

FDG-PET Images Quantified by Probabilistic Atlas of Brain and Surgical Prognosis of Temporal Lobe Epilepsy

*Sang Kun Lee, †Dong Soo Lee, †Jeong Seok Yeo, †Jae Sung Lee, *Yu Kyeong Kim,
*Myoung Jin Jang, *Kwang-Ki Kim, †Seok-Ki Kim, *Jong-Bai Oh, and ‡Chun-Kee Chung

Departments of *Neurology, †Nuclear Medicine, and ‡Neurosurgery, Seoul National University College of Medicine, Seoul, Korea

Summary: *Purpose:* This study evaluated the relation between hypometabolism, diagnosed by fluorodeoxyglucose positron emission tomography (FDG-PET), and the surgical outcome of a large and homogeneous series of cases of mesial temporal lobe epilepsy (mTLE), by using a probabilistic atlas of the human brain (statistical probabilistic anatomical maps: SPAM).

Methods: Ninety-five surgically proven intractable mTLE patients and 22 age-matched controls were spatially normalized to the average brain PET template of international consortium of brain mapping (ICBM). The diagnosis of mTLE was confirmed by the presence of hippocampal sclerosis on magnetic resonance imaging (MRI) and video-EEG monitoring. Counts from normalized PET images were multiplied by the probability from 98 volumes of interest (VOIs) of SPAM. Asymmetric indexes (AIs) reflecting the severity of hypometabolism were calculated by counts of selected 12 VOIs from SPAM images in both temporal lobes. Extent of hypometabolism was deter-

mined by the number of voxels showing decreased metabolism in each VOI segmented by SPAM.

Results: Of the 95 patients studied, 76 (80%) were seizure free, and 19 (20%) had postoperative seizures for the ≥ 2 -year follow-up period. No significant association between the severity of hypometabolism in each VOI of the temporal lobe and surgical outcome was identified ($p > 0.05$). The number of voxels showing decreased hypometabolism was not significantly different between the good- and poor-outcome groups ($p > 0.05$).

Conclusions: Our results demonstrated that focal severity and extent of hypometabolism quantified by a probabilistic atlas of brain were not related to the surgical outcome in mTLE patients who had hippocampal sclerosis on MRI. We should develop a more localized and specified anatomic map for mTLE for further results. **Key Words:** FDG-PET—Mesial temporal lobe epilepsy—Statistical probabilistic anatomic map (SPAM)—Surgery—Prognosis.

The role of [^{18}F] fluorodeoxyglucose-positron emission tomography (FDG-PET) is well established in the diagnosis of lateralization of a seizure focus in mesial temporal lobe epilepsy (mTLE). In the interictal state, the epileptogenic temporal lobe demonstrates decreased glucose metabolism in $\sim 80\%$ of these patients (1–4). Furthermore, recent studies suggest that FDG-PET may be a reliable indicator of clinical outcome after surgery (5–7). The presence of a hypometabolic temporal lobe is predictive of favorable surgical outcome in mTLE (1,6–9).

However, the presence of a specific focal hypometabolic region related to surgical outcome is still a controversial issue. Some studies have suggested that the asymmetry index of the mesial temporal lobe might be a

better predictor for a good outcome, although on average, the asymmetry index of the lateral temporal lobe is greater than that of the mesial temporal lobe (1,10). Other studies have found that uncus (8), lateral (5), anterolateral (9), or temporopolar regions (11) seem to correlate better with a good surgical outcome.

The visual assessment of FDG-PET is a widely used approach in clinical situations, but the results depend on the observers' experience (12). Sometimes objective data are needed to support subjective analysis in cases of subtly decreased metabolism. For that reason, methods of objective quantification have been developed. The use of regions of interest (ROIs) has been developed to quantify PET images. However, defining ROIs is not fully objective. The way in which ROIs are defined varies from one study to another, making data comparison very difficult. For example, results vary depending on ROI size. Other troublesome factors are variations in ROI shape from image to image because of intersubject variability and the proportion of gray matter sampled. More-

Accepted March 30, 2002.

Address correspondence and reprint requests to Dr. S. K. Lee at Department of Neurology, Seoul National University, College of Medicine, 28 Yeunkeun dong, Chongno gu, Seoul, Korea 110-744. E-mail: sangunlee@dreamwiz.com

over, the process is very time consuming when a large number of ROIs are involved.

To solve these problems, voxel-based approaches, such as statistical parametric mapping (SPM) have been introduced (13–15), and these methods facilitate the interpretation of PET brain images in a clinical setting. However, if we are interested in a specific anatomic area such as the hippocampus, another method is needed because SPM does not provide information about anatomic structure.

Recently many kinds of brain mapping methods have been developed, including automated registration and segmentation. One of these is statistical probabilistic anatomic mapping (SPAM) (16). This was designed to overcome cross-subject variations in brain structure, as a project of the International Consortium for Brain Mapping (ICBM). SPAM consists of 98 brain structures including multiple cortical gyri, white matter, cerebrospinal fluid, etc. Most of the studies that have used SPAM have been concerned with anatomic differences and volume measurements in magnetic resonance imaging (MRI) images, but application to functional images also has been suggested (17). We have already demonstrated the clinical usefulness of SPAM to support visual assessment of PET images in mTLE (18).

In this study, we applied SPAM to the PET images of patients with mTLE to evaluate the relation between the degree and extent of hypometabolism on FDG-PET and surgical outcomes in a large and homogeneous series of mTLE.

METHODS

Patients and controls

Ninety-five consecutive patients of intractable mTLE (62 male, 33 female; mean age, 27.6 ± 16.8 years) were included in this study. They underwent FDG-PET and anterior temporal lobectomy between 1995 and 1998. Presurgical evaluation included MRI to evaluate structural lesions and hippocampal sclerosis (19), video-electroencephalographic (EEG) monitoring, FDG-PET scans, interictal and ictal single-photon emission computed tomography (SPECT) if possible, neuropsychological evaluation, and the intracarotid amobarbital procedure. Patients were diagnosed with mTLE in this study if (a) a definite unilateral hippocampal sclerosis

showed on the brain MRI, and (b) the anterior temporal ictal onset was identified during video-EEG monitoring or if an invasive study with intracranial electrodes confirmed a mesial temporal onset. As a result, all patients had a definite hippocampal sclerosis diagnosed on MRI. Patients with space-occupying lesions identified by MRI were excluded. Patients with bitemporal independent ictal onsets confirmed by invasive study also were excluded.

Twenty-two healthy volunteers underwent FDG-PET as a control group. They were of mean age 28 ± 9 years. Sixteen were men, and six were women. None of the subjects had any history of neurologic or psychological disease, and they were not taking any drugs known to affect PET studies. Informed consent was obtained from each volunteer after each was given an explanation about the purpose and procedures of this study. The average asymmetry index of 21 controls for total temporal lobe was 1.66 ± 2.77 (Table 1). The procedure was approved by IRB of Seoul National University Hospital.

Surgical outcome

All patients had been followed up for ≥ 2 years after surgery. Patients were categorized as either free of disabling seizure (Engel class I; good outcome) (20) or not (poor outcome).

PET imaging

For those subjects undergoing PET, 370 MBq (10 mCi) of [^{18}F]FDG was injected intravenously, with the patients' eyes open and the room lights dimmed. Images were acquired ~ 30 min after tracer injection, by using a CTI ECAT Exact 47 PET camera (Siemens, Knoxville, TN, U.S.A.). After taking a transmission scan for 5 min with a Ge-68 rod source, the emission scan was performed for 25 min in two-dimensional mode.

Emission scan images were reconstructed by using a back-projection method with a Shepp-Logan filter (cut-off frequency of 0.35), and the attenuation effects were corrected with transmission images. The resolution [full width, half maximum (FWHM)] of the PET camera was $6.2 \times 6.2 \times 4.3$ mm, and the dimension of the image matrix was 128×128 pixels.

Registration of PET images with SPAM

We applied the statistical probabilistic anatomic map (SPAM) images of ICBM to calculate the PET counts

TABLE 1. Asymmetry index (%) of controls

	Total T	Med T	Lat T	Amy	HF	Phg	STg	MTg	ITg
Avg	1.66	-1.27	2.41	-3.08	-2.80	-0.56	1.39	0.65	1.04
SD	2.77	3.03	3.01	6.36	4.03	3.18	3.44	3.04	5.69

AI was calculated by the equation $(Rt - Lt)/(Rt + Lt) \times 200$.

T, temporal lobe; Med, medial; Lat, lateral; Amy, amygdala; HF, hippocampal formation; Phg, parahippocampal gyrus; STg, superior temporal gyrus; MTg, middle temporal gyrus; ITg, inferior temporal gyrus; Avg, average; SD, standard deviation; AI, asymmetry index.

objectively (Fig. 1). SPAM consists of 98 volumes of interest (VOIs) images including bilateral cortical gyri, and each image consists of the probability from 0 to 1 that it belongs to a specific region.

FDG-PET images were count- and spatially normalized by using a 12-parameter affine (linear) transformation to the ICBM PET template provided in SPM99 software (Wellcome Department of Cognitive Neurology, London, U.K.). The counts from normalized PET images were multiplied by the probability from 98 VOIs of SPAM by using a program developed with Matlab (Mathworks Inc., Natick, MA, U.S.A.). The template we used in this study was an average of MRI images from 152 young normal volunteers of the ICBM. With this multiplication of normalized PET and SPAM, the probability-weighted counts were obtained for all VOIs. As a result, 98 VOIs, including bilateral cortical gyri segmented by SPAM, were overlaid on the patient's spatially normalized PET.

Computing time

It took <10 min for each subject to normalize PET images by using SPM99b with an IBM-compatible personal computer (Pentium III 600-MHz CPU and 128-Mb memory). Probability-weighted counts were calculated by using the MATLAB program in batches for multiple subjects, and calculation took <1 min per subject.

Severity of hypometabolism: calculation of asymmetric indexes

We selected six pairs of VOIs to represent the temporal lobe. These consisted of the superior temporal gyrus,

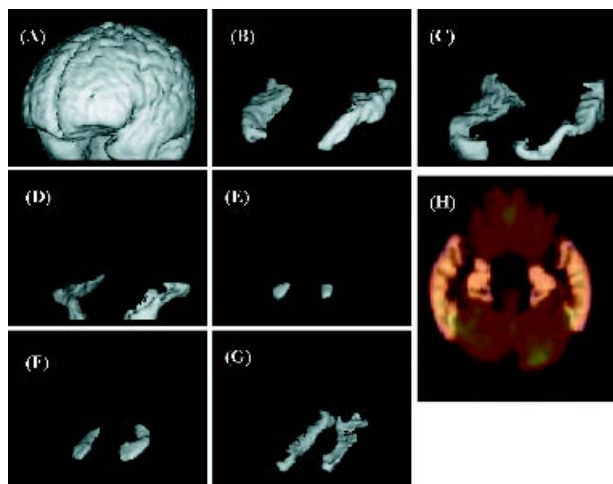


FIG. 1. The volume of interest (VOI) for each anatomic structure was defined by using statistical probabilistic anatomic map (SPAM) images of the International Consortium for Brain Mapping (ICBM), which is defined on an ICBM standard template and consists of the probability, from zero to one, that it belongs to a specific region: (A) whole brain, (B) superior temporal, (C) middle temporal, (D) inferior temporal, (E) amygdala, (F) hippocampus, (G) parahippocampal gyrus. H: Overlaid SPAM of the temporal lobe on the patient's spatially normalized positron emission tomography scan.

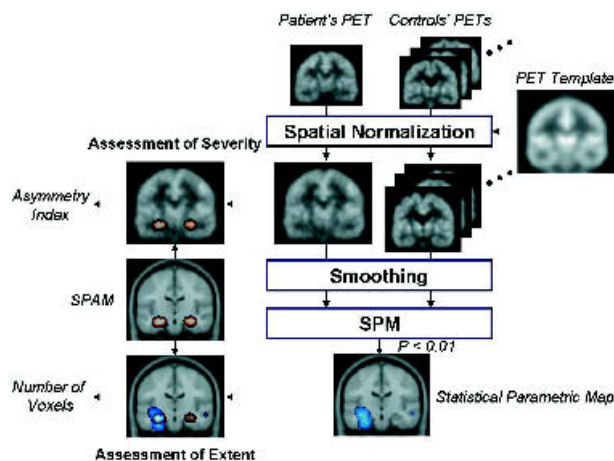


FIG. 2. Assessment of severity and extent of hypometabolism. Asymmetric indexes were calculated on six pairs of volumes of interest (VOIs) to represent the temporal lobe. Significant decrease of regional metabolism was estimated by comparing the positron emission tomography images with those of controls by using statistical parametric mapping. The extent of hypometabolic area for each VOI was determined by counting the number of voxels with significantly decreased hypometabolism in each VOI segmented by SPAM.

middle temporal gyrus, inferior temporal gyrus, hippocampus, parahippocampal gyrus, and the amygdala in each hemisphere (Figs. 1 and 2). The counts from normalized PET images were multiplied by the probability from these selected six pairs of VOIs of SPAM to assess the severity of hypometabolism. Asymmetric indexes (AIa) were calculated by using the equation $(C - I) \times 200 (\%) / (C + I)$ where C and I are mean counts of contralateral and ipsilateral VOIs to the resected temporal lobe, respectively.

When the VOI contralateral to the resected temporal lobe was hypometabolic, AI had a negative value, and when AI was positive, the resected temporal lobe was hypometabolic.

We calculated means and standard deviations (SD) of AIs in each pair of VOIs. Student's *t* test was applied to test the relation between AI of each VOI and the surgical outcome. P values <0.05 were considered significant.

Extent of hypometabolism determined by SPM and SPAM

The differences between [^{18}F]-FDG-PET scans of each patient and those of the controls were statistically analyzed by using SPM 99 software (Institute of Neurology, University College of London, U.K.; Fig. 2). Before statistical analysis, all the images were spatially normalized into the ICBM standard template (see the registration of PET images with SPAM). Subtle differences between the transformed image and the template were removed by the nonlinear registration method, by using the weighted sum of the predefined smooth basis function used in discrete cosine transformation. Spatially

normalized images were then smoothed by convolution with an isotropic gaussian kernel with 16-mm FWHM. The effect of global difference was removed by normalizing the count of each voxel to the global count of the cortical area (proportional scaling in SPM 99). A significant decrease of regional metabolism was estimated by comparing their PET images with those of controls by using T statistics for each voxel (Fig. 2). The voxels with p values <0.01 were considered to have significant difference, and parametric images of T values for significant voxels were composed for further analysis.

A VOI for each anatomic structure was defined by SPAM. Voxels with probability >0.5 were included in each VOI. The extent of the hypometabolic area for each VOI was determined by counting the number of voxels with significantly decreased hypometabolism in each VOI segmented by SPAM. We compared the number of significant voxels in VOIs of frontal, temporal, parieto-occipital, and thalamic areas between the good and the poor surgical-outcome groups. Volume of each voxel was 8 mm³ (2 × 2 × 2 mm).

Comparison with visual analysis

We compared the results of SPAM with those of visual analysis. Two observers (D.S.L. and Y.K.K.) graded subjectively the metabolic abnormalities in both temporal lobes on FDG-PET in a blinded fashion (grades 0–4). The hypometabolism of the ipsilateral temporal regions was graded considering extent and severity. The higher grade means more severe hypometabolism on the unilateral temporal lobe. Grade 0 means no asymmetric metabolism. The agreement between two observers was calculated. We also evaluated the correlation between visual grading and AI in the SPAM method.

RESULTS

Of the 95 patients studied, 76 (80%) were seizure free, and 19 (20%) had postoperative seizures at the 2-year follow-up evaluation. Figure 3 shows the AIs of six VOIs of the temporal lobe and the whole temporal lobe in the group of patients who became seizure free and the group of patients who did not become seizure free.

No significant association between the severity of hypometabolism of each location (six VOIs of each temporal lobe and the whole temporal lobe) and surgical outcome could be identified ($p > 0.05$). We also compared the clinical outcome with the range of AIs of controls (Table 1). If the AI in each pair of VOIs was within 2 SD of normal controls, we assumed the AI as normal. The clinical outcome was not different between the patients with AI of normal range and those with AI outside this range ($p > 0.05$). There also was no correlation between clinical outcome and the AIs outside this normal range ($p > 0.05$).

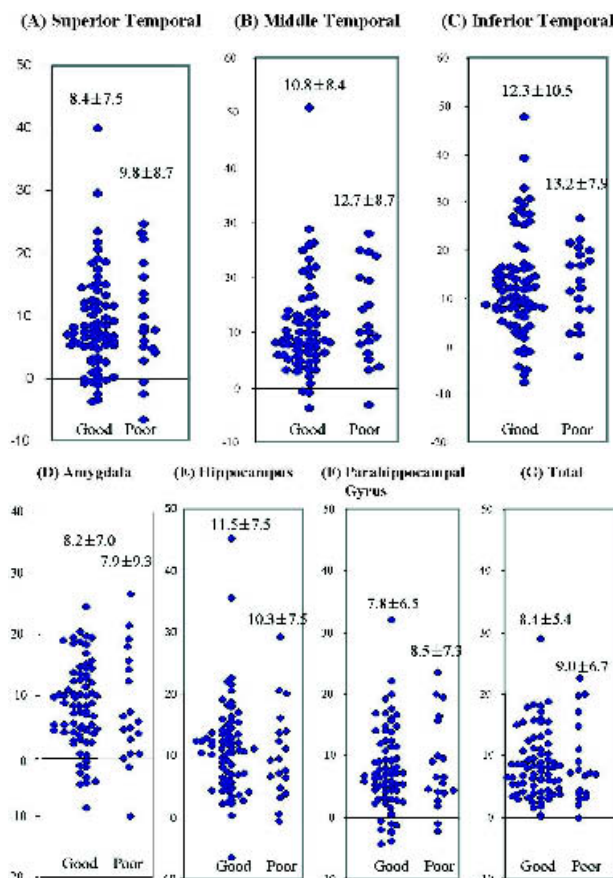


FIG. 3. Asymmetry indexes (AIs) of six volumes of interest (VOIs) of temporal lobe and the whole temporal lobe in the group of patients who became seizure free (good) and the group of patients who did not become seizure free (poor). When the VOI contralateral to the resected temporal lobe was hypometabolic, the AI had a negative value, and when the AI was positive, the resected temporal lobe was hypometabolic. Parentheses are the means ± standard deviations.

There was no difference in the number of voxels with significantly decreased hypometabolism in each lobe determined by SPM and SPAM between the good and the poor surgical-outcome groups ($p > 0.05$; Table 2).

The visual grading and AI with the SPAM methods were significantly correlated ($p < 0.0001$, Table 3). The agreement between two observers (Y.K.K. and D.S.L.) was good (weighted kappa score = 0.535; Table 4). There was no correlation between clinical outcome and the degree of hypometabolism by visual analysis ($p > 0.05$; Table 5).

DISCUSSION

We applied SPAM to the PET images of patients with mTLE to evaluate the relation between degree and extent of hypometabolism on FDG-PET and surgical outcome in a large and homogeneous series of mTLE. Identifying ROIs on two-dimensional slices of PET images has been

TABLE 2. Extent of hypometabolic area and surgical outcome

	Temporal		Frontal		Parietooccipital		Thalamus	
	Ipsilateral	Contralateral	Ipsilateral	Contralateral	Ipsilateral	Contralateral	Ipsilateral	Contralateral
Good	2,536 ± 1,741	470 ± 629	1,223 ± 1,343	525 ± 744	1,297 ± 1,785	344 ± 1,066	1,223 ± 1,343	525 ± 744
Poor	2,415 ± 2,075	223 ± 340	1,992 ± 2,716	603 ± 1,198	1,583 ± 1,807	201 ± 472	244 ± 353	60 ± 150

Differences between the 18F FDG-PET scans of each patient and those of the controls were statistically analyzed using SPM 99 software. The extent of the hypometabolic area for each VOI was determined by counting the number of voxels with significantly decreased hypometabolism in each VOI segmented by SPAM. The numbers of significant voxels in VOIs of frontal, temporal, parietooccipital, and thalamic areas were compared between the good and the poor surgical-outcome groups.

Data are expressed as means ± standard deviations. Temporal VOIs include hippocampal formation, amygdala, parahippocampal gyrus, inferior temporal gyrus, middle temporal gyrus, and superior temporal gyrus. Frontal VOIs include superior frontal gyrus, middle frontal gyrus, inferior frontal gyrus, lateral frontoorbital gyrus, medial frontoorbital gyrus, medial frontal gyrus, precentral gyrus, and insula. Parietooccipital VOIs include postcentral gyrus, angular gyrus, supramarginal gyrus, superior parietal lobule, precuneus, occipital pole, inferior occipital gyrus, middle occipital gyrus, superior occipital gyrus, lingual gyrus, lateral occipitotemporal gyrus, and medial occipitotemporal gyrus.

Ipsilateral, ipsilateral to the epileptogenic temporal lobe; contralateral, contralateral to the epileptogenic temporal lobe; VOI, volume of interest.

used to quantify metabolic activity and to support visual assessment (21). The AI, defined by comparing counts of regions with their contralateral counterparts, was found to be the most sensitive marker of hypometabolism in patients with TLE (22). However, reporting techniques based on ROI analysis also vary according to observers: it is not fully objective and is time consuming. To overcome this shortcoming, a variety of observer-independent analysis methods have been studied, including SPM and three-dimensional stereotactic surface projections (12). SPM is now widely used for analyzing functional brain images and has been applied to FDG-PET (13), especially for cases of TLE (14). This approach reduced observer variability, but the methods were still not fully objective because they lacked information about anatomic structures. Observers must determine where the area of decreased metabolism belongs. This is particularly difficult when the areas concerned are on small structures. SPAM can give us this anatomic information by automated registration and segmentation of brain structures.

During SPM processing, data from small structures are blurred by a partial volume effect combined with a smoothing process, which is capable of downgrading significant values to be insignificant. Conversely, SPAM methods have a problem when the ROI is too large. We used predefined VOIs for the temporal lobe such as su-

perior, middle, and inferior temporal gyri. They covered the area of the temporal lobe from anterior to posterior sections. Small deficits only in the anterior temporal pole could be masked because of an averaging effect by the normal counts of the posterior section. We should develop a specific VOI of the anterior temporal lobe to ascertain small deficits confined to that lobe.

We found no significant association between the severity of hypometabolism of six VOIs in the temporal lobe or extent of hypometabolism and surgical outcome, although FDG-PET provides an excellent localizing technique. Several studies have shown that the presence of a hypometabolic temporal area is predictive of favorable postsurgical outcome for seizure control (1,6–9). Furthermore, postoperative seizure outcome is improved in those patients with hypometabolism restricted to the temporal lobe (8). Patients with extratemporal hypometabolism tend to have a higher likelihood of postoperative seizure activity (6,8,23). However, two others series (24,25), examining the correlation between PET images and seizure control after temporal lobectomy, showed no difference in seizure control and the presence of PET abnormalities.

The prognostic value of the exact location of the hypometabolism within the temporal lobe is still being debated. Some data also suggest that patients with mesial temporal hypometabolism on PET have a higher prob-

TABLE 3. Correlation between visual grading and AI in SPAM methods

VOIs of SPAM	Correlation between AI and visual grading			
	DSL		YKK	
	rho	p Value	rho	p Value
Total temporal lobe	0.480	0.000	0.483	0.000
Medial temporal structure	0.421	0.000	0.473	0.000
Lateral temporal structure	0.498	0.000	0.518	0.000

The ASI of the SPAM method and the hypometabolic grading by visual analysis were significantly correlated ($p < 0.0001$, Spearman's two-tailed correlation test).

VOI, volume of interest; AI, asymmetric index; rho, Spearman rank correlation coefficient; DSL, Dong Soo Lee; YKK, Yu Keong Kim; SPAM, statistical parametric anatomic map.

TABLE 4. *The agreement between two observers was good*

	Gr 0	Gr 1	Gr 2	Gr 3	Gr 4	Total
Gr 0	0	2	3	0	0	5
Gr 1	2	17	5	0	1	25
Gr 2	0	5	10	6	1	22
Gr 3	0	2	3	9	2	16
Gr 4	0	0	3	6	9	18
Total	2	26	24	21	13	86

Weighted kappa score was 0.5353 (95% CI, 0.4168 ~ 0.6538).
G, grade; CI, confidence interval.

ability of becoming seizure free postoperatively than do patients with hypometabolism in other parts of the temporal lobe (1,8). However, other studies have indicated that lateral temporal lobe (5,26) or temporal pole hypometabolism (11) are better predictors of a seizure-free postoperative course. The results of our study differ from these previous reports in part because our series consisted of a large and homogeneous group of mTLE with strict criteria. All patients had definite hippocampal atrophy on MRI. Most previous studies included patients who had different etiologies, such as mesial sclerosis, tumor, dysplasia, or even no pathologic diagnosis (7,9), or who only underwent temporal resection (1,5,26). Such a mixture of etiologies with different prognoses may have resulted in heterogeneous patterns in PET images. This may also explain the controversial results of previous studies.

The presence of PET hypometabolism in patients with complex partial seizures of temporal origin usually reflects underlying temporal lobe focal gliosis and neuronal loss (25,27). The severity and anatomic distribution of neuronal loss is poorly correlated with the degree and spatial extent of PET hypometabolism (25,27,28). In patients with a mesial temporal lobe focus on EEG, hypometabolism ipsilateral to the seizure focus occurs more frequently and to a greater degree in the lateral than in the mesial temporal cortex (10). Hypometabolism in the lateral temporal region cannot be taken as evidence for an epileptogenic focus in the lateral neocortex. Other studies have found multiple areas of hypometabolism within and outside the temporal lobe (6,7,29). The cause of this hypometabolism remains controversial. Hypometabolism other than at the seizure focus may be due to physiologic dysfunction in regions functionally associated with the mesial temporal lobe, rather than cell loss in these regions (10,29). Henry et al. (28) found no cor-

relation between hypometabolism in any cortical region and the degree of hippocampal cell loss on pathology. Diaschisis due to cell loss alone cannot account for these findings. It might also represent the structural abnormalities that are below the resolution of routine structural histopathologic studies (30). Lateral temporal hypometabolism may also be due to repeated seizures spreading to the temporal neocortex (31). Alterations in synaptic organization due to repeated seizures rather than neuronal loss, which can occur in experimentally kindled animals, could underlie metabolic changes (32). One study, comparing preoperative and postoperative glucose consumption in mesiobasal and lateral temporal lobe epilepsy, demonstrated marked increases in the regional cerebral metabolic rate of glucose, both in the ipsilateral and—significantly—in the contralateral hemisphere. Moreover, there was a trend toward a normalization of glucose metabolism in the ipsilateral temporal neocortex in patients with mTLE (33). Another study showed that patients who became seizure free after removal of a vascular malformation also had a significant regional increase of FDG uptake (34). If hypometabolism other than the epileptogenic focus might be due to physiologic dysfunction in regions associated with the mesial temporal lobe or to seizure spread, the hypometabolic areas in mTLE would not be an important indicator for prediction of surgical outcome, although they can correctly lateralize the seizure focus in a high proportion. Our results are consistent with this hypothesis. However, the predictive value of FDG-PET regarding surgical outcome in TLE still has clinical implications. In our study, we recruited a homogeneous series of mTLE cases. However, in some clinical settings of TLE, FDG-PET imaging can be useful as a screening procedure in presurgical evaluation to assess the localization of seizure focus and surgical outcome. There are patients with electrophysiologic localization of seizure onset to one temporal lobe, but without any accompanying definite hippocampal sclerosis on MRI. All the previous results are applicable to these patients. FDG-PET also can provide valuable data in patients with nonlocalized surface ictal EEGs. Theodore et al. (31) showed a close association between invasive EEG and PET localization.

We applied only one surgical technique on all patients (e.g., standard anterior temporal lobectomy with amygdalohippocampectomy). We resected 3.5 cm of lateral

TABLE 5. *Correlation between clinical outcome and the results of visual analysis*

	Parameter estimate	Standard error	Wald χ^2	Pr > χ^2	Adjusted OR (95% CI)
Visual DSL	-0.0425	0.2017	0.0443	0.8333	0.958 (0.645 ~ 1.423)
Visual YKK	0.0822	0.2171	0.1435	0.7048	1.086 (0.709 ~ 1.662)

There was no correlation between the clinical outcome and hypometabolic grading by visual analysis.
Pr, probability; OR, odds ratio; CI, confidence interval.

temporal cortex from the temporal tip for the left TLE and 4.5 cm of lateral temporal lobe for the right TLE. The surgical outcome is not significantly correlated with the laterality. Furthermore, the distribution of right and left TLE patients was not significantly different between the good- and the poor-outcome groups. However, there are some limitations in our study. We did not see specific hypometabolic patterns. Even though there is no focal hypometabolic area that can predict surgical outcome, certain specific combinations of hypometabolic areas may mean that different seizure foci and pathogenesis may be related with poor surgical outcome.

Our results demonstrated that focal severity and extent of hypometabolism quantified by a probabilistic atlas of brain were not related to the surgical outcome in mTLE patients who had hippocampal sclerosis on MRI. SPAM is useful for the quantification of VOIs in the PET data of patients with mTLE. We should develop a more localized and specific anatomic map for mTLE to improve results.

Acknowledgment: We deeply appreciate the support and collaboration of Dr. Alan Evans, who provided SPAM data from Montreal Neurological Institute.

REFERENCES

1. Delbeke D, Lawrence SK, Abou-Khalil BW, et al. Postsurgical outcome of patients with uncontrolled complex partial seizures and temporal lobe hypometabolism on ^{18}F FDG-positron emission tomography. *Invest Radiol* 1996;31:261–6.
2. Engel J, Kuhl DE, Phelps ME, et al. Comparative localization of epileptic foci in partial epilepsy by PCT and EEG. *Ann Neurol* 1982;12:529–37.
3. Theodore WH, Newmark ME, Sato S, et al. ^{18}F -fluorodeoxyglucose positron emission tomography in refractory complex partial seizures. *Ann Neurol* 1984;14:429–37.
4. Abou-Khalil BW, Siegel GJ, Sackellares JC, et al. Positron emission tomography studies of cerebral glucose metabolism in chronic partial epilepsy. *Ann Neurol* 1987;22:480–6.
5. Theodore WH, Sato S, Kufta C, et al. Temporal lobectomy for uncontrolled seizure: the role of positron emission tomography. *Ann Neurol* 1992;32:789–94.
6. Swartz BE, Tomiyasu U, Delgado-Escueta AV, et al. Neuroimaging in temporal lobe epilepsy: test sensitivity and relationships to pathology and postoperative outcome. *Epilepsia* 1992;33:624–34.
7. Radtke RA, Hanson MW, Hoffman JM, et al. Temporal lobe hypometabolism on PET: predictor of seizure control after temporal lobectomy. *Neurology* 1993;43:1088–92.
8. Manno EM, Sperling MR, Ding X, et al. Predictors of outcome after anterior temporal lobectomy: positron emission tomography. *Neurology* 1994;44:2331–6.
9. Wong CYO, Geller EB, Chen EQ, et al. Outcome of temporal lobe epilepsy surgery predicted by statistical parametric PET imaging. *J Nucl Med* 1996;37:1094–100.
10. Sackellares JC, Siegel GJ, Abou-Khalil BW, et al. Differences between lateral and mesial metabolism interictally in epilepsy of mesial temporal origin. *Neurology* 1990;40:1420–6.
11. Dupont S, Semah F, Clemenceau S, et al. Accurate prediction of postsurgical outcome in mesial temporal lobe epilepsy. *Arch Neurol* 2000;57:1331–6.
12. Drzezga A, Arnold S, Minoshima S, et al. ^{18}F -FDG PET studies in patients with extratemporal and temporal epilepsy: evaluation of an observer-independent analysis. *J Nucl Med* 1999;40:737–46.
13. Signorini M, Paulesu E, Friston K, et al. Rapid assessment of regional cerebral metabolic abnormalities in single subjects with quantitative and nonquantitative [^{18}F]FDG PET: A clinical validation of statistical parametric mapping. *Neuroimage* 1999;9:63–80.
14. Swartz BE, Thomas K, Simpkins F, et al. Rapid quantitative analysis of individual ^{18}F FDG-PET scans. *Clin Positron Imaging* 1999;2:47–56.
15. Van Bogaert P, Massager N, Tugendhaft P, et al. Statistical parametric mapping of regional glucose metabolism in mesial temporal lobe epilepsy. *Neuroimage* 2000;12:129–38.
16. Mazziotta JC, Toga AW, Evans A, et al. A probabilistic atlas of the human brain: theory and rationale for its development: The International Consortium for Brain Mapping (ICBM). *Neuroimage* 1995;2:89–101.
17. Penhune VB, Zatorre RJ, MacDonald JD, et al. Interhemispheric anatomical differences in human primary auditory cortex: probabilistic mapping and volume measurement from magnetic resonance scans. *Cereb Cortex* 1996;6:661–72.
18. Kang KW, Lee DS, Cho JH, et al. Quantification of F-18 FDG-PET images in temporal lobe epilepsy patients using probabilistic brain atlas. *Neuroimage* 2001;14:1–6.
19. Jack CR. Epilepsy: surgery and imaging. *Radiology* 1993;189:635–46.
20. Engel J Jr, Van Ness PC, Rasmussen TB, et al. Outcome with respect to epileptic seizures. In: Engel J Jr, ed. *Surgical treatment of the epilepsies*. 2nd ed. New York: Raven Press, 1993:609–21.
21. Henry TR, Mazziotta JC, Engel J Jr, et al. Quantifying interictal metabolic activity in human temporal lobe epilepsy. *J Cereb Blood Flow Metab* 1990;10:748–57.
22. Theodore WH, Fishbein D, Dubinsky R. Patterns of cerebral glucose metabolism in patients with partial seizures. *Neurology* 1998;38:1201–6.
23. Blum DE, Ehsan T, Dungan D, et al. Bilateral temporal hypometabolism in epilepsy. *Epilepsia* 1998;39:651–9.
24. Engel J Jr, Babb TL, Phelps ME. Contributions of positron emission tomography to understanding mechanisms of epilepsy. In: Engel J Jr, Ojemann GA, Luiders HO, et al., eds. *Functional mechanisms of human brain function*. New York: Raven Press, 1987:209–18.
25. Theodore WH, Katz D, Kufta C, et al. Pathology of temporal lobe foci: correlation with CT, MRI, and PET. *Neurology* 1990;40:797–803.
26. Newberg AB, Alavi A, Berlin J, et al. Ipsilateral and contralateral thalamic hypometabolism as a predictor of outcome after temporal lobectomy for seizures. *J Nucl Med* 2000;41:1964–8.
27. Engel J Jr, Brown WJ, Kuhl DE, et al. Pathological findings underlying focal temporal lobe hypometabolism in partial epilepsy. *Ann Neurol* 1982;12:518–29.
28. Henry TR, Babb TL, Engel J Jr, et al. Hippocampal neuronal loss and regional hypometabolism in temporal lobe epilepsy. *Ann Neurol* 1994;36:925–7.
29. Henry TR, Mazziotta JC, Engel J Jr. Interictal metabolic anatomy of mesial temporal lobe epilepsy. *Arch Neurol* 1993;50:582–9.
30. Friston KJ. Statistical parametric mapping: ontology and current issues. *J Cereb Blood Flow Metab* 1995;15:361–70.
31. Theodore WH, Sato S, Kufta CV, et al. FDG-positron emission tomography and invasive EEG: seizure focus detection and surgical outcome. *Epilepsia* 1997;38:81–6.
32. Sloviter RS. The functional organization of the hippocampus dentate gyrus and its relevance to the pathogenesis of temporal lobe epilepsy. *Ann Neurol* 1994;35:640–54.
33. Hajek M, Wieser HG, Khan N, et al. Preoperative and postoperative glucose consumption in mesiobasal and lateral temporal lobe epilepsy. *Neurology* 1994;44:2125–32.
34. Dasheiff RM, Rosenbeck J, Matthews C, et al. Epilepsy surgery improves regional glucose metabolism on PET scan. *J Neurol* 1987;234:283–8.