간질발작의 진행에 따른 발작기 SPECT의 혈류증가 양상

성균관 대학교 의과대학 삼성서울병원 간질연구소[1], 신경과[2], 신경외과[4], 핵의학과[3]

신원철[1,2] · 홍승봉[1,2] · 태우석[1,2] · 손영민[1,2] · 서대원[1,2] · 김병준[2] · 홍승철[1,4] · 김상은[3]

Topographic Changes of Ictal Hyperperfusion During Progression of Clinical Seizures

Won Chul Shin, M.D.[1,2], **Seung Bong Hong**[1,2], M.D., **Woo Suk Tae**[1,2], M.S., **Young-Min Shon**[1,2], M.D., **Dae Won Seo**[1,2], M.D., **Byoung Joon Kim**[2], M.D., **Seung-Chyul Hong**[1,4], M.D., **Sang Eun Kim**[3], M.D.

Epilepsy program[1], Departments of Neurology[2], Nuclear Medicine[3] and Neurosurgery[4], Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Abstract

Purpose: To investigate ictal hyperperfusion patterns during semiologic progression of seizures, we performed SPECT subtraction in 50 patients with temporal lobe epilepsy (TLE). **Materials and Methods:** The patients were categorized into five groups according to semiologic progression during ictal SPECT (group-1 having only aura; group-2 having motionless staring with or without aura; group-3 having motionless staring and then automatism with or without aura; group-4 having motionless staring and then dystonic posturing with or without aura and automatism; group-5 having motionless staring, automatism, then head version and generalized seizures with or without aura and dystonic posturing). **Results:** In group-1, three patients showed ipsilateral temporal hyperperfusion and two had bilateral temporal hyperperfusion with ipsilateral predominance. In group-2, three (42.9%) patients showed bilateral temporal hyperperfusion with unilateral predominance and four (57.1%) revealed insular hyperperfusion of epileptic side. In group-3, 15 patients (88.2%) showed bilateral temporal hyperperfusion with unilateral predominance and 12 (70.6%) insular hyperperfusion. In group-4, 11 patients (84.6%) showed basal ganglia hyperperfusion on the opposite hemisphere to the side of the dystonic posturing. In group-5, there were multiple hyperperfusion areas in the frontal, temporal and basal ganglia regions. However, the injection times of radiotracer in five groups were relatively short and similar. **Conclusions:** The semiologic progression in TLE seizures were related to the propagation of hyperperfusion from ipsilateral temporal lobe to contralateral temporal lobe, insula, basal ganglia, and frontal lobe. Not only the radiotracer injection time but also semiologic progression after the injection was significant in determining hyperperfusion pattern of ictal SPECT. **(Korean J Nucl Med 2001;35:352-363)**

Key Words : Temporal Lobe Epilepsy, Ictal Hyperperfusion, SPECT Subtraction, Seizure Progression

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Corresponding Author: Seung Bong Hong, M.D., PhD

Associate professor, Department of Neurology, Director of Epilepsy Program, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-Dong, Kangnam-Gu, Seoul, 135-710, Korea

Tel: +82-2-3410-3592, Fax: +82-2-3410-0052

E-mail: sbhong@smc.samsung.co.kr

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Introduction

Because the clinical features of seizures are produced from the activation of certain regions of the brain and its spread to adjacent areas, detailed analysis of ictal semiology can often provide insight into the lateralizing information of seizure focus and seizure propagation pathway.[1-4]

However, the correlation of anatomical information and semiology is incomplete due to limitations of EEG.

Much of the knowledge regarding seizures of mesial temporal lobe epilepsy (TLE) has been derived from careful correlation of clinical data using video-EEG monitoring, or from results obtained during the intra-operative recording and brain stimulation as well as from presurgical EEG recording with invasive electrodes.[1-3, 5-8] But the scalp EEG cannot reflect the precise anatomical information and state of subcortical or deep structures, such as the basal ganglia and insula. Although intracranial electrodes can provide a more precise localization of seizure focus,[9] they record only a small portion of the brain tissue.[10] Brain SPECT (single photon emission computed tomography) demonstrates the local changes in the regional cerebral blood flow of the whole brain, which occur during or soon after seizures. The brain SPECT has been used widely for detection of epileptogenic focus and for analysis of seizure semiology. Regional cerebral blood flow during seizures is known to reflect brain activation and its spread pathway. Moreover, the patterns of relative hyperperfusion are congruent with the clinical symptomatology. There are several studies that demonstrated the relationship between seizure semiology and anatomical localization using brain SPECT[11] or PET.[12] However, topographic changes of ictal hyperperfusion during semiological progression of seizures have not been studied.

To identify the cerebral distribution of ictal hyperperfusion during the clinical progression of seizures, we categorized patients with TLE into five groups according to the progression degree of clinical seizures and performed SPECT subtraction with their interictal and ictal SPECT images.

Materials and Methods

Patient information. This study included 50 patients (25 men, 25 women) with intractable unilateral mesial TLE, who had an excellent surgical outcome (Engel class I) after anterior temporal lobectomy with amygdalohippocampectomy at Samsung Medical Center from 1997 to 2000. All subjects underwent long-term video-EEG monitoring, interictal and ictal SPECT, volumetric MRI, neuropsychological tests and 18F-fluorodeoxyglucose (FDG)-PET if necessary. The epileptogenic focus was determined by presurgical evaluation and epilepsy surgery.

Clinical characteristics registered for each subject included age at the time of seizure onset, the duration of epilepsy, seizure frequency, existence of aura and secondarily generalized seizures, and semiology of seizures.

Seizure analysis. All patients underwent long-term video-EEG monitoring. Patients were tested during the seizure by a staff from the monitoring unit (technologists, nurses or physicians) for their responsiveness and asked to remember items (color and object). The patients were judged as unconscious during the seizure if they were not able to interact normally with the observer and were amnesic afterwards. Patients were continuously checked for orientation and responsiveness after seizures. Postictally, after patients had regained consciousness and were able to follow commands, they were again interviewed to see if they (a)

recalled having an aura before that seizure and could describe it, (b) had any memory of what had occurred during the seizure and, (c) had dysnomia by asking them to name objects. Among a total of 155 seizures from 50 patients, we evaluated only 50 seizures (including five auras) in which ictal SPECT was performed. We noted all features from every seizure and recorded each feature with its time of onset, duration, and end. Specifically, we looked for auras, motionless staring, oro-alimentary or extremity automatisms, dystonic posturing of extremities, head included and secondarily generalization. Aura was counted only if the patients announced it at the beginning of the seizure or were able to recall having it during the postictal interview. The duration of aura was calculated from the time of pressing the seizure button to the patient's uttering the end of aura. The durations of complex partial seizures and secondarily generalized seizures were measured from the time of pressing the seizure button or the first ictal changes of clinical behavior or EEG to the cessation of ictal EEG discharges.

Patients with mesial TLE show similar and typical seizure semiology. The common features of mesial temporal lobe origin seizures are abdominal aura, motionless stare, oro-alimentary or extremity automatism, and unilateral dystonic posturing. These features usually occur with a constant sequence (abdominal aura, motionless staring, oro-alimentary or extremity automatism, unilateral dystonic posturing). As a previous literature[1] suggested, we selected major characteristic features of mesial TLE seizures and categorized them into five groups according to the progression of seizure semiology as follows; group-1 with only aura (n=5; 2 men, 3 women), group-2 having motionless staring with or without aura (n=7; 3 men, 4 women) during their seizures, group-3 having motionless staring and then automatism with or without aura (n=17; 10 men, 7 women), group-4 having motionless staring and then dystonic posturing, with or without aura and automatism (n=13; 7 men, 6 women), and group-5 having motionless staring, automatism, and then head version or generalized tonic-clonic seizures with or without aura and dystonic posturing (n=8; 3 men, 5 women).

Interictal and ictal SPECT studies. Brain SPECT scan was performed at 30~60 minutes after injection of 25 mCi ^{99m}Tc-ethyl cysteinate dimer (ECD) using a three-headed Triad XLT system (Trionix Research Laboratory, Twinsburg, OH) equipped with low-energy, high-resolution collimators. The transaxial system resolution of this camera was 6.9 mm full width at half maximum. Images were reconstructed by filtered back-projection using a Butterworth filter. Attenuation correction was performed using Chang's method (attenuation coefficient = 0.12 cm^{-1}).[13]

Interictal SPECT studies were performed when the patients had no documented seizure activity during the last 24-hour period or more. For ictal studies, patients received the radiotracer injection during aura or clinical seizures. The patients were continuously monitored by long-term video-EEG monitoring system during this phase. As soon as seizures were witnessed or made aware by pressing a seizure button, a trained EEG technician or nurse injected the radiotracer intravenously. The case of postictal injection was rejected.

MRI (magnetic resonance imaging). The MRI scanning was performed with a GE Sigma 1.5-Tesla scanner (GE Medical Systems, Milwaukee, WI, USA). SPGR (Spoiled Gradient Recalled) volumetric MRI was scanned with the parameters of no gap, 1.6 mm thick, 124 slices, TR/TE=30/7, flip angle=45, number of excitations (NEX)=1,

coronal. The voxel dimension was 0.86×0.86× 1.6 mm. FLAIR (FLuid Attenuated Inversion Recovery) was scanned with oblique coronal, 1.0 mm gap, 4.0 mm thickness, 32 Slice, TR/TE = 10002/127.5, 1 NEX, and axial images of FLAIR was also obtained with 2.0 mm gap, 5.0 mm thickness. T2 image was scanned with 0.3 mm gap, 3.0 mm thickness, 56 slice, TR/TE = 5300/99 ms, flip angle=90, 3 NEX, oblique coronal. T2 axial images were scanned also with 2.0 mm gap and 5.0 mm thickness.

Image Processing for SPECT subtraction with MRI co-registration. SPECT subtraction was processed on an off-line SUN Ultra 1 Creator workstation (Sun Microsystems, CA, USA) with a commercial software package ANALYZE 7.5 (Biomedical Imaging Resource, Mayo Foundation, MN, USA). All biomedical images were transferred from each scanner consoles to the Unix workstation by 4 mm DAT device.

SPECT Subtraction procedure consisted of the following steps.[14]

1) Ictal-interictal SPECT registration. Before subtracting each voxel value between the ictal and interictal SPECT images, three-dimensional position of interictal SPECT was transformed to the ictal SPECT. In all cases, RMSD (root mean square distance) was within 1 voxel. Correct registration is important for improving sensitivity of the subtraction technique. And inaccurate registration may produce a false perfusion difference. ***2) Normalization of radioisotope uptake level.*** Different radioisotope uptake levels were normalized as each patient had different uptake level of radioisotope. And normalization factor was calculated over the whole brain.[15] ***3) Ictal-transformed interictal SPECT subtraction.*** To get the cerebral perfusion difference, ictal SPECT was subtracted by transformed and normalized interictal SPECT. Difference in the radioisotope uptake level was calculated by pixel-by-pixel subtraction. ***4) Noise erasing.*** To erase the subtraction noise, the standard deviation of each subtracted SPECT was calculated. Two SD were adjusted to erase the noise. ***5) MRI-subtracted SPECT registration.*** For localization of difference images, we co-registered subtracted SPECT with SPGR MRI of the patient's whole brain. In most cases, the error ranges of SPECT-MRI registration were within three voxels (voxel size : 0.86×0.86×1.6 mm).

Interpretation of subtracted SPECT. Ictal hyperperfusion of subtracted SPECT was considered significant only when rCBF (regional cerebral blood flow) difference in each pixel of brain SPECT image between ictal and interictal states was greater 2SD. The location of significant ictal hyperperfusion was decided on MRI by SPECT-MRI co- registration. For determining significant rCBF changes, we included brain regions showing larger than three voxels (3.56 mm × 3 = 10.68 mm) with a significant difference of intensity values between ictal and interictal SPECT images. In cases of multi-regional rCBF changes, we decided significant changes in order of larger rCBF area and greater intensity change by color lookup table (red is the highest intensity value while violet is the lowest intensity value).[16,17] In earlier works, brain regions with a large rCBF change were more closely related with epileptogenic focus.[15]

Results

Demographic and clinical data. Of the 50 patients (Table 1), 25 were men and 25 were women. Their mean age was 31 years (range, 5-56). The mean age at the seizure onset was 16 years (range, 2-56); the mean duration of epilepsy history was 14 years (range, 2-37); and the mean

Table 1. Clinical information of the patients.

	Group-1 (n=5)	Group-2 (n=7)	Group-3 (n=17)	Group-4 (n=13)	Group-5 (n=8)	Total (n=50)
Sex(men:women)	2:3	3:4	10:7	7:6	3:5	25:25
Age(years old)	27.3±8.3	24.5±12.2	31.4±8.9	34.8±10.5	24.7±8.1	30.8±10.3
Age of seizure onset (years old)	11.7±2.1	11.7±7.9	18.3±8.1	19.4±14.6	11.2±6.6	16.1±10.5
Seizure frequency (per month)	20.3±17.9	8.1±11.5	2.8±1.7	3.7±4.5	3.4±2.7	5.0±7.2
Duration of seizure history (years)	16.7±8.7	14.2±8.7	13.3±8.1	15.5±1.2	13.3±6.4	13.7±7.2
Side of seizure focus	2R, 3L	3R, 4L	9R, 8L	3R, 10L	4R, 4L	21R, 29L
Seizure semiology during ictal SPECT						
Aura	5(100%)	5(71.4%)	13(76.5%)	7(53.9%)	4(50%)	34(68%)
Motionless staring	0	7(100%)	17(100%)	13(100%)	8(100%)	45(90%)
Automatism	0	0	17(100%)	11(84.6%)	8(100%)	36(72%)
Dystonic posturing	0	0	0	13(100%)	7(87.5%)	20(40%)
Secondarily generalization	0	0	0	0	8(100%)	8(16%)
EEG finding during ictal SPECT						
Unitemporal onset	2	5(71.4%)	11(64.7%)	8(61.5%)	5(62.5%)	31(62%)
Bitemporal onset with unitemporal predominance	0	2(28.6%)	5(29.4%)	3(23.1%)	3(37.5%)	13(26%)
Non-lateralized	0	0	1(5.9%)	2(15.4%)		3(6%)

Values are mean ± standard deviation. R= right, L= left ; Group-1 with only aura; group-2 having motionless staring with or without aura; group-3 having motionless staring and then automatism with or without aura; group-4 having motionless staring and then dystonic posturing, with or without aura and automatism; group-5 having motionless staring, automatism, and then head version or generalized tonic-clonic seizures with or without aura and dystonic posturing.

frequency of seizures was 5 per month (range, 1-40/month).

EEG findings during ictal SPECT (Table 1). Ictal EEG was reviewed during ictal SPECT in all patients. There was no patient who had subdural or depth electrode recording. In group-1 with only aura, there were no overt EEG changes in three but transient rhythmic ictal discharges visible only at the sphenoidal electrode in two. The ictal SPECT EEG was lateralized in 44 patients (88%). Thirty-one patients (62%) showed unilateral temporal onset and 13 patients (26%) had bilateral temporal onset with unilateral predominance. Three patients with only aura showed no EEG changes. Ictal SPECT EEG of the remaining three patients (6%) were not lateralized. However, in these three patients, some other seizures during EEG monitoring period were lateralized and the neuroimaging studies of these patients were concordant to the side of ictal onset.

Table 2. Semiology at the time of radiotracer injection and the injection time of radiotracer.

	Group-1 (n=5)	Group-2 (n=7)	Group-3 (n=17)	Group-4 (n=13)	Group-5 (n=8)	Total (n=50)
Semiology at the Radiotracer injection						
Abdominal aura	5((100%)	0	0	0	0	5(10%)
Motionless staring	0	7(100%)	4(23.5%)	2(15.4%)	2(25%)	15(30%)
Automatism	0	0	13(76.5%)	5(38.5%)	2(25%)	20(40%)
Dystonic posturing	0	0	0	6(46.2%)	3(37.5%)	9(18%)
Head version	0	0	0	0	1(12.5%)	1(2%)
Ictal SPECT						
Injection time of radioisotope(sec)*	20.0±9.5	26.3±8.4	28.3±16.7	24.3±9.3	22.7±6.7	25.7±12.2
Total seizure duration (sec)	39.3±11.9	75.2±34.2	90.4±26.3	81.3±27.6	128.3±38.0	88.6±33.1

*Injection time of radioisotope from seizure onset.

Group-1 with only aura; group-2 having motionless staring with or without aura; group-3 having motionless staring and then automatism with or without aura; group-4 having motionless staring and then dystonic posturing, with or without aura and automatism; group-5 having motionless staring, automatism, and then head version or generalized tonic-clonic sezures with or without aura and dystonic posturing.

Injection time of radiotracer and semiology at the injection (Table 2). The mean duration of all seizures was 89 seconds (range, 25-188), and the mean time of the radiotracer injection after seizure onset was 26 seconds (range, 12-76).

There was no significant difference of radiotracer injection time among the five groups (p=0.84, Kruskal-Wallis test). However, the mean seizure durations of groups-2, 3, 4 and 5 were longer than that of group-1 (p=0.009, Kruskal-Wallis test)

Conventional SPECT, brain MRI. Ictal SPECT showed areas of hyperperfusion at the epileptic foci in all subjects [right temporal (n=21) and left temporal (n=29) regions]. No false lateralization was observed. Interictal SPECT demonstrated a focal and unilateral temporal hypoperfusion that is concordant to the seizure focus in 31 patients (60%).

Brain MRI showed structural lesions in 37 patients (74%). There were hippocampal sclerosis in 34 and suspicious tumorous lesion at mesial temporal region in three patients.

The pathology showed hippocampal sclerosis in 43 patients (86%), cortical dysplasia in six (12%) and oligoastrocytoma in one.

Ictal hyperperfusion patterns in subtracted SPECT (Table 3, Fig. 1). We excluded the patients whose seizures were not lateralized by ictal SPECT or subtracted SPECT. Subtracted SPECT showed ictal hyperperfusion at the temporal lobe of seizure origin in all patients (21 right; 29 left).

All patients in group-1 (n=5) had abdominal aura. Subtracted SPECT showed unilateral temporal hyperperfusion in three patients and bilateral temporal hyperperfusion with ipsilateral predominance in two. Two with bilateral temporal hyperperfusion had right hippocampal sclerosis on MRI and diffuse hyperperfusion in the right temporal lobe and focal hyperperfusion in the left temporal area on subtracted SPECT

Table 3. The locations of ictal hyperperfusion in subtracted SPECT

	Group-1 (n=5)	Group-2 (n=7)	Group-3 (n=17)	Group-4 (n=13)	Group-5 (n=8)
Temporal lobe					
Unilateral(ipsilateral)	3(60%)	4(57.1%)	2(11.8%)	4(30.8%)	2(25%)
Bilateral with ipsilateral predominance	2(40%)	3(42.9%)	15(88.2%)	9(69.2%)	6(75%)
Insular cortex					
Ipsilateral	1(20%)	4(57.1%)	5(29.4%)	4(30.8%)	4(50%)
Bilateral	0	0	7(41.2%)	2(15.4%)	3(37.5%)
None	4(80%)	3(42.9%)	5(29.4%)	7(53.9%)	1(12.5%)
Basal ganglia					
Ipsilateral	0	2(28.6%)	6(35.3%)	5(38.5%)	2(25%)
Bilateral	0	0	2(11.8%)	6(46.2%)	5(62.5%)
None	0	5(71.4%)	9(52.9%)	2(15.4%)	1(16.7%)
Frontal lobe					
Ipsilateral	0	2(28.6%)	2(11.8%)	5(38.5%)	1(12.5%)
Bilateral	0	1(14.3%)	5(29.4%)	4(30.8%)	7(87.5%)
None	0	4(57.1%)	10(58.8%)	4(30.8%)	0

Group-1 with only aura; group-2 having motionless staring with or without aura; group-3 having motionless staring and then automatism with or without aura; group-4 having motionless staring and then dystonic posturing, with or without aura and automatism; group-5 having motionless staring, automatism, and then head version or generalized tonic-clonic seizures with or without aura and dystonic posturing; Ipsilateral = ipsilateral side to the epileptic focus; Contralateral = contralateral side to the epileptic focus.

In group-2 (n=7), the aura was observed in five patients (four epigastric rising sensation and nausea, and one dizziness). Three patients (42.9%) showed bilateral temporal hyperperfusion with diffuse whole temporal lobe hyperperfusion in the epileptogenic side and focal hyperperfusion in contralateral temporal lobe. Four patients (57.1%) showed hyperperfusion in the ipsilateral insula to the epileptic focus (Fig. 1B).

In group-3 (n=17), aura was reported in 13 patients (76.5%); seven with epigastric rising sensation with nausea, three with dizziness, two with fear, and one with jamaris vu. All patients had motionless staring and extremity or oroalimentary automatism; five patients (29.4%) with only extremity automatism, four (23.5%) with only oroalimentary automatism, eight (47.1%) with both extremity and oroalimentary automatism. Fifteen patients (88.2%) showed bilateral temporal lobe hyperperfusion, 12 (70.6%) ipsilateral or bilateral insular hyperperfusion to the epileptic side, eight (47.1%) ipsilateral or bilateral basal ganglia hyperperfusion, seven (41.2%) ipsilateral or bilateral frontal lobe hyperperfusion, and five (29.4%) contralateral frontal lobe hyperperfusion (Fig. 1C).

In group-4 (n=13), the aura was noticed in seven patients (53.9%) (four epigastric rising sensation with nausea, one dizziness and two fear). All patients had dystonic posturing of contralateral hand to the epileptogenic focus as well as motionless staring. Eleven patients (84.6%) had extremities and/or oroalimentary automatism. Nine patients (69.2%) showed

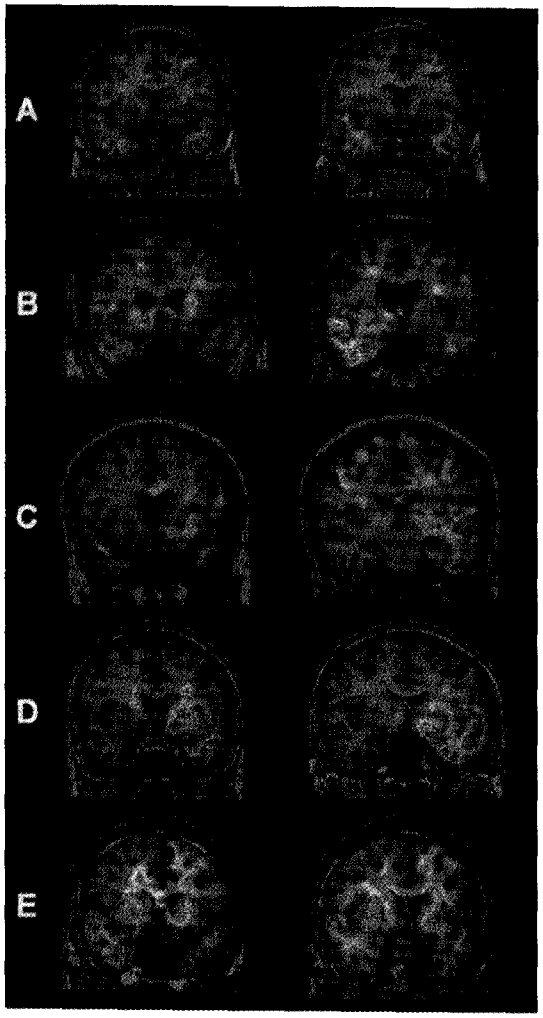

Fig. 1. Images of subtracted SPECT with MRI co-registration in each group (A). Ictal hyperperfusion on left temporal lobe with subtle right temporal change in a 37 year-old woman with left temporal lobe epilepsy (group-1) (B). Ictal hyperperfusion on right temporal lobe and ipsilateral insular cortex in a 25 year-old man with right temporal lobe epilepsy (group-2) (C). Forty-two year-old man with left temporal lobe epilepsy showing ictal hyperperfusion of left temporal lobes, its adjacent insula and small portions of basal ganglia (group-3) (D). Ictal hyperperfusion on left temporal lobe, basal ganglia and insula in a 34 year-old man with left temporal lobe epilepsy (group-4) (E). 28 year-old man with right temporal lobe epilepsy showing ictal hyperperfusions on bilateral multiple brain regions with right temporal predominance (group-5).

bilateral temporal lobe hyperperfusion, six (46.2%) ipsilateral insular hyperperfusion to the epileptogenic side, nine (69.2%) ipsilateral frontal hyperperfusion, and four (30.8%) contralateral frontal hyperperfusion. The ipsilateral basal ganglia hyperperfusion to the epileptic side was observed in 11 patients (84.6%) and bilateral basal ganglia hyperperfusion in six (46.2%) (Fig. 1D). In three patients without ipsilateral basal ganglia hyperperfusion, one patient showed ictal hyperperfusion in ipsilateral basal frontal region and the other two in contralateral basal ganglia.

In group-5 (n=8), the aura was reported in four patients (50%) (two epigastric rising sensation with nausea, and two dizziness). All patients had motionless staring, automatism and head version with secondarily generalization. Dystonic posturing was observed in seven patients (87.5%). Bilateral temporal lobe hyperperfusion was seen in six patients (75%), ipsilateral insular hyperperfusion to the epileptogenic side in four (50%), ipsilateral basal ganglia hyperperfusion in seven (87.5%), contralateral basal ganglia hyperperfusion in five (62.5%), ipsilateral frontal hyperperfusion in eight (100%), and contralateral frontal hyperperfusion in seven (87.5%) (Fig. 1E).

Discussion

Many of the ictal clinical phenomena of mesial TLE occur as the result of activation of temporal lobe and seizure spread to another regions (contralateral temporal lobe, ipsilateral or contralateral basal ganglia, frontal and parietal lobes) by various anatomical pathways. It is postulated that in a significant proportion of TLE seizures, the constellation of clinical behavioral manifestation seen initially or shortly after seizure onset may be due to seizure spread to the contralateral temporal or extratemporal structure.[6]

Therefore, clinico-anatomical correlation in sequences of clinical seizure progression could demonstrate seizure spread pathways to other brain areas and origin of specific behavior during seizures as well as the location of the epileptic focus. Ictal hyperperfusion apparently reflects not only the origin of epileptic discharges but also their spread to adjacent cortical areas,[18] and provides information on the regions of brain activation. Ictal SPECT is not a mere consequence of EEG seizure activity, but may provide insight into the functional organization of more complex seizure-related symptoms such as automatisms and motionless stare.[6,19] The patterns of relative hyperperfusion are congruent with the clinical symptomatology. It has been systemically studied partial seizures by using the ^{14}C-2-deoxyglucose technique in rats.[20] The resulting brain images revealed five distinct seizure-activation patterns representing progressively larger and more complex levels of seizure-mediating neuronal organization and these patterns ranged from restricted limbic ones to those extending to the ipsilateral basal ganglia and finally to those that even included most parts of the neocortex. Others reported of changes in blood flow or blood distribution in the ictal state by using ictal SPECT[11,21] and interictal state by using PET.[12] In these studies, dystonic posturing has been shown to correlate with increased cerebral blood flow of the contralateral basal ganglia in ictal SPECT and hypometabolism of ipsilateral basal ganglia to the seizure focus in interictal PET.

It is a common assumption that auras reported by patients with partial seizures indicate which part of the brain the seizure starts from and thus provide useful localizing information. It has been suggested that is a were strong association between epigastric sensations and temporal lobe epilepsy.[22-24] One study reported that the epigastric aura occurred during seizure discharge restricted to one temporal lobe.[6] Abdominal auras have been shown to arise not only from mesial temporal structures but also from other brain regions such as insula, frontal lobe olfactory area, centromedian nucleus, and basal ganglia.[20, 25-27] Because the duration of aura is short generally, it is very difficult to obtain ictal SPECT during the aura. In our study, the patients of group-1 had unusually prolonged aura, which made ictal SPECT possible. We assume that a long duration of aura implies persistent ictal discharges confined within a limited region of brain. Two patients had aura of longer duration than others (51 seconds and, 60 seconds, respectively). They showed bilateral temporal hyperperfusion with ipsilateral predominance while three patients with shorter duration had unilateral temporal hyperperfusion. This finding suggests that when the aura persists, seizure discharges can move go to the contralateral side before spreading to ipsilateral extratemporal structures.

Motionless staring with unresponsiveness is a distinctive clinical behavioral manifestation consistently seen at the onset of temporal lobe seizures in patients achieving significant improvement in seizure control after anterior temporal lobectomy.

It was reported that motionless stare was found in 46% of the complex partial seizures with regional hippocampal-amygdala ictal discharge and in 65% of complex partial seizures with unifocal hippocampal ictal discharge.[6,7] But, other studies suggested that bilateral change in EEG background rhythm was always present during impaired responsiveness.[7,26] More recent observation have documented that motionless stare can also be observed in seizures arising in the frontal and/or occipital lobes.[6] Our result suggests that the motionless staring with unresponsiveness may be

related with hyperperfusion in insular cortex or frontal lobe.

The automatism, like motionless stare, is commonly associated with the hippocampal-amygdala complex and infrequently mesial and orbital frontal lobe, the cingulate gyrus, and subcortical regions.[7] It was usually associated with bilateral ictal discharges,[8] and unilateral automatisms in temporal lobe seizures were generally ipsilateral to the seizure focus.[28] It has been reported that repetitive upper extremity automatisms are also due to ictal activation of basal ganglia.[3] Subtracted SPECT of our study showed hyperperfusion in bilateral temporal lobes (88.2%), ipsilateral insular cortex (70.6%) and ipsilateral basal ganglia (47.1%) in patients who had automatism without dystonia during seizures. This result suggests that various mechanisms are associated with generation of ictal automatisms. Although the injection time and seizure duration of group-3 were similar to group-2, group-3 had a tendency to involve insula and basal ganglia involvement.

Clinical and anatomical data support the hypothesis that ictal dystonic posturing is caused by the spread of the ictal discharge to the subcortical structures and especially to the striatal region.[12,29] Ictal SPECT studies have shown activation of basal ganglia on the side of the seizure origin when contralateral dystonic posturing is present.[11] Dystonic posturing was significantly associated with more severe hypometabolism in the striatal and in the orbitofrontal regions ipsilateral to the seizure focus.[12] There is anatomic and experimental evidence for projection to basal ganglia structures from the amygdala and hippocampus.[30-32] It can be also produced by seizure spread from the temporal lobe to the frontal region.[29,33,34] In our study, the basal ganglia hyperperfusion was observed in 76.9% of patients with dystonic posturing and this result is in accord with previous studies.[11,12,29] Our results showed that ictal dystonia was associated with hyperperfusion of bilateral basal ganglia as well as ipsilateral one to the side of dystonia.

In ictal SPECT, the early injection of radiotracer has been considered as the most important factor for seizure localization. The radiotracer injection during the earlier part of a seizure may reflect the ictal propagation limited to the structures surrounding the epileptogenic focus while the injection during the later part of a seizure tends to show the more widespread propagation with extensive hyperperfusion. However, cerebral uptake of radiotracer takes over 30 to 60 seconds after the injection.[35-37] Therefore, the ictal SPECT may reflect not only the brain activity at the time of injection but also cerebral perfusion changes over 30-60 seconds thereafter.

In our study, most of the patients showed ictal hyperperfusion in bilateral temporal lobes. There are several reasons why those structures are frequently involved even in all different groups. Ictal discharges arising from hippocampus easily spread to neighboring structures (amygdala, parahippocampal structures in temporal lobe, and insula) and contralateral temporal lobe within a relatively short period.[38] Secondly, ictal hyperperfusion may occur in not only brain region with ictal EEG discharges but also neighboring areas receiving efferent fibers from that region. So the extent of perfusion changes could be broader than the region of ictal EEG discharges.

The more extensive hyperperfusion of ictal SPECT was observed in some patients with later injection of radiotracer in the same group. But others showed uncoupling of injection timing and the extent of hyperperfusion. Therefore, other factors (total extent of EEG seizure spreading and the intensity of ictal discharges) as well as

injection timing may affect the pattern of ictal hyperperfusion. Although the injection time (mean injection time=25.512.5 seconds) and ictal manifestations at the injection time were similar among different groups in our study, the patterns of ictal hyperperfusion were quite different. This finding suggests that not only the injection time but also semiological progression after the injection are important to determine hyperperfusion patterns of ictal SPECT.

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