

EPIRES 00436

## Interictal cerebral metabolism in partial epilepsies of neocortical origin

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(Received 31 July 1991; revision received 4 September 1991; accepted 4 September 1991)

*Key words:* Partial epilepsy; Neocortex; Cerebral metabolism

We performed interictal [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography (FDG PET) in 24 patients with partial epilepsy of neocortical origin. Two-thirds of patients had regions of hypometabolism. The zone of intracranially recorded electrographic ictal onset was always located in a region of hypometabolism, in those with hypometabolism. Hypometabolic regions in partial epilepsies of neocortical origin were usually associated with structural imaging abnormalities. Regional hypometabolism occasionally occurred without localizing ictal scalp EEG and cerebral magnetic resonance imaging findings, however. FDG PET may be useful in directing placement of intracranial electrodes for presurgical evaluation of refractory neocortical seizures.

### INTRODUCTION

The epileptogenic zone in partial epilepsies of adults and older children often can be localized to limbic (histologically allocortical-juxtallocortical) or neocortical structures<sup>2</sup>. Interictal [<sup>18</sup>F]fluorodeoxyglucose (FDG) positron emission tomography (PET) demonstrates typical patterns of interictal hypometabolism in mesial (limbic) temporal lobe epilepsy<sup>1,3,5,6,8–10,14,19,21,25–28,31</sup>. These interic-

tal metabolic patterns of mesial temporal lobe epilepsy have proved useful in lateralizing and localizing epileptogenic zones for surgical treatment of refractory complex partial seizures<sup>4</sup>. Regional patterns of interictal metabolism in partial epilepsies of neocortical origin have not been fully described nor established as useful in presurgical evaluation. We report a series of interictal FDG PET studies in patients whose refractory partial seizures originated in neocortical structures, based on intracranial electrophysiologic ictal recording and on marked decrease in seizure frequency after these structures were resected. We also assess PET in presurgical evaluation by comparing regional metabolic abnormalities with intracranial electrophy-

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siologic ictal localization and with results of other means of localizing the epileptogenic zone.

## METHODS

### *Selection and clinical characteristics of subjects*

All 156 adults with intracranial electrophysiologic (depth electrode or subdural grid array) monitoring at UCLA, during the period from 1979 to 1989, were considered for inclusion in this study. Subjects were included if (1) intracranial electrographic ictal onsets were localized to a neocortical area, (2) technically adequate interictal cerebral FDG PET was performed before any neurosurgical procedure (including intracranial electrode placement) with no evidence of cranial malpositioning (lateral head tilt) during scanning, and (3) technically adequate cranial X-ray computed tomography (XCT) or magnetic resonance imaging (MRI) was performed pre-operatively. Subject identification numbers were assigned by site of intracranial electrographic ictal onset (see complete list under METHODS: Analysis of Correlative Data).

Twenty-four subjects (14 women and 10 men) were included in this study. Average age at FDG PET was 28 years (with a range of 17–43 years). Average duration of epilepsy prior to FDG PET was 14 years (with a range of 1–26 years). Subjects had normal neurologic examinations, except that subject F3 had mild right arm and leg hyperreflexia, subject F10 had mild left pedal hypoplasia and mild left pedal dorsiflexor weakness, subject T2 had mild hyponomia and mild right central facial paresis, subject T7 remembered 2 of 4 phrases after 5 min, subjects O1 and O2 had mild hyponomia, subject O3 had right homonymous hemianopia, and subject O5 had right superior quadrant-anopia.

Subjects underwent corticectomy or anterior temporal lobectomy with resection of the site of intracranial electrographic ictal onset, except for subjects T8 and O1, both of whom had no resection due to intracranial electrographic ictal onset at apparent language (comprehension)-committed sites. Resected tissue included neocortical lesions in 14 subjects, with 1 glial neoplasm, 5 arteriovenous malformations, 3 glial or neuroglial

hamartomata, and 5 focal gliotic and encephalomalacic lesions. No histopathologic abnormalities were found with multiple stains for light microscopy in 6 intact surgical specimens. No final pathologic diagnosis was rendered for 2 damaged specimens. Each subject who underwent resection had greater than 80% reduction in seizure frequency postoperatively (through the time of writing, a period of 1–10 years across the group, averaging 3.5 years of follow-up).

### *Fluorodeoxyglucose PET procedure*

FDG PET studies were performed with the deoxyglucose method<sup>18</sup>. Three tomographic instruments were used for imaging in the cerebral axial plane: (1) ECAT scanner (Ortec, Knoxville, TN), with spatial resolution of approximately 13 mm in plane and 19 mm axially (full width at half maximum)<sup>17</sup>, for subjects F4, F11, O1, O3 and O4; (2) NeuroECAT scanner (CTI-Siemens, Knoxville, TN), with resolution of approximately 9 mm in plane and 11 mm axially<sup>11</sup>, for subjects F1, F2, F3, F5, F6, F7, F8, T3, T4, T6, T7, T8 and O2; and (3) CTI-831 scanner (CTI-Siemens, Knoxville, TN), with resolution of approximately 6 mm in plane and 7 mm axially (unpublished results), for subjects F9, F10, T1, T2, T5, and O5. Scans were performed under resting ambient conditions<sup>16</sup> in wakefulness. Interictal state during scanning was documented by observation and continuous scalp EEG for 30 min before and 60 min after FDG injection. Attenuation correction was performed by the geometric method.

### *Analysis of FDG PET images*

Two investigators (T.R.H. and J.E. Jr.) examined each interictal FDG PET scan independently. Neocortical epilepsy patients' scans were intermixed with those of 15 normal adult volunteers and of 180 adult mesial temporal lobe epilepsy patients. Investigators were unaware of the identity of each scan's subject. Study scans were compared with 10 normal FDG scans. Replicable metabolic landmarks defined boundaries of 10 large metabolic divisions (frontal, lateral temporal, mesial temporal, parietal, occipital, cingulate, basal ganglial, thalamic, cerebellar and brainstem areas), outlined on a normal template scan. Local decreases

in activity on images were rated as hypometabolism if (1) the local hypointensity was seen on adjacent areas of more than one image plane and (2) local intensity was unequivocally decreased, on comparison of intensity relationships between this area and other areas of that scan with intensity relationships among relevant areas of scans of normal subjects. (The investigators did not find hypermetabolism on any scans.) The location and sharpness of demarcation from adjacent eumetabolic areas were specified for each hypometabolic area; where hypometabolic areas extended across more than one metabolic division, the division(s) with the most severe hypometabolism were noted.

Replicability of independent, blind FDG scan evaluations between investigators was assessed by  $\kappa$  correlation<sup>13</sup>. Any disagreements were settled in favor of the clinical interpretation of the Laboratory of Nuclear Medicine; in most cases the clinical interpretation had been performed by one of the authors (J.C.M.), who was aware that the scans were performed on epilepsy patients, but unaware of details of the epilepsy during interpretation. Linear dimensions, within and across image planes, of agreed hypometabolic regions were estimated from known pixel-and-object-size relationships and interplanar spacing. Summarized findings of 5 of these FDG scans (those of subjects F4, F5, O1, O3 and O4) have been included in a published series with different selection criteria<sup>4</sup>; the other 19 FDG scans have not been previously reported.

#### *Analysis of correlative data*

Ictal semiologic data were derived by chart review of epileptologists' histories (for patients' subjective ictal phenomena) and reports of intensive monitoring at UCLA (for patients' ictal behaviors during intensive monitoring). The initial and subsequent subjective or objective semiologic manifestations of each subject's habitual seizure type were classified with criteria proposed by the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE)<sup>2</sup>. The ILAE Classification recommends use of only the first ictal manifestation for localization of the ictal onset zone; the localization(s) related to the first manifestation for each subject were con-

sidered 'initial'. Any additional localizations related to other manifestations occurring later during simple partial seizures were considered 'early'. Several subjects had peculiar and stereotyped feelings that could not be further described, at the onset of simple partial seizures; one subject (T6) had no simple partial seizures and complex bilateral automatisms during complex partial seizures; each of these manifestations was classified as 'non-localizing'.

Ictal and interictal scalp-sphenoidal EEG was interpreted and reviewed by each patient's primary epileptologist-electroencephalographer at UCLA, with consensus of the epilepsy surgery group. Initial ictal changes for each subject's entire set of seizures were classified in 1 of 4 categories: (1) unilaterally focal (involving a consistent group of electrodes unilaterally at seizure onset), (2) bilaterally focal (involving 2 distinct and contralateral groups of electrodes at onset), (3) nonlocalizing (involving most or all electrodes bilaterally at onset) and (4) artifactually obscured (where myogenic or other artifacts consistently obscured earliest electrocerebral ictal changes). (Interictal abnormalities did not add significant localizing information to ictal onsets in these 24 patients, so were not included among data correlated with PET in the current study.)

Cranial magnetic resonance imaging (MRI) and X-ray computed tomography (XCT) studies were performed on various instruments at UCLA and referring institutions. MRI and XCT interpretations were those of the neuroradiologists who supervised the studies; one author (T.R.H.) reviewed each scan to exclude obvious errors in interpretation (none of which were found) and to estimate the dimensions of any cortical abnormalities. Equivocal changes, such as possible focal atrophy, were noted in several MRIs; only definitely abnormal findings were analyzed here.

Seizures were recorded with subdural electrode arrays (subjects F2, F3, F6, F9, F10, F11, T1, T2, T4, T5, T6, T7, T8, O2 and O5), depth electrodes (subjects F4, F5, O1, O3 and O4) or both (subjects F1, F7, F8 and T3). Localization of electrographic ictal onset on depth electrode recordings was determined by visual analysis of the field pattern of the earliest paroxysmal change<sup>30</sup>; recordings were

interpreted by one of the authors (W.W.S., J.E. Jr. or M.W.R.) with consensus of the epilepsy surgery group. Localization of electrographic ictal onset on subdural electrode recordings was determined by the same method (where visual analysis revealed beta activity at 9 or fewer contiguous electrodes on 1-by-1-cm arrays, i.e., a 'focal' onset) or by the recently described dipole method<sup>22</sup>; recordings were interpreted by one of the authors (W.W.S. or M.W.R.) with consensus of the epilepsy surgery group.

Intracranial ictal onsets were localized to: dorso-lateral (premotor) frontal cortex in 7 patients (on the left in cases F1, F3, F4, F6 and F7 and on the right in F2 and F5), the right frontal operculum in F8 and F9, the right supplementary motor area in F10 and F11, left anterolateral temporal cortex in T1 and T2, mid lateral temporal cortex on the right in T3 and left in T4 and T5, posterolateral temporal cortex on the right in T6 and left in T8, left posteroinferior temporal cortex in T7, left anterolateral occipital cortex in O1 and O2, and posterolateral occipital cortex on the right in O4 and left in O3 and O5.

## RESULTS

### *Replicability of FDG PET analysis*

Agreement of independent FDG scan evaluations between investigators was very good. Both investigators (who were unaware of the identities of scans' subjects) considered all 15 FDG scans of normal control subjects to be normal. For scans of neocortical partial epilepsy subjects, there was complete agreement between investigators in rating the entire FDG scan as normal or abnormal and in rating frontal, occipital, cingulate, basal ganglial, cerebellar and brainstem divisions as normal or abnormal. Two disagreements each for lateral temporal, mesial temporal and thalamic divisions and one disagreement for a parietal division on the 24 neocortical epilepsy scans resulted in  $\kappa$  values for shared discrimination (agreement corrected for chance)<sup>13</sup> of 0.84 for lateral temporal, of 0.81 for mesial temporal, of 0.66 for parietal and of 0.71 for thalamic divisions. (None of these disagreements involved the area of intracranial electrographic ictal onset in any individu-

al.) Where more than one division was considered abnormal in a scan, there was no disagreement on the division(s) with most severe hypometabolism. There was no disagreement on sharpness of demarcation of hypometabolic from eumetabolic areas.

### *FDG PET findings*

Interictal FDG PET findings were of 3 types: (1) normal metabolism (in 8 subjects, F1, F4, F5, F6, F10, F11, T4 and T6); (2) focal hypometabolism, defined as a small (estimated at 4 cm or less in greatest dimension) neocortical region of severe hypometabolism with sharp demarcation from adjacent eumetabolic cortex (in 3 subjects, F2, T8 and O2); and (3) diffuse hypometabolism, defined as a more widespread region of variably mild to severe hypometabolism in one hemisphere, with graded demarcations from adjacent eumetabolic cortex (in 14 subjects); subject T8 had focal hypometabolism on one side and diffuse hypometabolism contralaterally, so is counted twice in these totals. Diffuse hypometabolism involved one cortical lobe in 7 subjects and more than one lobe in 7 subjects. Of the 7 subjects with multilobar diffuse hypometabolism, 5 had variable severity of hypometabolism across affected areas, such that one smaller area of most severe hypometabolism could be recognized within the larger area of cortical hypometabolism. Diffuse hypometabolism often included mesial temporal, thalamic or basal ganglial hypometabolism ipsilateral to neocortical hypometabolism. Cingulate, cerebellar and brainstem metabolism was normal on all scans.

### *Comparison of PET localization with the intracranial ictal onset zone and histopathology*

In all 16 subjects who had hypometabolism, the zone of intracranial electrographic ictal onset was located in a region of focal or diffuse hypometabolism (see Table I). The region of hypometabolism consistently appeared more extensive than the zone of intracranial electrographic ictal onset.

The electrographic ictal onset zone was located in the most severely hypometabolic portions of the hypometabolic region, in the 5 subjects who had variable severity of multilobar diffuse hypometabolism (F8, F9, O1, O3 and O4). The patient with

TABLE I

Accuracy of noninvasive localizations as determined by intracranial ictal electrophysiologic localizations

	Lobe of intracranial ictal onset zone			Totals
	Frontal	Temporal	Occipital	
<i>FDG PET</i> <sup>1</sup>				
Correct	5	6*	5	16*
Incorrect	0	0	0	0
Normal	6	2	0	8
<i>MRI/XCT</i> <sup>2</sup>				
Correct	3 <sup>+</sup>	8	4	15 <sup>+</sup>
Incorrect	1	0	0	1
Normal	7	0	1	8
<i>EEG onset</i> <sup>3</sup>				
Correct	5	7	3	15
Incorrect	0	0	0	0
Correct/ incorrect	0	0	2**	2**
Nonlocalizing	3	1	0	4
Obscured	3	0	0	3
<i>Semiology</i> <sup>4</sup>				
Correct	1 <sup>++</sup>	2 <sup>++</sup>	5 <sup>++</sup>	8 <sup>++</sup>
Incorrect	9	2	0	11
Nonlocalizing	1	4	0	5

<sup>1</sup> Regional hypometabolism on FDG PET is considered correctly localizing if the hypometabolic zone includes the intracranial ictal onset zone.

<sup>2</sup> Regional abnormality on cranial MRI and XCT is considered correctly localizing if the abnormal area includes the intracranial ictal onset zone.

<sup>3</sup> Focal ictal onset on scalp-sphenoidal EEG is considered correctly localizing if the electrode(s) habitually involved in ictal onset overlies the area of the cortical ictal onset zone subsequently determined by intracranial monitoring. Bilateral independent scalp EEG onsets at 2 distinct sets of electrodes are considered both correctly and incorrectly localizing if intracranial onsets underlie only 1 of the sets of scalp electrodes, because 2 discrete zones of scalp EEG onset incorrectly predict 2 foci of intracranial onset (in this study of unifocal partial epilepsy).

<sup>4</sup> The *initial* subjective or objective semiologic manifestation of each subject's habitual seizure type is considered correctly localizing if *any* of the sites of ictal onset predicted by the particular manifestations coincided with the intracranial ictal zone.

\* Subgroups identified with an asterisk include 1 subject (T8) who had bilateral interictal hypometabolism, which involved the intracranial ictal zone.

<sup>+</sup> Subgroups identified with a cross include 1 subject (F3) who had bilateral (bifrontal) atrophy on MRI, which involved the intracranial ictal zone.

\*\* Subgroups identified with a double asterisk include 2 subjects (O2 and O3) who had bilateral independent scalp electrographic ictal patterns with onset at distinct sets of electrodes, one correctly and the other incorrectly localizing.

<sup>++</sup> Subgroups identified with a double cross include subjects (F5, T8, O4) who had initial ictal semiology localizing to multiple cerebral regions, one of which coincided with the intracranial ictal zone.

bilateral hypometabolism (T8) had electrographic seizure onset in the most severely hypometabolic area (a region of focal hypometabolism at the left occipitotemporal junction), with no semiologic or ictal scalp EEG evidence for a second type of seizure originating elsewhere.

Spatial patterns of multilobar diffuse hypometabolism that included the frontal lobe were not unique to any particular site of ictal onset, since they occurred in patients with frontal, temporal or occipital seizures. The same was true of multilobar patterns of diffuse hypometabolism that included the temporal lobe. All 4 patients with multilobar diffuse hypometabolism that included occipital hypometabolism had seizures of occipital origin, however.

Regional (diffuse or focal) hypometabolism was seen in all 5 subjects with occipital epileptogenic zones (100%), in 6 of 8 with neocortical onset temporal lobe seizures (75%) and in 5 of 11 with neocortical onset frontal lobe seizures (45%). The trend toward decreased frequency of hypometabolism in neocortical frontal seizures is not statistically significant (at  $P < 0.05$  by Fisher's exact test).

Regional hypometabolism was not significantly associated with presence of a histopathologic lesion. Among 6 subjects with histopathologically normal tissue specimens, 3 had hypometabolism and 3 did not; among 14 subjects with histopathologic lesions, 11 had hypometabolism and 3 did not. The region of focal hypometabolism was approximately the same size as the resected lesion, in the 2 subjects with focal hypometabolism who had resective surgery. A region of diffuse hypometabolism included the site of a histopathologic lesion in the other 12 subjects with both hypometabolism and lesions; this spatial relationship was clear, even allowing for imprecision in estimating the location of the lesion on PET images, because regions of diffuse hypometabolism were consistently much larger (by at least several centimeters in each axis) than resected lesions.

#### Comparison of PET localization with other noninvasive localizations and the intracranial ictal onset zone

Structural neuroimaging was normal in 8 sub-

jects, though 4 of these did not have MRI due to its unavailability at the time of their presurgical evaluations. Any abnormalities seen on XCT were also seen on MRI (if performed), while MRI showed abnormalities in 8 subjects with normal XCT (and in 6 subjects with abnormal XCT). All focal cortical abnormalities on MRI or XCT, occurring in 11 subjects, were small (1–4 cm in greatest planar dimension) and were located at or near the site of intracranial electrographic seizure onset. Atrophic (larger than 5 cm, in each case) or noncortical (cerebral white matter) abnormalities, occurring in 5 subjects (F3, F8, T2, T3 and T5), could be bilateral (e.g., F3 had bilateral anterior frontal atrophy) or distant from the site of electrographic ictal onset (e.g., F8 had multiple puncta of T2 increase in right temporal subcortical white matter, but right frontal opercular ictal onset). Focal hypometabolism appeared co-localized with a focal cortical abnormality (MRI) in the 3 subjects in whom focal hypometabolism was seen (F2, T8 and O2). Diffuse hypometabolism included and extended beyond the location of a focal cortical abnormality (MRI or XCT) in 6 subjects and beyond the location of an atrophic or noncortical MRI abnormality in 5 subjects. Table IIA summarizes coincidence of PET and MRI/XCT abnormalities in individual subjects.

Initial ictal changes on scalp-sphenoidal EEG were unilaterally focal in 15 subjects, bilaterally focal in 2 subjects, nonlocalizing in 4 subjects, and consistently obscured by myogenic or other artifacts in 3 subjects (see Table I). The 2 subjects with bilateral focal ictal onsets each had 2 distinct, but adjacent topographic patterns of right and left parasagittal extracranial EEG changes at onsets of behaviorally indistinguishable seizures; each had a single zone of initial ictal changes on intracranial recordings. Relationships between PET and ictal scalp EEG findings are summarized in Table IIB.

Initial ictal semiology provided misleading localizing information in many patients. For example, initial ictal semiology was incorrectly localizing (usually as focal somatosensory hallucinations localizing to anterior parietal neocortex) in 9 of 11 neocortical onset frontal lobe seizures, as summarized in Table I; 8 of these 9 had early (but not initial) ictal manifestations that were suggestive of

TABLE II

*Comparisons of interictal FDG PET findings with other findings*

Abnormal findings are considered correctly localizing, except where explicitly stated to the contrary. Terms for findings are defined in Methods and Results. Abbreviations: FCA, focal cortical abnormality; ANA, atrophic or diffuse cortical abnormality.

IIA. MRI/XCT	FDG PET	
	Hypometabolism	Normal
MRI/XCT:		
FCA	9*	2
ANA	5 <sup>+</sup>	0
Normal	2**	6

\* Includes 1 bilateral localization (T8) by PET.

<sup>+</sup> Includes 1 incorrect localization (F8), 1 bilateral localization (F3), and 3 correct unilateral localizations by MRI.

\*\* Includes 1 subject with normal MRI and XCT (F7) and 1 with normal XCT but no MRI (O1).

IIB. Ictal scalp-sphenoidal EEG	FDG PET	
	Hypometabolism	Normal
EEG onset:		
Unifocal	10*	5
Bilateral	2 <sup>+</sup>	0
Other	4**	3 <sup>++</sup>

\* Includes 1 bilateral localization (T8) by PET.

<sup>+</sup> Includes 2 bilateral independent ictal onset patterns on scalp EEG (O2 and O3), one of which was incorrectly localizing in each case.

\*\* Includes 2 nonlocalizing (F7 and T2) and 2 artifactually obscured (F2 and F9) ictal onsets on EEG.

<sup>++</sup> Includes 2 nonlocalizing (F4 and F10) and 1 artifactually obscured (F11) ictal onsets on EEG.

IIC. Initial ictal semiology	FDG PET	
	Hypometabolism	Normal
Semiology:		
Correctly localizing	7*	1
Incorrectly localizing	6	5
Nonlocalizing	3	2

\* Includes 1 bilateral localization (T8) by PET.

the correct localization. Comparative PET and initial ictal semiologic localizations are summarized in Table IIC.

Correctly localizing regions of diffuse hypometabolism occurred in 2 patients who had nonloca-

lizing scalp-sphenoidal EEG initial ictal changes and who had normal MRI (subject F7) or nonspecific changes on MRI (subject T2); subject F7 had incorrectly localizing initial ictal semiology, while subject T2 had semiology consistent with the intracranial ictal zone. Each of the other 14 patients who had regions of focal or diffuse hypometabolism also had focal cortical abnormalities on MRI or unilaterally focal initial ictal changes on scalp-sphenoidal EEG; in this series, such ictal scalp EEG and MRI information was consistently accurate in directing placement of intracranial electrodes.

## DISCUSSION

Interictal cortical hypometabolism is highly associated with the site of intracranial electrographic ictal onset and with localized structural imaging abnormality in our patients with partial epilepsies of neocortical origin. 'Diffuse hypometabolism' (as we define this type of regional hypometabolism) was seen more commonly than normal metabolism (58% versus 33% of the group studied) in patients with neocortical seizures, as is the case in mesial (limbic) temporal lobe epilepsy (TLE)<sup>1,3,5,6,8-10,14,19,21,25-28,31</sup>. In these patients with neocortical seizures, any unilateral region of diffuse hypometabolism consistently included the smaller zone of intracranially recorded electrographic ictal onsets, as in mesial TLE<sup>6</sup>. Regions of diffuse hypometabolism included and were more widespread than associated cortical abnormalities on structural imaging and than histopathologic lesions in resected tissue of our patients with neocortical seizures, as in mesial TLE<sup>3,20</sup>. Interictal FDG PET often is abnormal where MRI is normal in mesial TLE, at least with nonquantitative clinical interpretation of MRI<sup>1,20,27</sup>. Only one neocortical seizure patient had hypometabolism and normal MRI, though 5 had cortical hypometabolism and atrophic or noncortical abnormalities on MRI; these atrophic or noncortical MRI abnormalities sometimes failed to correctly lateralize or did not include the neocortical ictal onset zone. Frontal and parietal subcortical white matter MRI abnormalities, with normal temporal lobe MR imaging, have also been reported in probable mesial

TLE<sup>20,29</sup>. Thus, FDG PET and MRI can provide nonredundant information in presurgical evaluation of neocortical epilepsies.

Sharply demarcated, small foci of severe interictal hypometabolism were observed at the epileptogenic site in 3 patients with partial epilepsies of neocortical origin, a finding not reported in patients with mesial TLE. 'Focal hypometabolism' (as we define this term) has also been reported by other investigators in probable neocortical seizures<sup>23,24,26</sup>. This focal hypometabolism may simply reflect a focal ablative lesion; all 3 of our subjects with focal hypometabolism also had focal cortical abnormalities on MRI at or near the epileptogenic site; the 2 who had surgical resection had histopathologic lesions. Alternatively, focal hypometabolism in some neocortical seizures may reflect less spatially disseminated mechanisms of epileptogenesis than those typical of mesial TLE. This issue could be addressed in part with prospectively applied methods of precise registration of PET and MRI images<sup>32</sup> and of determining subdural grid electrode location on MRI images<sup>12</sup>, so that (1) it could be determined whether focal hypometabolism on PET coincides precisely with focal cortical abnormality on MRI and (2) the electrical field at ictal onset could be spatially correlated with regional PET and MRI abnormalities. Precise spatial co-registration of metabolic and electrographic information is also required to determine whether postoperative seizure control is better when interictally dysfunctional (hypometabolic) tissue beyond the zone of intracranial electrographic ictal onset is resected along with the ictal onset zone.

Mesial and lateral temporal hypometabolism, without or with ipsilateral extratemporal hypometabolism, is characteristic of both neocortical temporal seizure origin (in this series) and mesial temporal lobe epilepsy with or without mesial temporal histopathologic lesions<sup>7,10,19</sup>. A third group deserves comment, that of patients with intracranially recorded mesial temporal ictal onsets and ipsilateral neocortical temporal lesions. In the time period covered in this study, we saw 8 patients who had low-grade neoplastic (5 patients), hamartomatous (2 patients) or focal encephalomalacic (1 patient) lesions that were confined to neocortical tis-

sue, which was resected at anterior temporal lobectomy for refractory complex seizures of depth-electrode-recorded mesial temporal ictal onset (with depth electrode contacts in multiple limbic and neocortical temporal sites bilaterally); none had evident histopathologic abnormalities in mesial temporal tissue; preoperative interictal FDG studies, reviewed in the same way as for this study, revealed mesiolateral temporal hypometabolism ipsilateral to lobectomy in 5, normal metabolism in 2, and bilateral hypometabolism (including mesiolateral temporal hypometabolism ipsilateral to lobectomy) in one. Thus, mesiolateral temporal hypometabolism is commonly seen in mesial temporal seizures with a lesion (usually hippocampal sclerosis) in the mesial temporal area, in mesial temporal seizures with an ipsilateral neocortical temporal lesion (and without a mesial temporal lesion), in neocortical temporal seizures with a neocortical temporal lesion, and in mesial or neocortical temporal seizures with no histopathologic lesion in resected tissue (but with significant improvement in seizure control postoperatively). Mesiolateral temporal hypometabolism, therefore, in itself gives no conclusive evidence for presence or absence of a histopathologic lesion nor for limbic versus neocortical ictal onset.

Occipital hypometabolism was observed only in the 5 subjects with neocortical occipital ictal onsets and in one subject with an occipitotemporal junction abnormality on structural imaging and posterior neocortical temporal ictal onsets. Occipital hypometabolism is rare in mesial temporal lobe epilepsy<sup>4,7</sup>. Occipital hypometabolism within a multilobar hypometabolic zone may be particularly associated with occipital epileptogenesis in adult partial epilepsies.

Normal interictal metabolism was seen in a higher proportion of those with neocortical frontal seizures than in those with neocortical temporal or occipital seizures. The same was true for structural imaging, as would be expected, given a strong association of abnormal PET with abnormal MRI and XCT across the entire neocortical partial seizure group. The trend (toward fewer imaging abnormalities in the frontal seizure group) cannot be explained by an increased tendency for frontal sei-

zure patients to reach the stage of intracranial electrographic monitoring on the basis of extracranial ictal EEG information, since ictal EEG was less often correctly localizing in frontal seizure patients than in extrafrontal seizure patients. Similarly, interlobar differences in localizability by ictal semiology also fail to explain this trend.

Interictal FDG PET findings are complementary to those of ictal extracranial EEG and of ictal semiology in neocortical seizures. Ictal semiology is sometimes very useful in identifying a rather limited neocortical area of probable ictal onset, as in focal clonic or tonic motor seizures. Initial ictal subjective and behavioral manifestations may, however, reflect propagation of seizure discharges away from the actual site of electrographic onset; additionally, multiple sites of seizure onset may produce the same ictal manifestation<sup>15</sup>.

FDG PET may prove particularly useful for patients with complex partial seizures and without auras or simple partial seizures, where extracranial EEG and MRI are normal or not specifically localizing; this group currently cannot be offered resective procedures for refractory seizures. Our data support the use of regional hypometabolism on FDG PET to direct the placement of intracranial electrodes, in order to maximize the likelihood of recording the earliest ictal electrographic changes for determination of neocortical resection.

#### ACKNOWLEDGEMENTS

Dr. Henry's work was partially supported by the Merritt-Putnam Clinical Research Fellowship of the Epilepsy Foundation of America. This work was also partially supported by NIH Grants NS 02808 and NS 20806. We thank Dr. J. Bruce Jacobs, Dr. David E. Kuhl, Dr. Robert B. Lufkin, Dr. Michael R. Sperling, Dr. Paul C. VanNess, Dr. M. Anthony Verity, Dr. Harry V. Vinters and Dr. Gabriel H. Wilson for providing clinical interpretations of EEG, MRI, PET and histopathologic studies and information on postoperative seizure control. We thank Sally Mouilleseaux and Kay Neff for assistance in preparing the manuscript.



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