Neurophysiological and Neuroimaging Assessment of Complex Partial Seizures

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ABSTRACT

Background: CPS (complex partial seizures) represents the commonest type of refractory epilepsy and proper management of such seizures necessitates proper localization of the seizure focus. The techniques of EEG (electroencephalography) remain the principal investigation for localizing seizure foci. When clinical features and EEG are not localizing and structural neuroimaging studies are normal, functional imaging will be of great value. Objective: To specify the sensitivity of EEG as a localizing & lateralizing tool in the diagnosis of CPS and to compare the EEG findings with imaging studies. Methods: The study was conducted on 30 patients (13 males and 17 females) with CPS. Patients were assessed by clinical examination, interictal video EEG monitoring, brain MRI (Magnetic Resonance Imaging) study and interictal SPECT (Single Photon Emission Computed Tomography). Results: The localizing sensitivity of interictal EEG was 100%. The lateralizing sensitivity was 83.3%. The localizing and lateralizing sensitivity of MRI were both 30%. Qualitative SPECT had localizing and lateralizing sensitivities of 83.3% and 80.7% respectively. Quantitative SPECT had localizing and lateralizing sensitivities of 80% and 76% respectively. When EEG and SPECT findings were combined together, the lateralizing sensitivity was 100%. Conclusion: EEG is still the principal investigating tool for localizing seizure foci and confirming the site suggested by clinical features and SPECT is a useful diagnostic tool, especially when combined with EEG. (Egypt J Neurol Psychiat Neurosurg. 2010; 47(1): 99-106)

Key Words: Epilepsy, Complex partial seizures, EEG, SPECT.

INTRODUCTION

Electroencephalography (EEG) remains a very important tool in investigating patients with epilepsy. Also EEG is an essential tool in patients with established seizure disorders, in differentiating between various types of seizures. EEG abnormalities were detected in 70-90% of patients with temporal lobe epilepsy as reported by others. MRI of the brain is an important tool of investigation in the field of epilepsy researches. It provides valuable anatomic information and ensures recognition of almost all mass lesions, mesial temporal sclerosis and focal cortical dysplasia that may be responsible for the patients' seizures.

SPECT is a direct method of measuring cerebral blood flow (CBF) in three dimensions and an indirect method of measuring cerebral metabolism. Epileptic seizures represent enhanced neuronal activity that results in significant increase in cerebral brain metabolism and cerebral blood flow. An important application of SPECT in patients with epilepsy is to localize the epileptic focus in patients with refractory complex partial seizures, especially those of temporal lobe origin. Ictal SPECT could detect and localize the abnormalities in 80-100% of CPS patients as reported by McNally et al. and Lee et al. While in interictal SPECT in patients with CPS, abnormalities have been found to be in 70-90% of cases.

Aim of Work: To specify the sensitivity of EEG as a localizing & lateralizing non-invasive tool in the diagnosis of CPS and to compare the EEG findings with those of MRI and SPECT studies.

MATERIALS AND METHODS

Subjects:
30 epileptic patients with complex partial seizures were collected from the epilepsy outpatient clinic, Kasr El-Aini Hospital, Cairo University. 13 patients were males (43%) and 17 were females (57%). Their age ranged between 13 and 46 years with a mean of (25.8±9.3 years).

All patients were diagnosed as having complex partial seizures according to the ILAE classification, based on the detailed clinical symptomatology of seizures from an eyewitness (mostly a relative) and
from the patient, if possible and verified by the EEG findings.

**Exclusion criteria:**
1. Patients with other types of seizures.
2. Patients with subnormal mentality.
3. Patients with risk factors that may alter cerebral perfusion as diabetes mellitus, hypertension, dyslipidemia.
4. Patients with psychiatric disorders.
5. Patients with normal or non-localized interictal EEG record.

**Methods:**
All patients were subjected to the following battery of assessment:
1. Full history taking from the patient and more important from an eye witness.
2. Complete general and neurological examination.
3. Laboratory investigations including: blood glucose level, liver and kidney functions, lipid profile and uric acid.
4. Interictal EEG studies: We used 14 channels digitized Schwarzer GmbH, Medical diagnostic equipment and a digital video-camera (Panasonic AG 6040) recording machine.
5. Magnetic resonance imaging (MRI) of the brain: at the MRI unit of the Radiology Department of Kasr El-Aini Hospital using General electric medical system signal 1.0 Tesla. Moreover, the localizing and lateralizing values of MRI of the brain were also assessed. The lateralizing value of the MRI is defined as the ability of MRI to demonstrate a pathological lesion in the ipsilateral side of origin of the epileptic seizure (right or left), diagnosed by clinical or interictal EEG findings. Whereas, the localizing value is reported when the MRI can localize this lesion in a specific area of the brain.15
6. Radionuclide SPECT: Intercital radionuclide SPECT studies were performed for all patients in the Department of Nuclear Medicine, Cairo University, using Tc-99m-HMPAO16. Both qualitative and quantitative analyses were done.

**Statistical analysis:**
An IBM compatible PC was used to store and analyze the data and to produce graphic presentation of important results. Calculations were done by means of statistical software packages namely: "MICROSTAT" and "ABSTAT". Data were tabulated and statistically analyzed to evaluate the difference between various parameters done to the studied patients. The statistical analysis included; the arithmetic mean, standard deviation, standard error, hypothesis Student’s "t", X², and Pearsons’ Correlation tests.

### RESULTS

I. **Clinical Results:**

1. **Seizure description:**
   - **Age of seizure onset:** ranged from 1.5 to 40 years with a mean of (17.3±9.3 years).
   - **Duration of illness:** The duration of complex partial seizure ranged from 3 to 20 years with a mean of (8.5±4.9 years).
   - **Past history:** 5 patients (16.7%) reported past history of febrile convulsions, 5 patients (16.7%) gave a history of head trauma, 2 patients (6.6%) reported a history of brain operation (one patient reported evacuation of abscess and the other of blood evacuation) prior to seizure onset and 1 patient (3.3%) reported past history of meningitis.
   - **Family history:** 5 patients (16.7%) reported family history of epilepsy.
   - **Seizure semiology:**
      - 1. **Aura:**
         - 27 patients (90%) had an aura preceding their seizures, 18 patients (60%) had one type of aura (Table 1) and 9 patients (30%) reported more than one type of aura (Table 2).
      - 2. **Seizure frequency:**
         - The frequency of epileptic attacks in the last year among our patients ranged from 1/month to 20/month (mean of 7.1±5.9). 3 patients (10%) had no seizures for more than one year.
      - 3. **Antiepileptic treatment:**
         - 15 patients (50%) were taking monotherapy, 12 patients were on bitherapy while 3 patients (10%) were taking polytherapy (Table 3).
      - 4. **Postictal symptoms:**
         - 9 patients (30%) presented with amnesia, postictal sleep was present in 5 patients (13.3%), while confusion was present in 2 patients (6.6%).

2. **Clinical correlations:**
   No statistical correlation was found between fits frequency and sex of patients (P=0.2), age of onset (P = 0.6), duration of illness (P=0.7) or antiepileptic drugs (P=0.7).
   A statistically significant positive correlation was found between history of febrile convulsions and the fits frequency (P=0.03).
   No significant correlation was found between febrile convulsions and both age at onset or family history of epilepsy (P=0.1 and P=0.4 respectively).
   Furthermore, Four over five (or 80%) of the patients having history of febrile convulsions showed unilateral epileptic discharges in the EEG.
record, while one patient showed bilateral epileptic discharges. Also, MRI abnormalities were found in four of the five patients with history of febrile convulsions, but these abnormalities were not limited to MTS which was found in 2 patients of them. History of head trauma didn’t correlate to specific EEG or MRI findings.

II. EEG Results:

All patients had EEG abnormalities in the form of: spike/sharp and slow wave complexes in 26 patients (86.6%) and the remaining 4 patients (13.4%) had temporal intermittent delta activity together with sharp waves.

Unilateral epileptogenic discharges were found in 25 patients (83.3%), while the remaining 5 patients (16.7%) showed bilateral epileptogenic discharges.

III. Brain MRI results:

Abnormal brain MRI was found in 10 patients (33.3%), while 20 patients (66.7%) showed normal MRI (Table 4).

IV. Interictal SPECT Results:

1) Qualitative SPECT Results:

By visual inspection interictal SPECT revealed abnormal findings in 25 patients (83.3%); including 70% with unilateral hypoperfusion and 13.3% with bilateral hypoperfusion. The remaining 5 patients (16.7%) showed a normal finding.

2) Quantitative SPECT Results:

Quantitative computer analysis of interictal SPECT revealed that 24 patients (80%) had hypoperfusion areas of the brain; including 63.3% with unilateral hypoperfusion and 16.7% with bilateral hypoperfusion. While 6 patients (20%) had a normal finding.

V. Comparisons:

1) Diagnostic Sensitivity of EEG, MRI and SPECT:

Diagnostic sensitivity in detecting abnormalities among complex partial seizures patients was 100% for EEG, 33.3% for MRI and 83.3% & 80% for qualitative & quantitative SPECT respectively.

When MRI and SPECT (qualitative and quantitative) were combined the sensitivity in detecting abnormality was (86.6% and 83.3% respectively).

2) Localizing and lateralizing sensitivities of EEG, MRI and SPECT:

The sensitivity of EEG in localizing the epileptic focus was (100%), for MRI it was (31%) whereas it was (83.3%, 80%) for qualitative and quantitative SPECT. The lateralizing sensitivity of the EEG was (83.3%), for MRI it was (31%) and (80.7% and 76%) for qualitative and quantitative SPECT respectively.

The localizing sensitivity was (83.3%) on combining EEG and SPECT, while it was (100% and 96.7%) on combining EEG and SPECT (qualitative and quantitative respectively), and it had lower values of (80.7% and 76%) on combining the MRI and (qualitative and quantitative) SPECT.

3) Topographic concordance between EEG and SPECT:

Comparison of both techniques revealed that 11 patients (36.6%) had an identical localization of the epileptic focus and 5 patients (16.7%) had a larger area of epileptic discharges than that of hypoperfusion, 4 patients (13.3%) had bilateral epileptogenic discharges which was lateralized on SPECT, 3 patients (10%) showed bilateral hypoperfused area on SPECT, while was lateralized by the EEG and 5 patients (16.7%) had a normal test on SPECT test.

4) Topographic concordance between EEG and MRI:

Four patients (13.3%) showed identical localization of the epileptic focus and the MRI abnormalities; 2 patients (6.7%) had the same laterality but with larger area of epileptic discharges than that of the MRI findings, 2 patients (6.7%) had bilateral epileptogenic discharges while were lateralized and localized in the MRI, and the remaining 2 patients (6.7%) showed bilateral or diffuse pathology in the MRI.

Table 1. Number and Percentage of patients having one type of aura.

<table>
<thead>
<tr>
<th>Types of Aura</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epigastric</td>
<td>6</td>
<td>20%</td>
</tr>
<tr>
<td>Psychic symptoms</td>
<td>4</td>
<td>13.3%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>3</td>
<td>10%</td>
</tr>
<tr>
<td>Fear</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Visual hallucinations</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>1</td>
<td>3.3%</td>
</tr>
</tbody>
</table>
### Table 2. Number and Percentage of patients having different types of auras.

<table>
<thead>
<tr>
<th>Types of Aura</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epigastric and Auditory Hallucinations</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>Vertigo and Visual Hallucinations</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>Fear and Auditory Hallucinations</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>Fear and Vertigo</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Sensory symptoms and Vertigo</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Fear and Psychic symptoms</td>
<td>1</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

### Table 3. Antiepileptic drugs used among the 30 patients in the study group.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>10</td>
<td>33.3%</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>5</td>
<td>16.7%</td>
</tr>
<tr>
<td><strong>Bitherapy:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid + Carbamazepine</td>
<td>9</td>
<td>30%</td>
</tr>
<tr>
<td>Carbamazepine + Phenytoin</td>
<td>2</td>
<td>6.7%</td>
</tr>
<tr>
<td>Valproic acid + Phenytoin</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td><strong>Polytherapy:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid + Carbamazepine + Phenytoin</td>
<td>3</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Table 4. MRI findings in our patients.

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abnormal findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mesial temporal sclerosis:</td>
<td>4</td>
<td>13.4%</td>
</tr>
<tr>
<td>- Temporal lobe atrophy:</td>
<td>2</td>
<td>6.7%</td>
</tr>
<tr>
<td>- Parietal lacunar infarction:</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>- Frontal gliotic changes:</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>- Left hemiatrophy:</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>- Occipital leukodystrophy:</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td><strong>Normal finding</strong></td>
<td>20</td>
<td>66.7%</td>
</tr>
</tbody>
</table>

**Figure 1.** Interictal EEG in case No. 20 (32 year-old male) showing sharp waves over Left tempo-parietal epileptogenic dysfunction in the bipolar transverse montage.
**DISCUSSION**

The techniques of EEG remain the principal investigation for localizing seizure foci or confirming the site suggested by clinical features\(^{17}\). When clinical features and EEG are not localizing and structural neuroimaging studies are normal, functional imaging with SPECT will be of great value\(^{4}\).

In our study, history of febrile convulsions was demonstrated in 16.7% of our patients. This coincides with other studies which reported that 13-20% of patients with complex partial seizures had history of febrile convulsions\(^{19,20,21}\). While another study\(^{22}\) reported higher incidence up to 58% which could be attributed to different patient selection as most of the patients had MTS revealed by MRI of the brain, while in our study MTS was demonstrated in only 13.3% of patients. On the other hand, Lee et al.\(^{23}\) failed to confirm an association between febrile convulsions and partial epilepsy.
In our study, significant positive correlation was demonstrated between the history of febrile convulsions and frequency of complex partial seizures (P=0.03). In our patients, febrile convulsions were recurrent and prolonged and occurred in the presence of low grade fever. This goes in agreement with the previously reported study done by Annegers et al. However, we failed to demonstrate correlation between febrile convulsions and the age of onset (P=0.1), or the presence of a family history of epilepsy (P=0.4). This goes in agreement with the study done by Olivia et al.

Most of our patients with positive history of febrile convulsions showed lateralized epileptic discharges in the EEG record. This finding was previously reported in other studies. In our study, the frequency of auras was 90% which is within the range reported by other studies which ranged from 50-95%. This discrepancy is probably due to difference in patient selection. We also found that, epigastric aura was more common when the epileptic discharges were localized to the temporal lobe specially the right side. This was in agreement with the studies done by Palmini and Gloor, who found an association between viscerosensory auras including epigastric sensations and the right temporal lobe. While Williamson didn’t find lateralizing significance of the viscerosensory auras.

There was also good correlation in our study between psychic aura, fear, vertigo and the left temporal lobe which was also reported by others.

In our study, interictal scalp EEG revealed abnormalities in all the patients. Our findings are similar to the studies done by Pataraia et al. and Bocti et al., who also found EEG abnormalities in 100% of their patients with complex partial seizures.

In our work, the interictal EEG showed unilateral epileptic discharges in 83.3% of patients. This figure is within the range reported in other studies which ranged from 62% in the study of Cendes et al. to 94.7% in the work of Lee et al.

Localized interictal EEG abnormalities were detected in all our patients. This finding was equal to that found by Lee et al., who found localized abnormalities using interictal EEG in all their CPS patients. The authors excluded all patients without prominent EEG localization, like our study. While Spanaki et al. reported that, interictal scalp EEG was localizing in 53% of patients. Our higher figure is due to exclusion of patients with normal or non-localizing EEG records.

Our MRI results revealed abnormalities in 10 patients (33.3%), of which 4 patients had MTS (13.3%). These results are nearly similar to those of Maton et al., who reported MTS in 20% of patients with refractory epilepsy. On the other hand, Spanaki et al. reported abnormalities in 63% of their patients with refractory complex partial seizures, with 24% of them having mesial temporal sclerosis. Furthermore, MRI lateralized the abnormalities in 30% of our patients and localized the pathology in 30% of the patients. However, Mitchell et al. reported localizing and lateralizing sensitivities of 64% using volumetric MRI studies which were not used in our work.

Interictal SPECT showed localized hypoperfusion areas (83.3% and in 80%) of our patients in qualitative and quantitative SPECT respectively. This matches with the results of previous studies, in which abnormalities have been found to be in 70%-90% of cases. Furthermore, the lateralizing sensitivities, in our study, were 80.7% and 76% for qualitative and quantitative studies respectively. This also matches with the results of the studies of Spencer and Olivia et al. On the other hand, Rabinowicz et al. reported 100% lateralizing sensitivity of qualitative interictal SPECT in patients with CPS. This high figure may be due to patient selection; as all patients had unilateral MRI changes.

Concerning the topographic concordance between the EEG and SPECT findings in the present study, we found that SPECT hypoperfused areas were ipsilateral to EEG epileptic focus in 60% of the patients. This figure was lower than that obtained by Carrilho et al., who found 92% concordance between SPECT and EEG. In our study, 16.7% of patients showed normal qualitative SPECT which were localized by EEG. False normalization can occur if the patient had developed an epileptic seizure (passed unnoticed or during sleep) prior to interictal scan (within the last 24 hours). In such case, the scan may be normalized by temporary increase of flow to an otherwise hypoperfused area, thus balancing flow to the hemisphere.

Conclusion

In complex partial seizures, EEG is still the principal investigating tool for localizing seizure foci and confirming the site suggested by clinical features and SPECT is a useful diagnostic tool, especially when combined with EEG.

REFERENCES


