Composite SISCOM Perfusion Patterns in Right and Left Temporal Seizures

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Objective: To compare composite subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging (also known as SISCOM) patterns between right and left medial temporal-onset seizures to document neuroanatomical involvement in perfusion patterns.

Design: A retrospective comparative survey.

Setting: Epilepsy monitoring unit in a tertiary care referral center.

Participants: Subjects with temporal lobe epilepsy (TLE) who underwent ictal single-photon emission computed tomography studies.

Main Outcome Measures: Comparison of ictal perfusion pattern changes in subjects with right and left temporal seizures.

Results: Composite subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance images showed similar regions of hyperperfusion change in the ipsilateral anteromedial temporal–corpus striatum–insula region in both groups. In the midbrain reticular formation, there was a significant difference in hyperperfusion between the left and right TLE groups. In addition, the right, but not the left, TLE group shows contralateral hypoperfusion of the temporoparietal junction.

Conclusions: While anteromedial temporal–corpus striatum–insula perfusion patterns are similar, there are brainstem and hemispheric perfusion pattern differences in right and left TLE seizures, confirming pathophysiological differences between the groups. These findings help define neuronal network involvement in TLE seizures, and may explain the differences in clinical symptoms of right and left TLE seizures.

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Recent advances in neuroimaging have enabled measurement of brain function during the ictal state. Notably, single-photon emission computed tomography (SPECT) allows measurement of changes in cerebral perfusion patterns during seizures.1,2 Ictal SPECT-documented perfusion changes are related to electrographic seizure patterns,3 and provide valuable insight into neuronal network function in epilepsy.4

By using subtraction SPECT, previous investigators5-6 have demonstrated patterns of ictal perfusion changes associated with alteration of consciousness in epileptic seizures. Given the differences in ictal symptoms of right and left temporal lobe epilepsy (TLE) seizures,7 which are suggestive of differences in pathophysiological features between groups, analyzing right and left TLE seizures together may have confounded the differences of perfusion due to laterality of seizure onset. This study identifies hyperperfusion and hypoperfusion patterns in subjects with medial temporal-onset seizures according to the side of seizure onset and compares the patterns between groups. In addition, we interpret results in the context of neuronal network function in epilepsy and discuss findings of global perfusion changes in the context of clinical symptoms of right and left temporal lobe seizures.

Methods

Patients and Clinical Variables

We retrospectively analyzed 32 consecutive patients with medically intractable TLE who underwent ictal and interictal SPECT studies. The study protocol was approved by the Saint Louis University institutional review board. All patients underwent long-term video electroencephalographic (EEG) monitoring, ictal and interictal SPECT studies, and high-resolution magnetic resonance imaging (MRI). Two of us (K.K. and M.E.B.) reviewed long-term video-
**Table. Baseline Characteristics of the Subjects**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TLE Group</th>
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<tbody>
<tr>
<td></td>
<td>Left (n = 17)</td>
</tr>
<tr>
<td>Age, y†</td>
<td>32.4 (11.7)</td>
</tr>
<tr>
<td>Sex§</td>
<td>Male 7 (41)</td>
</tr>
<tr>
<td></td>
<td>Female 10 (59)</td>
</tr>
<tr>
<td>SPECT scanner protocol§</td>
<td>1 6 (35)</td>
</tr>
<tr>
<td></td>
<td>2 11 (65)</td>
</tr>
<tr>
<td>Injection time, s†</td>
<td>32.1 (12.3)</td>
</tr>
<tr>
<td>Symptoms during ictal SPECT injection</td>
<td></td>
</tr>
<tr>
<td>Motionless staring (n = 6)</td>
<td>3</td>
</tr>
<tr>
<td>Automatism (n = 14)</td>
<td>7</td>
</tr>
<tr>
<td>Dystonic posturing (n = 7)</td>
<td>4</td>
</tr>
<tr>
<td>Versive head movements (n = 5)</td>
<td>3</td>
</tr>
<tr>
<td>EEG pattern at injection</td>
<td></td>
</tr>
<tr>
<td>Ipsilateral temporal δ (n = 17)</td>
<td>9</td>
</tr>
<tr>
<td>Ipsilateral temporal δ (n = 3)</td>
<td>2</td>
</tr>
<tr>
<td>Bitemporal δ (n = 3)</td>
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</tr>
<tr>
<td>Bitemporal δ (n = 1)</td>
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<tr>
<td>Diffuse δ (n = 4)</td>
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<tr>
<td>Seizure duration, s†</td>
<td>89.0 (37.2)</td>
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<tr>
<td>Pathological diagnosis (n = 20)</td>
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<tr>
<td>Hippocampal sclerosis</td>
<td>10</td>
</tr>
<tr>
<td>Subcortical heterotopia</td>
<td>0</td>
</tr>
<tr>
<td>DNET*</td>
<td>1</td>
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</table>

*Abbreviations: DNET, dysembryoplastic neuroepithelial tumor; EEG, electroencephalographic; NA, data not applicable; SPECT, single-photon emission computed tomography; TLE, temporal lobe epilepsy.
†Data are given as number of subjects in each group unless otherwise indicated.
‡Comparison of left and right TLE groups using the 2-tailed unpaired t test.
§Data are given as number (percentage) of each group.

EEG monitoring results during ictal SPECT studies to determine the time of seizure onset and end, the time of radiopharmaceutical injection, seizure symptoms, and EEG localization. The epileptogenic focus was localized based on the long-term scalp video-EEG, neuroimaging studies, intracranial EEG (if available), and surgical outcomes.

**IMAGE ACQUISITION AND PROCESSING FOR COMPOSITE SUBTRACTION ICTAL SPECT COREGISTERED TO MRI STUDIES**

The SPECT images were obtained using 2 different protocols because of an upgrade of the SPECT scanner at our institution. Both protocols produce comparable results. SPECT acquisition and composite subtraction ictal SPECT coregistered to MRI studies were performed as previously described.

In summary, after SPECT-to-SPECT coregistration and SPECT normalization, the normalized interictal SPECT image was matched to the template SPECT image. The variables generated for the normalized interictal SPECT image were then applied to the normalized ictal SPECT image. The transformed interictal and ictal SPECT images were subtracted and segmented in binary format to show only voxel intensities greater than 1 SD (for hyperperfusion studies) or less than 1 SD (for hypoperfusion studies). These subtracted images were then added together to make the final composite image. The composite SPECT image was coregistered to the template MRI using the coregistration coordinates of the template SPECT image and MRI.

**RESULTS**

Thirty-two patients with medial temporal-onset seizures were included. Baseline demographic and physiological variables were not different between subjects with right and left TLE (Table). One subject in the left TLE group had a simple partial seizure. All other subjects had complex partial seizures. No subject had secondarily generalized tonic-clonic seizures.

**HYPERPERFUSION PATTERNS**

Composite subtraction ictal SPECT coregistered to MRI images of the right and left TLE groups showed similar areas of hyperperfusion changes in the ipsilateral anteromedial temporal–corpus striatum–insula, bilateral orbitofrontal, bilateral thalamus, and contralateral temporal regions (Figure 1 and Figure 2). Significant hyperperfusion in the region of brainstem tegmentum was observed in the left, but not the right, TLE group.

**HYPOPERFUSION PATTERNS**

Visual inspection of hypoperfusion changes showed the most prominent involvement in the cerebral midline structures and cerebellar hemispheres, bilaterally (Figure 3 and Figure 4). However, hemispheric asymmetries in the right and left TLE groups were also present. Significant contralateral hypoperfusion of the temporo-parietal junction was observed in the right, but not the left, TLE group. In addition, larger regions of hypoperfusion were seen throughout the contralateral occipital lobe in the right TLE group (Figure 4).

Figure 5 shows hyperperfusion of limbic structures, surrounded by hypoperfusion of hemispheric cortical structures in the left TLE group.
Figure 1. Transaxial subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging (SISCOM) sections through the entire brain, showing regions of hyperperfusion. Images in the upper half of the figure represent the left temporal lobe epilepsy (TLE) group, while images in the lower half of the figure represent the right TLE group. Common regions of 1-SD change occur for 15 subjects in the left TLE group and for 14 subjects in the right TLE group; the difference in color scales, which are depicted below the composite SISCOM images of each group, is shown. The anteromedial temporal–corpus striatum–insula region shows a contiguous region of highly significant hyperperfusion in both groups. The ipsilateral anterior temporal regions show similar degrees of hyperperfusion in the left (15 of 17 subjects) and right (13 of 15 subjects) TLE groups (P < .001 for both). In addition, there is significant hyperperfusion of the bilateral thalamus and orbitofrontal and contralateral temporal regions. The left TLE group shows a contiguous region of hyperperfusion involving the anteromedial temporal–corpus striatum–insula region, posterior thalamus, and brainstem tegmentum. The pattern of brainstem involvement is absent in the right TLE group.
Our study suggests that the most commonly hyperperfused areas, the anteromedial temporal–corpus striatum–insula, represent the primary neuronal network activated during a temporal lobe seizure. This finding is consistent with the growing evidence that “partial” epilepsy involves not only a localized brain region but also interconnected structures in preferential patterns of neuronal networks.

Several studies using positron emission tomography,\(^1\) SPECT,\(^4\) functional MRI,\(^5\) and structural MRI\(^6\) have documented widespread interictal abnormalities in patients with TLE, implicating extensive effects of focal epileptic seizures and supporting the concept of neuronal network involvement of epilepsy. In addition, intracranial electrocorticographic recordings of preferential ictal propagation patterns, which are the best documented work in defining ictal neuronal networks, suggest widespread neuroanatomical involvement in TLE.\(^7\)\(^-\)\(^8\)

Previous parametric mapping studies\(^9\)\(^-\)\(^12\) of TLE showed ictal hyperperfusion in the ipsilateral anteromedial temporal region. While initial studies\(^12\) did not show involvement of deep gray matter structures, subsequent studies have confirmed involvement of the corpus striatum alone\(^2\) and the corpus striatum and the insula.\(^3\) Recently, Isnard et al\(^4\) performed depth electrode record-

ings of the insula and demonstrated insular cortex involvement in all of 81 recorded TLE seizures, confirming the extremely common involvement of the insula. In addition, intracranial EEG studies\(^5\) of the basal ganglia show changes dependent on seizure propagation. Based on correlative analysis of global ictal brain perfusion changes, Blumenfeld et al\(^6\) have proposed neuronal networks involving the basal ganglia and temporal structures and separate neuronal networks involving the thalamus, while Tae et al\(^7\) have proposed an ictal activation of the cortical-thalamic-hippocampal-insular network. However, intracranial EEG data suggest that the centromedian thalamic nuclei participate little in the direct spread of complex partial seizures.\(^8\) Given the correlation of ictal SPECT and EEG patterns,\(^4\) intracranial electrographic studies support our findings of a primary anteromedial temporal–corpus striatum–insula neuronal network activation in TLE.

While we found no significant asymmetry of hyperperfusion in the anteromedial temporal–corpus striatum–insula regions (the primary neuronal network) of the right and left TLE groups, there were differences in brainstem and hemispheric perfusion patterns. The differences between the right and left TLE groups from other studies\(^9\)\(^-\)\(^12\) using parametric analysis are inconsistent. The first of these studies\(^12\) did not show significant hyperperfusion changes in the brainstem tegmentum. In the
Figure 3. Transaxial subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging sections through the entire brain, showing regions of hypoperfusion. Images in the upper half of the figure represent the left temporal lobe epilepsy (TLE) group, while images in the lower half of the figure represent the right TLE group. Common regions of 1-SD change occur for 10 subjects in the left TLE group and for 11 subjects in the right TLE group. Hypoperfusion changes in both groups showed prominent involvement of the cerebral cortex, with the most pronounced involvement in the cerebral midline structures bilaterally. There are also regions of significant hypoperfusion of the bilateral cerebellar hemispheres in both groups. However, significant contralateral hypoperfusion of the temporoparietal junction was present in the right, but not the left, TLE group.
second study, Blumenfeld et al. found perfusion changes of the midbrain tegmentum, proposing a neuronal network involving the midbrain tegmentum, other brainstem structures, and the thalamus. In the third study, Tae et al. found significant ictal midbrain hyperperfusion in subjects with right and left TLE compared with a group of control subjects, but not when comparing with interictal and ictal scans. In 2 studies, right temporal scans were rotated so the entire group would show changes on the left side, which would explain why they did not find a difference in brainstem perfusion between right and left TLE onset studies.

As in previous studies, we found large regions of ictal hypoperfusion in the cerebral hemispheres, which tended to involve midline hemispheric structures. In addition, Blumenfeld et al. have proposed that regions of association cortex are primarily involved in ictal hypoperfusion in TLE. Comparing between right and left TLE groups, we did find asymmetries of involvement, with both groups showing greater involvement of the left pos-

Figure 4. Hypoperfusion patterns in the right and left temporal lobe epilepsy (TLE) groups. Hypoperfusion composite subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance images in axial, coronal, and sagittal planes, with the second column showing the left TLE group and the third column showing the right TLE group. The lowest intensity value of significance is represented by the transition of color scales between shades of green for both groups of images. This image serves to show regions of hypoperfusion asymmetry, such as significant contralateral hypoperfusion of the temporoparietal junction, which was present in the right, but not the left, TLE group. In addition, there is a larger region of hypoperfusion throughout the contralateral occipital lobe in the right TLE group, as seen on the axial images.
terior hemisphere, with significant hypoperfusion over the left temporoparietal region in the right TLE group (Figure 4).

There are ictal signs and symptoms that indicate lateralization of seizure onset. Some of these signs are relatively common, such as ictal dystonia, which lateralizes the ictal-onset zone to the contralateral hemisphere. Other signs, such as postictal aphasia (lateralizing to the dominant hemisphere), are explained by language function differences between the temporal lobes. However, the underlying pathophysiological basis of other ictal phenomena, such as ictal automatisms with preserved responsiveness, which are documented to localize seizure onset to the right temporal lobe, is uncertain. Our patient population showed typical TLE ictal symptoms, which correlate with the associated perfusion patterns. Because ictal automatisms with preserved responsiveness are relatively uncommon, they could not be studied using the sample size of the present study. However, the perfusion pattern differences of the right and left TLE groups provide a theoretical framework to explain some of the symptom differences of the groups, assuming that perfusion changes represent probabilities of ictal involvement in the pathophysiological mechanisms of TLE.

The differences in perfusion of the brainstem tegmentum correlate with the region of brainstem reticular formation. Given the clinical similarities between groups, it is appropriate to compare probabilities of regional perfusion changes. In this context, the greater than 60-fold difference in probabilities of hyperperfusion of the brainstem tegmentum between the left and right TLE groups is significant. Therefore, the hyperperfusion asymmetry in the brainstem reticular formation may explain why right temporal seizures, compared with left temporal seizures, cause a lesser degree of loss of consciousness in ictal automatisms with preserved responsiveness. Study of larger groups of patients and verification of the precision and accuracy of different image-processing techniques that allow direct statistical comparisons of changes between groups will be important in ongoing studies.

In conclusion, right and left TLE seizures show similar regions of hyperperfusion in the anteromedial temporal–corpus striatum–insula region in both groups. However, there are extratemporal perfusion asymmetries in patients with right, compared with left, TLE. Differences in perfusion of the brainstem tegmentum in the region of the reticular formation may explain some symptom differences between right and left TLE, such as relative preservation of consciousness in right TLE in ictal automatisms with preserved responsiveness.

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Figure 5. Images show 2 sagittal planes through the left temporal lobe in the left temporal lobe epilepsy group; sections through the insula (A-C) and through the corpus striatum (D-F) are shown. B and E show hyperperfusion subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging (SISCOM). C and F show hypoperfusion SISCOM. Common regions of 1-SD change occur in 15 subjects for hyperperfusion and in 10 subjects for hypoperfusion. The lowest intensity value of significance is represented as the transformation from green to yellow in the hyperperfusion images (B and E) and between shades of green in the hypoperfusion images (C and F). The hyperperfusion images show the anteromedial temporal region involvement and clearly demarcated involvement of the insula (B) and corpus striatum (E). In this plane, the hypoperfusion images (C and F) show diffuse involvement in the cerebral hemisphere, surrounding the region of hyperperfusion involving limbic structures (B and E).
Author Contributions: Study concept and design: Hogan and Kaiboriboon. Acquisition of data: Hogan, Kaiboriboon, Bertrand, and Rao. Analysis and interpretation of data: Hogan, Kaiboriboon, and Acharya. Drafting of the manuscript: Hogan and Kaiboriboon. Critical revision of the manuscript for important intellectual content: Hogan, Kaiboriboon, Bertrand, Rao, and Acharya. Statistical analysis: Hogan and Kaiboriboon. Administrative, technical, and material support: Hogan, Kaiboriboon, Bertrand, and Rao. Study supervision: Hogan.

REFERENCES


Calendar of Events: A New Web Feature

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