SPECT perfusion changes during ictal automatisms with preserved responsiveness in patients with right temporal lobe epilepsy

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ABSTRACT

Ictal automatism with preserved responsiveness (APR) has been reported, particularly in nondominant temporal lobe epilepsy (TLE), but its pathophysiology remains poorly understood. This study sought to investigate the relationship between APRs and increased cerebral blood flow (CBF) using ictal single photon emission computed tomography (SPECT) in TLE.

Forty-seven subjects with right mesial TLE (15 with and 32 without APR) were enrolled. Patients with APR (APR+) were subdivided into four groups according to degree of responsiveness during seizures. Cerebral blood flow changes during these seizures were semiquantitatively assessed by subtraction ictal SPECT coregistered to MRI (SISCOM).

Hyperperfusion in temporal regions did not vary significantly between the APR+ and APR− groups. Cerebral blood flow changes in the frontal area, insula, cingulum, and occipital area were also nonsignificant. However, hyperperfusion in the ipsilateral parietal areas was more frequent in the APR− group than in the APR+ group. Furthermore, hyperperfusion of the contralateral basal ganglia showed an inclination to be more common in the APR− group, but without statistical significance.

The study suggested that the involvement of the parietal association cortex during seizure may play an important role in ictal loss of consciousness in TLE. Further studies will be needed to elucidate the pathophysiology of changes in consciousness during temporal lobe seizures.

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1. Introduction

Ictal automatism with preserved responsiveness (APR) is defined as the ability of patients to respond verbally or to follow motor commands during seizure [1]. Automatism with preserved responsiveness is an uncommon phenomenon in temporal lobe epilepsy (TLE), but has been reported in several studies, especially in nondominant temporal lobe epilepsy [1–4]. The prevalence of APR remains controversial, but Ebner et al. reported an occurrence rate of 5.7% in TLE and 10% in right TLE [1].

Previous reports suggested that impaired level of consciousness (LOC) in temporal lobe seizures may result from focal abnormal ictal activity in the temporal and subcortical networks, which has been linked to widespread impaired function of the connected cortical or subcortical regions [5–8]. However, in prior studies, the inclusion of subjects with inhomogeneous etiologies and epilepsy syndromes [7] and the use of data from different diagnostic tests or types of seizure [5,6] and from the late ictal and postictal periods [5] made detecting LOC and its interpretation difficult. Automatism with preserved responsiveness in TLE therefore may be a useful model for determining the mechanism of changed LOC in temporal lobe seizures in cases with relatively less language deterioration caused by early ictal spreading from the ipsilateral temporal lobe toward the dominant hemisphere.

Ictal single photon emission computed tomography (SPECT) is an effective evaluation tool for focal increases in cerebral blood flow (CBF) associated with an ictal increase in neuronal metabolic activity [9]. Moreover, ictal perfusion changes associated with alterations in LOC in epileptic seizures suggest extensive neuronal network involvement during the ictal period in patients with TLE [10].

In the present study, we analyzed the characteristic hyperperfusion patterns of patients with APRs compared with those with ictal unresponsiveness in right TLE using subtraction ictal SPECT coregistered to MRI (SISCOM).

2. Methods

2.1. Patients enrolled

We retrospectively evaluated a group of consecutive patients with right TLE who underwent video-electroencephalography (EEG)

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monitoring and SPECT tests between March 2003 and March 2017 at one university-affiliated hospital. Epilepsy classification was determined based on the results of video-EEG monitoring, brain magnetic resonance imaging (MRI), PET, and SPECT images. Clinical characteristic data collected for each patient included duration of epilepsy, history of CNS infections and head trauma, and the presence of hippocampal sclerosis and other temporal lesions. If the subjects had undergone epilepsy surgery, surgical seizure outcomes were evaluated via outpatient clinic interview or participation in a phone interview.

We reviewed patient seizure videos and determined subject responsiveness during focal aware seizure (FAS) or focal impaired awareness seizure (FIAS) with automatism. Responsiveness was evaluated using the seizure interview protocol of our video-EEG monitoring unit. The interviews consisted of four categories including verbal (word memory, orientation, and verbal command) and nonverbal (motor command) questions. We defined 'preserved responsiveness' as more than one correct verbal or nonverbal response during ictal automatic behaviors. After independent review, the two reviewers (HR Park and YM Shon) resolved any disagreements by consensus.

In addition, subjects with APRs were subdivided into four groups according to degree of responsiveness during seizure: Groups 1 through 4 include subjects who responded correctly to only one (group 1), two (group 2), three (group 3), or all (group 4) of four categories.

The study was conducted with the approval of the Institutional Review Board of Samsung Medical Center, The Sungkyunkwan University of Korea, and informed written consent was obtained from all patients or from their family members.

2.2. Interictal and ictal SPECT studies

Brain SPECT scans were performed 30–60 min after the injection of 25 mCi 99mTc-ethyl cysteinate dimer (ECD) using a three-headed Triad XLT system (Trionix Research Laboratory, Inc., Twinsburg, OH). Interictal SPECT studies were performed when the patients had no documented seizure activity for more than 24 h. For ictal studies, patients underwent radiotracer injection during seizures. The time of radiotracer injection was defined as the time when the syringe plunger was fully depressed. Injection times were determined by reviewing video containing this information. We measured all subject SPECT injection times (the time interval between EEG seizure onset and radiotracer injection) and injection time index (the injection time divided by total seizure duration), and we excluded subjects whose injection time index on ictal SPECT was over 0.50.

Subtraction ictal SPECT coregistered to MRI analysis was performed on an offline workstation using ANALYZE 7.5 (Biomedical Imaging Resource, Mayo Foundation, Rochester, MN). Two neurologists (HR Park and YM Shon) who were blinded to patient information independently reviewed SISCOM images to determine regional hyperperfusion of cortical and subcortical structures. In addition, we defined 'Localized' as definite localized hyperperfusion in the temporal lobe, and 'lateralized' as hyperperfusion areas are only in the right hemisphere or dominancy of right hemisphere is obvious.

2.3. Statistical analysis

All data are presented as mean and standard deviation. The clinical characteristics of the APR group and control group were compared with Mann–Whitney U test for continuous variables and with Fisher's exact test for categorical variables. The comparison of hyperperfused areas on SISCOM images was analyzed by Fisher's exact test. The relationship between degree of APR and hyperperfusion in SISCOM images was analyzed using chi-square tests for trend. We compared hyperperfusion in ipsilateral and contralateral 13 brain regions in SISCOM image. Using the Bonferroni correction statistic, significance required P-values < 0.0019 in the comparison of regional hyperperfusion in SISCOM images. In other tests, P-values < 0.05 were considered

Table 1
Clinical characteristics of subjects with APRs and without APRs in right TLE.

	Subjects with APRs (N = 15)	Subjects with ictal unresponsiveness (N = 32)	p-Value
Age	26.5 ± 9.4	30.3 ± 11.8	0.338
Age at seizure onset	14.3 ± 8.3	18.6 ± 11.3	0.214
Male (%)	40.0	43.8	1.000
Hippocampal sclerosis (%)	60.0	75.0	0.324
Other temporal lesion (%)	6.7	21.9	0.250
History of head trauma (%)	0.0	9.4	0.541
History of CNS infection	6.7	21.9	0.250
SPECT injection time	28.6 ± 10.2	25.3 ± 13.1	0.174
Injection time index	0.31 ± 0.12	0.28 ± 0.11	0.345
Postoperative seizure-free rate (%)	75.0 (6/8)	80.6 (25/31)	1.000

APR: Ictal automatisms with preserved responsiveness, TLE: Temporal lobe epilepsy.
Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables. Significance requires p < 0.05.

statistically significant. Statistical analyses were performed with a commercially available software package (PASW version 18.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Demographics and clinical characteristics

A total of 47 patients with epilepsy with ictal onset in the right temporal lobe were included in this study. Among them, 15 subjects exhibited APR during seizure (APR + group), and the other 32 subjects exhibited ictal unresponsiveness (APR − group).

The demographics and clinical characteristics of the APR + group and APR − group are summarized in Table 1, and were similar between groups, including age, sex, duration of epilepsy, proportion of hippocampal sclerosis, other temporal lesions, and history of head trauma or CNS infection. Furthermore, SPECT injection time and injection time index were similar between the two groups. Eight of 15 subjects in the APR group and 31 of 32 subjects in the control group underwent epilepsy surgery, and the postoperative seizure-free rate was not significantly different between the two groups.

Fifteen subjects in the APR + group were subdivided into 4 groups according to the degree of responsiveness: 3 subjects were classified into group 1, 6 subjects into group 2, 4 subjects into group 3, and 2 subjects into group 4 (Table 2).

3.2. SISCOM images analysis

The results of SISCOM image analysis were summarized in the Table 3. The proportion of localized or lateralized hyperperfusion was not significantly different between the APR + group and the APR − group. Furthermore, we compared hyperperfusion in ipsilateral and contralateral 13 brain regions in SISCOM images with Bonferroni correction. Hyperperfusion in the ipsilateral and contralateral mesial, lateral temporal, and temporal stem areas were not significantly different between the two groups.

Table 2
Subdivision of subjects with APR group according to their degree of responsiveness.

Group	Number of categories with correct responses (among total of four)	No. of patients (%)
1	1	3 (20.0)
2	2	6 (40.0)
3	3	4 (26.7)
4	4	2 (13.3)

APR: Ictal automatisms with preserved responsiveness; The interviews consisted of four categories including verbal (word memory, orientation, and verbal command) and nonverbal (motor command) questions.