Facial Paresis in Patients with Mesial Temporal Sclerosis: Clinical and Quantitative MRI-based Evidence of Widespread Disease

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**Summary:** Purpose: To assess the frequency and significance of facial paresis (FP) in a well-defined cohort of mesial temporal lobe epilepsy (MTLE) patients.

**Methods:** One hundred consecutive patients with MRI findings consistent with mesial temporal sclerosis (MTS) and concordant electroclinical data underwent facial motor examination at rest, with voluntary expression, and with spontaneous smiling. Hippocampal, amygdaloid, and temporopolar (TP) volumetric measures were acquired. Thirty healthy subjects, matched according to age and sex, were taken as controls.

**Results:** Central-type FP was found in 46 patients. In 41 (89%) of 46, it was visualized at rest, with voluntary and emotional expression characterizing true facial motor paresis. In 33 (72%) of 46 patients, FP was contralateral to the side of MTS. By using a 2-SD cutoff from the mean of normal controls, we found reduction in TP volume ipsilateral to MTS in 61% of patients with FP and in 33% of those without (p = 0.01). Febrile seizures as initial precipitating injury (IPI) were observed in 34% of the patients and were classified as complex in 12 (26%) of 46 of those with FP and in five (9%) of 54 of those without (p = 0.02). The presence of FP was significantly associated with a shorter latent period and younger age at onset of habitual seizures, in particular, with secondarily generalized tonic-clonic seizures.

**Conclusions:** Facial paresis is a reliable lateralizing sign in MTLE and was associated with history of complex febrile seizures as IPI, younger age at onset of disease, and atrophy of temporal pole ipsilateral to MTS, indicating more widespread disease. **Key Words:** Mesial temporal lobe epilepsy—Hippocampal sclerosis—Facial paresis—Magnetic resonance imaging.

Although the first quantitative assessment of facial asymmetry was made by Darwin, in his 1872 discussion, “Sneering and Defiance” (Darwin, 1872), our interpretation of brain mechanisms controlling facial expression has relied on behavioral observations, physiologic excitation of the cerebral cortex, and clinical deductions based on localized brain trauma caused by disease and injury (Morecraft et al., 2004).

Unilateral facial paresis (FP) may result from a peripheral or a central lesion. Commonly, the peripheral lesion is infranuclear, as in Bell’s palsy. In such a case, paresis of the upper and lower segments of the face is found, although the upper part of the face is much less affected in central-type FP (Spillane, 1983).

Another aspect of FP is the existence of a clinical dissociation between voluntary and emotionally driven facial expressions (Privatdozentin et al., 2006). Emotional facial paresis (EFP) or mimic paresis refers to weakness of emotionally evoked facial movements such as smiling, with normal volitional activation. Conversely, volitional facial paresis (VFP) refers to a weakness of facial muscles on voluntary effort while emotional movements are preserved (Hopf et al., 1992).

Temporal lobe epilepsy (TLE) associated with mesial temporal sclerosis (MTS) has been recognized as a well-defined epilepsy syndrome and is the most common type of medically refractory epilepsy in adults requiring surgical treatment. The selection of these patients for surgery depends on the concordance of data from clinical, imaging, and electroencephalographic evaluations (Wieser, 2004).

Despite the neurologic examination in patients with TLE related to MTS generally being described as entirely normal (French et al., 1993), facial asymmetry with lower facial weakness has been studied as an important lateralizing sign in patients with epilepsy of temporal lobe origin. Facial weakness, especially during emotional expression, was observed in 26 to 86% of patients with TLE and was found to be contralateral to the epileptic temporal lobe in most of the patients, whereas it was uncommon in normal controls (Remillard et al., 1977; Cascino et al., 1993; Lessa et al., 1998).
1993; Jacob et al., 2003). In these patients, contralateral weakness was apparent at rest only rarely, being more obvious in voluntary movement and greatly enhanced by emotional expression. At times, marked asymmetry was noticed only when the patient was smiling (Remillard et al., 1977). Consequently, it was considered an EFP (Jacob et al., 2003).

The pathogenesis of facial asymmetry in TLE is not well understood. None of the previously reported series of patients with TLE and facial asymmetry had undergone quantitative magnetic resonance imaging (MRI) analysis. The aim of this study was to evaluate (a) the prevalence of facial asymmetry in a homogeneous cohort of patients with TLE related to MTS as the sole etiology; (b) its value as a lateralizing sign; (c) its condition of appearance and associated clinical findings, and finally (d) its correlation with quantitative MRI study of mesial and neocortical temporal lobe structures.

METHODS

Subjects

One hundred consecutive patients with drug-refractory mesial temporal lobe epilepsy (MTLE), who were considered possible candidates for epilepsy surgery, underwent a comprehensive presurgical evaluation at the Epilepsy Section of the Universidade Federal de Sao Paulo (UNIFESP), between March 2002 and February 2005. It consisted of a detailed clinical history, neurologic examination, high-resolution cerebral MRI, neuropsychological and psychiatric studies, and psychosocial assessments. Patients also underwent 2–6 days of continuous video-EEG monitoring with 32-channel EEG recording, with electrodes placed according to 10–10 system on the temporal lobe, including sphenoidal electrodes. All patients had clear MRI findings consistent with unilateral MTS and concordant interictal and ictal EEG data. Hippocampal sclerosis was defined if atrophy, an increased T2-weighted signal, a decreased T1-weighted signal, and disrupted internal structure of the hippocampus were present on visual inspection of MRI pictures (Kuzniecky et al., 1987; Berkovic et al., 1991; Jackson et al., 1993). The epileptogenic zone was determined by predominantly ipsilateral interictal epileptic abnormalities (80% cutoff) and unequivocal unilateral seizure onset recorded during prolonged video-EEG monitoring.

Clinical features were recorded prospectively according to a specific protocol developed for this study. Patients’ previous medical charts were also reviewed. Age at onset and type of initial precipitating injury (IPI), including febrile seizures, head trauma, hypoxia, and intracranial infection, usually before the age of 5 years, were recorded. Latent period between the IPI and onset of habitual seizures, age at first nonfebrile seizure, presence and age at onset of secondarily generalized tonic–clonic seizures (SGTCSs), and duration of epilepsy were also registered.

Estimation of the duration and frequency of seizures was based on a review of medical records and seizure calendars and specific questioning of the patient and family members. Age at onset of epilepsy was defined as the age at which habitual and recurrent seizures developed. The duration, or number of years of epilepsy, was defined as the interval between the age at onset and the time of the MRI.

The Ethics Committee of UNIFESP approved the study, and informed consent was obtained from all participants before their inclusion in this protocol.

Assessment of facial asymmetry

Short digital movies with both sound and video in standard MPEG format, with 1–2 min of duration, were taken under adequate light and head positioning, with all patients sitting and facing the camera. Patients were filmed under three conditions: at rest, during voluntary contraction of facial muscles when the patient was asked to show his teeth, and with emotional expression (e.g., smiling induced by a joke). Filming, better than photographs, is not limited to still pictures, allowing us to have a more accurate observation of the facial asymmetry. The whole examination was undertaken during the video-EEG monitoring and is available for review.

To ascertain observer bias, three neurologists (K.L., J.L., E.M.T.Y.), who did not have any information regarding the neurologic history, routine EEG recordings, or neuroimaging studies at the time of evaluation, independently examined all patients for the presence or absence of FP. Controversies were resolved by reexamination with the three investigators together.

Asymmetries were noted according to the degree of depression or diminished lateral and upward movement of the corner of the mouth and flattening of the nasolabial fold. Each patient was separated into one of three groups: left FP, no FP, and right FP.

Patients with asymmetries of growth, hemiatrophy, hemiparesis, a history of hemiparesis or Bell palsy in the past, or other lesions besides MTS were excluded.

At the time of this evaluation, none of the patients had undergone epilepsy surgical treatment.

Controls

Thirty control subjects, members of the hospital personnel and randomly selected healthy volunteers (15 women) with no history of head injury or significant medical or psychiatric illness were filmed and submitted to MRI studies under identical conditions with the patients. The mean age of the control group was 32.97 ± 8.83 years (range, 22–58 years), and two were left-handed.
Magnetic resonance imaging acquisition

The MR studies were performed on a 1.5-T Gyroscan (Philips Medical System, Eindhoven, The Netherlands) by using the same protocol for all patients and controls. This protocol included the following: sagittal T_1-weighted [repetition time (TR), 433 ms; echo time (TE), 13 ms; field of view (FOV), 25 cm; 6-mm slice thickness; matrix size, 256 × 512]; axial turbo-spin echo T_2-weighted (TR, 4,535 ms; TE, 100 ms; FOV, 23 cm; 6-mm slice thickness; matrix size, 256 × 512); axial gradient-echo T_2*-weighted (TR, 707 ms; TE, 23 ms; flip angle, 15 degrees; FOV, 23 cm; 6-mm slice thickness; matrix size, 205 × 256); inversion recovery (IR) T_1-weighted (TR, 5,620 ms; TE, 17 ms; inversion time [TI] = 400 ms), and fluid-attenuated inversion recovery (FLAIR) (TR, 8,000 ms; TE, 150 ms; TI, 2,350 ms) with the same section thickness, FOV, and matrix (3 mm, 23 cm, 256 × 512, respectively) in the coronal planes perpendicular to the long axis of hippocampus, including the totality of the temporal lobe; fast field echo (FFE) T_1-weighted (TR, 30 ms; TE, 4.6 ms; one acquisition average pulse sequence, flip angle, 45 degrees; FOV, 23 cm; 1.5-mm slice thickness with no gaps; matrix size, 228 × 512) in the coronal plane.

Imaging processing

FFE T_1-weighted images were transferred to a workstation and processed by using the software Easy Vision 4.2 (Philips Medical System, Eindhoven, The Netherlands). Images were reformatted in the coronal planes, perpendicular to the long axis of the hippocampus and reoriented to correct for head tilt. This software allows simultaneous viewing of all scans in three orthogonal planes: coronal, sagittal, and horizontal orientations. The volumes of the hippocampus, amygdala, and temporal poles were measured by the same rater (K.L.) to ensure consistency, and were performed entirely with the manual contouring function because of the complexity of the structures involved. A combination of thresholding and tracing was used to outline boundaries and to contour manually the boundaries of these temporal structures. Hippocampal (Watson et al., 1992), amygdaloid (Watson et al., 1992), and temporopolar volumes (Insauti et al., 1998) were measured according to previously published protocols. Once the outline of each of these structures was defined on serial sections, a three-dimensional binary image was created, and its volume was measured in voxels. The number of voxels was then multiplied by appropriate voxel size to give the volume of these structures in cubic millimeters or centimeters.

A ratio was used to correct the volumes of these temporal structures for interindividual differences in head size according to a previously validated method (Mathalon et al., 1993; Free et al., 1995). The mean intracranial volume (IcV) of the 30 controls was divided by the corresponding IcV of the patient, and then this ratio was multiplied by the measured volume of the hippocampus, amygdala, and temporal pole. This method estimates IcV by modeling its volume as a sphere. The diameter of the sphere was determined by the height of the intracranial vault, based on a coronal slice obtained at the level of the anterior commissure in a plane perpendicular to the anterior commissure–posterior commissure (AC-PC) line. Half this height defined the radius of the sphere, and the total area (tissue + CSF) of the index section (first bilateral appearance of the frontal ventricular horns) from an axial MRI sequence represented the area of a plane passing through the center of the sphere (Pfefferbaum et al., 1992). The volume of the sphere, or IcV, was calculated as follows:

Intracranial volume = 4/3 × radius × area of index section

The degree of asymmetry between the left and right hippocampal, amygdaloid, and temporopolar volumes was examined by calculating asymmetry ratios according to Bernasconi et al. as follows (Bernasconi et al., 1999):

Asymmetry index = (right − left)/[(right + left) × 0.5]

Statistical methods

All results were presented as mean ± standard deviation (SD) to define dispersion. Student’s t test (two-tailed), Mann–Whitney, Fisher’s Exact test, and chi-square tests were performed to compare the means over the study groups and to evaluate the significance of the association of different clinical characteristics between patient and control groups, and between patients with and without FP.

Each individual’s volumetric measurements of temporal structures were also standardized in relation to the value of normal controls by using a z-score transformation [(volume − mean control volume)/control volume SD]. Therefore, for any individual, a z-score of −2.0 on any volumetric measure indicates a raw value that is 2 SD below the mean of normal controls on that measure and was considered abnormal.

The level of statistical significance was set at p < 0.05 in all studies.

RESULTS

The patients’ mean age at the time of evaluation was 36.36 ± 9.68 years (range, 15–62 years); 44 (44%) were male patients, and five (5%) with left-hand dominance by self-report.

Prevalence

Among 100 patients with definite diagnosis of pure MTS, unilateral lower facial weakness was found in 46 (46%) (Fig. 1).

Value as lateralizing sign

Fifty-seven (57%) patients had left MTS; 26 (45.61%) of them had facial asymmetry, which in 22 (84.61%) was
OF 43 (43%) patients who had right MTS, 20 (46.51%) had asymmetry, with contralateral weakness in 11 (55%).

Therefore among the 46 patients with lower FP, this sign was contralateral to the site of seizure onset in 33. The presence of contralateral FP correctly predicted the side of the epileptogenic zone in 71.74% patients.

Condition of appearance
Among 46 patients with lower facial weakness, only two (4.34%) had FP solely during smiling, three (6.52%) had FP during smiling and voluntary movement, and 41 (89.13%), during smiling, voluntary expression, and at rest.

Clinical features
The distribution of clinical variables among the groups of patients with and without FP is compared in Table 1. A significant association was found between presence of FP and shorter latent period and younger age at onset of habitual seizures, in particular SGTCSs, as shown in Fig. 2.

Medical history in 42 (42%) patients disclosed the presence of an IPI, 34 (34%) of them described as febrile seizures, with similar frequency between both groups with...
TABLE 1. Clinical variables (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>With FP (n = 46)</th>
<th>Without FP (n = 54)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male, female)</td>
<td>14 M, 32 F</td>
<td>30 M, 24 F</td>
<td>0.01a</td>
</tr>
<tr>
<td>Age at IPI (yr)</td>
<td>2.00 ± 1.56</td>
<td>1.82 ± 1.73</td>
<td>0.73b</td>
</tr>
<tr>
<td>History of febrile seizures</td>
<td>17/46 (36.96%)</td>
<td>17/54 (31.48%)</td>
<td>0.13c</td>
</tr>
<tr>
<td>Simple febrile seizures</td>
<td>5</td>
<td>12</td>
<td>0.02b</td>
</tr>
<tr>
<td>Complex febrile seizures</td>
<td>12</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Latent period (yr)</td>
<td>4.54 ± 6.67</td>
<td>10.34 ± 7.03</td>
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<tr>
<td>Age at onset of habitual seizures (yr)</td>
<td>6.54 ± 7.18</td>
<td>12.16 ± 6.78</td>
<td>0.01b</td>
</tr>
<tr>
<td>Age at onset of SPSs (yr)</td>
<td>14.03 ± 9.74</td>
<td>14.80 ± 8.61</td>
<td>0.71b</td>
</tr>
<tr>
<td>Age at onset of CPSs (yr)</td>
<td>16.02 ± 11.85</td>
<td>14.49 ± 8.04</td>
<td>0.45b</td>
</tr>
<tr>
<td>Age at onset of SGTCSs (yr)</td>
<td>7.05 ± 6.76</td>
<td>12.05 ± 9.81</td>
<td>0.01b</td>
</tr>
<tr>
<td>Frequency of seizures (per mo)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPSs</td>
<td>5.90 ± 7.00</td>
<td>5.15 ± 6.15</td>
<td>0.36b</td>
</tr>
<tr>
<td>CPSs</td>
<td>3.81 ± 2.27</td>
<td>5.60 ± 8.46</td>
<td>0.66b</td>
</tr>
<tr>
<td>SGTCSs</td>
<td>1.12 ± 1.47</td>
<td>2.13 ± 5.12</td>
<td>0.36b</td>
</tr>
<tr>
<td>Mean duration of epilepsy (yr)</td>
<td>26.95 ± 11.52</td>
<td>23.81 ± 10.16</td>
<td>0.16b</td>
</tr>
</tbody>
</table>

CPSs, complex partial seizures; FP, facial paresis; F, female; IPI, initial precipitating injury; M, male; SGTCSs, secondarily generalized tonic-clonic seizures; SPSs, simple partial seizures.

aχ².  
bStudent’s t-test.  
cFisher’s exact test.

and without FP, but a predominance of complex febrile seizures existed among patients with FP as an IPI. Febrile seizures were defined as seizures occurring during a pyrexic illness before the age of 5 years. In patients with seizures and a history of so-called “meningitis” or “encephalitis,” further hospital records were obtained and, unless unequivocal evidence was present of an antecedent illness, these cases were classified as febrile seizures. If a definite history of focal onset was found, multiple separated seizures during the same febrile illness, a seizure lasting more than 30 min that became indistinguishable from convulsive status epilepticus, or seizures with transient postictal hemiparesis, the febrile seizure was classified as complex.

To date, 60 patients have undergone anterior temporal lobectomy (ATL). While awaiting surgery, eight patients became seizure free with medication, and one died. The remaining patients are at present either awaiting operation or have refused surgery. Twenty-nine patients without FP and 31 with FP were submitted to surgical treatment, and MTS was confirmed as the only pathologic finding in 100% of them. Postoperative follow-up has been for a mean of 2.9 years (range, 1 month to 4.5 years). With Engel’s classification (Engel et al., 1993), 70% of the patients without FP and 79% of those in the FP group are currently in class I (p = 0.91).

Magnetic resonance imaging

No statistically significant difference was noted in volumetric values of hippocampus and amygdala and in the asymmetry index of the temporal structures between both groups of patients with and without FP (Tables 2 and 3). However, a marginally significant difference in temporal pole volume was found ipsilateral to MTS between patients with and without FP (Table 2).

Amygdalar signal abnormality ipsilateral to MTS was observed in 20 (37%) of the patients without FP, whereas this change was present in 11 (24%) of the patients with FP (p = 0.15). Temporopolar signal abnormality was observed in 32 (59%) of the patients without FP, whereas this alteration was present in 30 (65%) of those with FP (p = 0.24). All patients with temporopolar signal abnormality had it ipsilateral to MTS, characterized by loss of gray–white matter definition on T2-weighted study, with the main finding being increased T2 signal and decreased signal in T1-weighted IR sequence.

Comparison of the z-score of volumetric results between both groups, by using the cutoff of 2 SD from the mean of normal controls, demonstrated abnormally small temporal pole volume ipsilateral to MTS in 61% of...
patients with FP compared with 33% of patients without (p = 0.01) (Table 4).

**DISCUSSION**

The neurologic examination in patients with MTLE is often described as normal. However, since the 1970s, experienced neurologists have called attention to the presence of facial asymmetry in these patients (Remillard et al., 1977).

A cohort of homogeneous medically refractory TLE patients with unilateral MTS on MRI and concordant interictal and ictal EEG findings were evaluated to determine the frequency of FP and its associated features. About half of our patients had unilateral FP, and it correctly lateralized the side of the epileptogenic temporal lobe in more than two thirds of our series. These results agree with the three studies that investigated the association of EFPs with TLE. Remillard et al. compared 50 patients with unilateral temporal lobe lesions with 25 normal subjects, and EFP was detected in 86% of them, contralateral to the side of lesion in 73% (Remillard et al., 1977). Cascino et al. found lower facial weakness more obvious with emotional expression and smiling in all 13 patients studied among 50 consecutive candidates for ATL, and it was always contralateral to the epileptic temporal lobe, as determined by ictal EEG recordings. The surgically excised tissue in all patients revealed MTS (Cascino et al., 1993). Jacob et al. found 36 (72%) of 50 MTLE patients exhibiting unilateral EFP, correctly predicting the side of ATL in 86% of the patients. This clinical sign was significantly associated with longer duration of epilepsy before surgery and left ATL (Jacob et al., 2003).

Hence, observation of FP in patients with MTLE may be a clinically useful sign that may assist in lateralizing the site of seizure onset. Nevertheless, this sign was encountered to be ipsilateral to the MTS in 28% of our patients. Studies in normal subjects have shown that the left hemisphere, controlled by the right cerebral hemisphere, moves more extensively and appears more intense during emotional facial expression than does the right hemiface [i.e., a right hemisphere dominance exists for emotional expression (Borod and Caron, 1980; Moscovitch and Olds, 1982; Borod and Koff, 1983; Borod et al., 1988)]. This might be the reason for the incidental finding of facial asymmetry in normal subjects and also the finding of more frequent ipsilateral FP among our patients with right MTS.

It is also important to point out that FP was evident during volitional and emotional expression, and at rest in 41 (89%) of 46 of our patients. Thus this clinical sign cannot be considered solely an emotional facial asymmetry. We believe that a true central FP is clinically evident in this group of MTLE patients.

The pathogenesis of facial asymmetry in TLE is not well understood. Contralateral facial weakness appears to be caused by an upper motor neuron lesion, suggesting

<table>
<thead>
<tr>
<th>TABLE 2. Volumetric measures and z-scores of temporal structures of patients with and without facial paresis</th>
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<tr>
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<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Hippocampus (contra)</td>
</tr>
<tr>
<td>Hippocampus (ipsi)</td>
</tr>
<tr>
<td>Amygdala (contra)</td>
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<tr>
<td>Amygdala (ipsi)</td>
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<tr>
<td>Temporal pole (contra)</td>
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<tr>
<td>Temporal pole (ipsi)</td>
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<tr>
<td>Temporal pole (ipsi)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD. Volumes are ipsilateral or contralateral to mesial temporal sclerosis. The p-value is based on Student’s t-test.

**TABLE 3. Volumetric asymmetry index**

<table>
<thead>
<tr>
<th></th>
<th>With FP (n = 46)</th>
<th>Without FP (n = 54)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampal asymmetry index</td>
<td>0.52 ± 0.25</td>
<td>0.61 ± 0.25</td>
<td>0.09</td>
</tr>
<tr>
<td>Amygdaloid asymmetry index</td>
<td>0.19 ± 0.14</td>
<td>0.10 ± 0.11</td>
<td>0.29</td>
</tr>
<tr>
<td>Temporal pole asymmetry index</td>
<td>0.19 ± 0.29</td>
<td>0.14 ± 0.11</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD. The p-value is from Student’s t-test.

**TABLE 4. Percentage of patients with and without facial paresis, with reduction in volumetric measures ipsilateral or contralateral to mesial temporal sclerosis by using a two standard deviation cutoff from the mean of normal controls**

<table>
<thead>
<tr>
<th></th>
<th>With FP (n = 46)</th>
<th>Without FP (n = 54)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampal volume (contra)</td>
<td>15</td>
<td>11</td>
<td>0.54</td>
</tr>
<tr>
<td>Hippocampal volume (ipsi)</td>
<td>87</td>
<td>96</td>
<td>0.09</td>
</tr>
<tr>
<td>Amygdaloid volume (contra)</td>
<td>2</td>
<td>4</td>
<td>0.65</td>
</tr>
<tr>
<td>Amygdaloid volume (ipsi)</td>
<td>22</td>
<td>11</td>
<td>0.15</td>
</tr>
<tr>
<td>Temporal pole volume (contra)</td>
<td>13</td>
<td>11</td>
<td>0.77</td>
</tr>
<tr>
<td>Temporal pole volume (ipsi)</td>
<td>61</td>
<td>33</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Contra, contralateral; FP, facial paresis; Ipsi, ipsilateral.

The p-value is based on the Chi² test.
that, in addition to temporal structures, suprasylvian areas may be involved (Remillard et al., 1977).

The limbic lobe forms a continuous ring of cortex around the medial edge of the cerebral hemisphere, and it is characterized by marked structural and functional heterogeneity that in many ways mirrors the features of the isocortex that it borders. For example, the anterior part of the cingulate gyrus is bounded dorsally by the supplementary (M2) and primary motor cortices (M1) and has structural and functional commonalities with these isocortical motor fields (Morecraft and van Hoesen, 1998).

Recent neuroanatomic studies in nonhuman primates have revealed that corticofacial axons arise from the cortex in the lower bank and fundus of the cingulate sulcus, termed areas 24c or M3 (Morecraft and van Hoesen, 1992) and 23c or M4 (Morecraft et al., 1996). These segments have been shown to be major cortical entry points for widespread and diverse limbic lobe inputs originating from intracingulate, retrosplenial, retrolateral, orbitofrontal, insular, temporopolar, amygdalar, hippocampal, perirhinal, entorhinal, parasubicunal, and parahippocampal sources; they are connected with the face area of M1 and M2 in a somatotopically organized fashion and also contain a cingulate face representation projecting directly to the facial nucleus (Morecraft and van Hoesen, 1998).

The epileptogenic foci in MTLE reside in deep mesial temporal lobe structures, and seizure activity from this region often propagates to the anterior cingulate cortex (Lieb et al., 1991). The most commonly reported somatomotor manifestations in TLE semiology occur in the face, neck, and upper extremities (Bossi et al., 1984). Orofacial movements involve both upper and lower facial musculature and include blinking, eye closure, bilateral facial contraction, contralateral hemifacial contraction, ipsilateral facial clonic jerks, periocular movements such as "lip smacking," and a general change in overall facial expression (Bossi et al., 1984; Kotagal et al., 1995; Guimarães et al., 2005; Hogan and Rao, 2006).

Suggestions have been made that these motor manifestations are a consequence of secondary generalization of a temporal epileptogenic focus, occurring through reciprocal cortico-cortical projections from mesial temporal structures to lateral temporal cortices, converging to the primary motor and premotor lateral cortices (Bossi et al., 1984). These somatomotor manifestations may occur because of direct amygdalar projections to the premotor lateral cortex (lateral area 6) (Morecraft et al., 2003); through indirect pathways from mesial temporal structures to ventral forebrain or brainstem where the nuclei of the cranial nerves are located (Hopkins and Hostege, 1978); or through direct amygdalocingulate projections (Morecraft et al., 2003, 2004).

Therefore these reciprocal limbic–motor interactions provide a plausible basis for anatomic–electrical–clinical correlations in facial paresis among MTLE patients, whether by their direct involvement in the initial pathologic process or by propagation of seizure discharges outside the temporal lobe, across the sylvian fissure, generating permanent facial-expression disruption in our patients.

In addition, formulated largely on the basis of clinical correlates is the suggestion that separate neural systems exist for mediating voluntary and emotional facial movements. As seen in our patients, it is probable that functional overlap in emotional and voluntary circuitry occurs at the cortical level as well as subcortically, because anterior cingulate and lateral region of the primary motor cortex are interconnected.

Evidence exists also that the pathologic changes in the brains of patients with MTLE often extend beyond the mesial temporal structures. The HHE syndrome, proposed by the Marseille School in the 1950s, consists of a combination of hemiconvulsions (one or many convulsions, sometimes an epileptic status) followed by an ipsilateral hemiplegia occurring in the first years of life (Gastaut et al., 1959/1960). Thereafter, a free interval of months or years, with possible regression of the motor deficit, results in the appearance of chronic epilepsy of psychomotor type. The free interval corresponds to the maturation of cerebral lesions, during which the ischemic necrosis is replaced by an important glial proliferation and irritative scarring (Gastaut et al., 1959/1960).

Although no association was found between FP and presence and age of IPI, we found that FP was significantly related to the type and severity of IPI. Therefore we hypothesize that the early childhood illness, represented by a history of complex febrile seizures, is probably critical to the pathophysiologic process that leads to FP. If prolonged febrile seizures cause damage to the hippocampus via neuroexcitotoxic damage, then it may be that not only the hippocampus is damaged. This is consistent with a milder version of the proposed mechanism for the HHE syndrome, in which diffuse rather than focal hippocampal lesion occurs, leading to a more subtle clinical sign represented by FP.

Previous MRI investigations of MTLE patients demonstrated a diverse range of structural abnormalities extending beyond the ipsilateral hippocampus (Sutula and Herrmann, 1999; Wieser, 2004). More-widespread disease among our TLE patients with FP could be demonstrated, because 61% of them had abnormally atrophic temporal pole, whereas 33% of those without FP had it ipsilateral to the MTS. Nevertheless, these findings were not associated with signal abnormalities and a higher degree of atrophy of the other temporal structures. It is important to point out that whereas marked damage in the structures of the mesial temporal lobe is reliably identified with quantitative MRI, subtle forms of cell loss and loss of connection fibers may remain below the detection threshold of current MRI volumetric measurement techniques (Jack, 1994).
Furthermore, the pathologic changes in MTLE, characterized by neuronal loss, gliosis, and deposition of corpora amylacea, can be progressive over time (Sutula and Hermann, 1999; Tasch et al., 1999). The significant correlation among the presence of complex febrile seizures, shorter latent period, and younger age at onset of habitual and intractable seizures, including SGTCs and presence of FP, may be related to more widespread pathologic changes in those with longer duration of TLE.

Further studies will be necessary to assess the correlation between facial asymmetry and the disruption of reciprocal connections between cingulate cortex and temporal structures in patients with MTLE. Longitudinal studies with prolonged follow-up of MTLE patients without FP would be required to assess whether FP develops later in life as a result of cumulative consequences and as an end state of years of poorly controlled epilepsy, considering the hypothesis that repeated generalized seizures cause progressive, more-widespread neuronal loss or dysfunction, or because of the static effect of an initial etiologic substrate. Of years of poorly controlled epilepsy, considering life as a result of cumulative consequences and as an end state of years of poorly controlled epilepsy, considering the hypothesis that repeated generalized seizures cause progressive, more-widespread neuronal loss or dysfunction, or because of the static effect of an initial etiologic substrate.

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