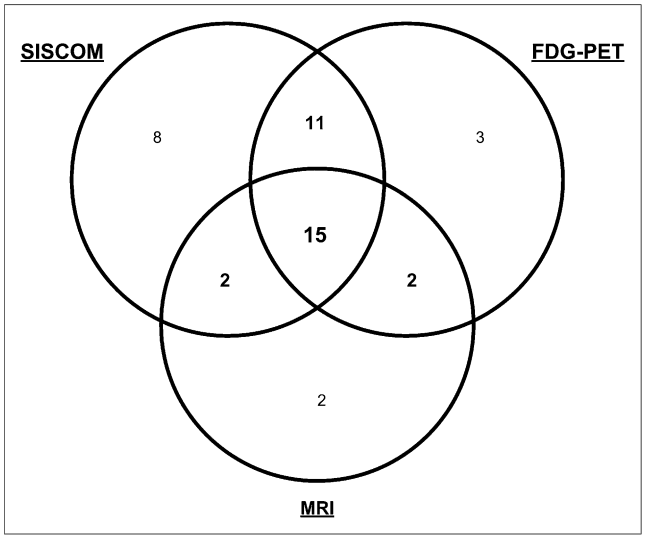

FIGURE 3. Number of patients with localizing-study results by MR imaging, SISCOM, and ^{18}F-FDG PET and their concordance.

TABLE 2
Neuroimaging Findings, Histopathologic Results, and Surgical Outcome of All Patients

Patient no./sex	Age (y)	PEZ	MRI	SISCOM	PET	Histopathology	Engel
1/F	11	F/R	F/R	F/R	F/R	i-EEG – MCD	I
2/F	4	Multifocal	Normal	Normal	Normal		
3/F	3	T/R	T/R	T/R	T/R	MCD	I
4/M	9	F/L	F/L	F/L	F/L	MCD	IV
5/M	1	T-O/R	T-O/R	T-O/R	T-O/R	MCD	II
6/M	10	P/L	Not-loc	Normal	Not-loc		
7/F	22	F/L	F/L	F/L	F/L		
8/M	12	P/R	Not-loc	P/R	Not-loc		
9/M	15	P/R	Normal	P/R	P/R		
10/F	12	F/L	F/L	Normal	Normal		
11/M	5	F/R	Normal	Lat/R	F/R	VNS	III
12/M	18	No PEZ	Normal	Normal	Normal		
13/M	4	P/R	Not-loc	P/R	Not-loc	Cortical tuber	IV
14/M	9	F/R	Not-loc	F/R	Not-loc	Cronic herpetic encephalitis	I
15/F	10	F/L	Normal	Normal	F/L	MCD	III
16/F	9	F/R	F/R	F/R	F/R	MCD	I
17/F	19	F/R	Normal	Normal	T/L		
18/M	4	F/L	Normal	T/R	F/L	MCD	II
19/F	10	F/R	F/R	F/R	F/R	i-EEG – MCD	II
20/M	8	T/R	Normal	T/R	T/R		
21/M	5	T/L	Normal	Normal	T/L	VNS	IV
22/F	9	T/R	T/R	T/R	T/R	Low-grade astrocytoma	IV
23/M	5	P/L	Normal	Normal	Normal	VNS	IV
24/F	11	F/L	Normal	F/L	F/L		
25/M	6	O/R	Normal	O/R	Normal		
26/F	20	P/R	Normal	T/L	Normal	VNS	IV
27/F	16	F/L	Normal	F/L	Normal		
28/F	12	T/L	T/L	T/L	T/L		
29/M	8	Lat/L	Normal	T-P/L	T-P/L		
30/M	4	F/R	F/R	F/R	Normal	MCD	I
31/M	11	F-T/L	F-T/L	F-T/L	Lat/L		
32/F	12	P-T/R	Normal	Normal	Normal		
33/F	4	F/L	F/L	F/L	F/L	MCD	IV*
34/F	1	T/R	T/L	T/R	T/R		
35/F	1	P-O/R	P-O/R	P-O/R	P-O/R	MCD	II*
36/M	16	F/R	Normal	F/R	F/R	MCD	IV
37/M	3	T/L	T/L	Normal	T/L	Low-grade glial tumor + cortical dysplasia	II
38/M	15	Lat/R	Normal	T/L	T/L	VNS	IV
39/M	9	P/L	P/L	P/L	P/L	MCD	I*
40/F	6	T/R	T/R	T/R	T/R	MCD	I*
41/F	3	P-O/R	Normal	Normal	Normal		
42/M	6	P-O/R	Normal	P-O/R	P-O/R		
43/F	5	Lat/R	Normal	Lat/R	Normal		
44/M	1	T-P-O/R	T-P-O/R	Normal	Normal		
45/M	13	O-R	Normal	T-O/R	O/R		
46/M	12	O-R	O/R	O/R	O/R		
47/M	4	Lat/R	Normal	Normal	F-P-T/R		
48/F	11	Lat/L	Not-loc	P-O/L	Not-loc		
49/F	15	P-R	P-T/R	P/R	P/R		
50/F	1	T-R	Normal	T/R	T/R		
51/F	6	F-P-R	F/R	F/R	F-P/R		
52/M	1	T-L	Not-loc	T/L	Not-loc		
53/M	9	F-L	Normal	F/L	F/L		
54/M	18	F-R	Normal	F/R	Normal		

*Engel evaluation at 6 mo.

F = frontal; R = right; MCD = malformation of cortical development; T = temporal; L = left; O = occipital; P = parietal; Not-loc = not-localizing study; VNS = vagus nerve stimulation; Lat = lateralizing study.

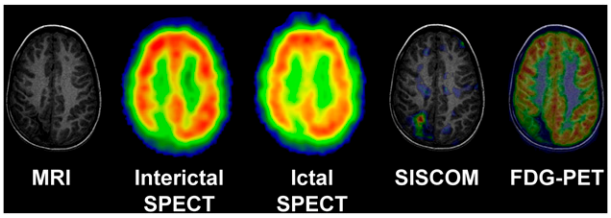

FIGURE 4. Multimodal neuroimaging studies of patient 8, a 9-y-old boy with drug-resistant complex partial seizures. MR imaging shows right parietal encephalomalacia, with concordant hypoactive zone in interictal SPECT and ^{18}F-FDG PET studies that were classified as not localizing. Ictal SPECT showed subtle hyperperfusion that was clearly depicted by SISCOM in area adjacent to malacia.

because they show only a hypometabolic area associated with the MR imaging–spotted lesion. Within this clinical context, a positive SISCOM finding concordant to PEZ can allow the option of surgical treatment to be considered.

Even though no significant difference was found between SISCOM and ^{18}F-FDG PET localizing-study proportions, the κ statistic showed only a moderate rate of concordance. This rate would suggest that the information provided by SISCOM and ^{18}F-FDG PET is not identical, making their contribution complementary. We agree with the explanation put forward by Carreño and Lüders (*22*) that SISCOM's capacity to demonstrate cerebral blood flow changes in the ictal state makes it a more suitable technique for defining the seizure-onset zone, whereas ^{18}F-FDG PET highlights the functional deficit zone.

If we consider only nonlesional MR imaging cases (26/54 [48%] of normal studies), SISCOM and ^{18}F-FDG PET showed equal sensitivity (13 [26%–50%]). As previously reported by our group and other authors (*14,17,23*), ^{18}F-FDG PET contribution is especially valuable in nonlesional MR imaging situations. In these particular cases, the information provided by SISCOM and ^{18}F-FDG PET can also be useful for guiding iEEG placement, minimizing the need for invasive studies, and reducing the craniotomy size of iEEG and the number of electrodes used (*11,17*).

Multimodal neuroimaging assessment in all 18 surgically intervened patients was deemed successful because their epileptic symptomatology was justifiable from histopathologic findings and also because 12 patients presented a favorable Engel outcome. It has already been shown that an incomplete resection of cortical dysplasia is the main predictor of poor postsurgical outcome (*24*). Of the 6 cases in which Engel outcome was unfavorable, 5 were due to incomplete resection and there was 1 case of new epileptogenic activity coming from a previously silent cortical tuber.

Although the number of patients undergoing resective surgery in this study is small, a favorable Engel outcome score is more likely in those cases when all techniques (video-EEG, MR imaging, SISCOM, and ^{18}F-FDG PET) exhibit concordant localizing-study results (8/10 [80%]).

This study holds some limitations; the use of a 3-T MR imaging unit could have improved MR imaging sensitivity. Moreover, our patient selection criteria may have led to an underestimation of MR imaging sensitivity, because those cases in which MR imaging was the only imaging study were not included. However, the use of MR imaging has never been questioned because not only does it establish the brain's anatomic structures for surgical planning, but also an MR imaging–identified lesion warrants surgical candidacy and predicts a favorable surgical outcome (*25–28*). The standard for EZ localization (PEZ) was defined as a result of video-EEG, clinical, and neuropsychologic data. Therefore, we agree that there is not enough evidence to consider PEZ as definitive and in some cases PEZ and EZ do not match. Nevertheless, the EZ is a theoretic concept that can be confirmed only after achieving postsurgical seizure freedom (*3*), hence, we consider PEZ as the strongest criterion available in the noninvasive presurgical evaluation of epileptic patients. This notion is supported because all intervened patients demonstrated histopathologic findings that justified the presence of epileptic symptomatology.

Consistent with the current literature in this field, our results suggest that nuclear medicine functional neuroimaging techniques can actively improve the decision-taking process in complex cases of pediatric epilepsy. Future work should focus on the elaboration of clinical guidelines that will contribute to a better use of multimodal neuroimaging procedures and the consequent optimization of evaluation for surgical candidacy.

It has been shown that long-term uncontrolled seizures can lead to progressive cognitive deterioration and brain atrophy (*29,30*) and that the longer the duration of epilepsy, the less likelihood of achieving a favorable long-term surgical outcome (*31,32*). Hence, any delay in surgical treatment should be reduced to a minimum. The use of radionuclide imaging is particularly useful in the pediatric population because of the complex nature of most cases and the limitations of the MR imaging (*5,7,33–35*). We believe that a multimodal neuroimaging approach should always be available in the assessment of pediatric drug-resistant epileptic patients.

CONCLUSION

SISCOM or ^{18}F-FDG PET assessment provided important complementary presurgical information that was concordant to the PEZ in three fourths of our sample. SISCOM was particularly useful in those cases in which MR imaging findings were abnormal but no epileptogenic lesion was identified. Even though the role of radionuclide imaging in adult epilepsy is mainly complementary, we believe that an accurate evaluation of drug-resistant epileptic pediatric patients should always consider SISCOM or ^{18}F-FDG PET evaluation. These techniques are useful and reliable tools that can extend the possibility of surgical treatment to patients who may have been considered untreatable with surgery without a nuclear medicine approach.

DISCLOSURE

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