Mesial Frontal Epilepsy and Ictal Body Turning Along the Horizontal Body Axis

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Objective: To evaluate the clinical utility of mesial frontal semiology.

Design: Retrospective case series.

Setting: Tertiary epilepsy referral center.


Main Outcome Measures: Inclusion criteria for both parts of the study were seizure localization by analysis of resection margins (mesial frontal, lateral frontal, orbitofrontal, nonfrontal) or intracranial exploration and an Engel class I outcome. In part 1, 84 patients had their habitual seizures analyzed by video encephalography using a semiology checklist of 47 items during the early phase (electrographic onset to 10 seconds) and late phase (rest of episode). Localization semiology was analyzed by χ² test with Bonferroni correction and cluster analysis when occurrence exceeded 10% in at least 1 region. In part 2, 144 patients had their habitual seizures screened with mesial frontal semiology from the first part of study during the early phase only.

Results: In part 1 of the study, the statistically significant localizing semiology for the mesial frontal region in the early phase was ictal body turning along the horizontal axis (57% of patients), crawling (57% of patients), restless (64.3% of patients), facial expressions of anxiety (42.9% of patients) and fear (35.7% of patients), grimacing produced by bilateral facial contraction (42.9% of patients), barking (32.1% of patients), head shaking (25% of patients), and pelvic raising (25% of patients) (all P < .001). In the late phase, recurrent utterance (21.4% of patients) was the additional statistically significant item (P < .002). In part 2 of the study, ictal body turning along the horizontal axis gave a 55.2% positive predictive value, which improved to 85.7% when clustered with restless, facial expressions of anxiety and fear, and barking.

Conclusions: Ictal body turning along the horizontal body axis and semiology with physiological movement are not only prevalent semiology items of mesial frontal lobe epilepsy but they distinguish mesial frontal from lateral frontal and orbitofrontal seizures.

Arch Neurol. 2008;65(1):71-77

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STUDY PART 1

Localization Steps and Video EEG Analysis

We retrospectively reviewed 152 patients (mean age, 30 years; range, 3-66 years; 62% male) who underwent presurgical evaluation leading to frontal lobe surgery at the University Department of Epileptology, Bonn, Germany, between 1997 and 2005. The location of resection was divided into mesial frontal, lateral frontal, and orbitofrontal using results of operation records and magnetic resonance imaging. When overlapping resections occurred, classification was made using data from intracranial exploration; otherwise, the patient would be excluded if no implantation was performed or if intracranial exploration did not provide localization to 1 of the 3 areas. The Engel outcome was determined in patients who had been followed up for at least 1 year (mean follow-up, 3.6 years). Only patients achieving an Engel Class I outcome were selected for video EEG analysis because the seizure foci in these patients were considered part of the resection and the semiology, as representative of such seizure foci. From 152 patients, 10 patients had overlapping resection margins (and no implantation or inconclusive implantation results); 9 patients, incomplete follow-up; and 49 patients, non-Class I outcomes. The remaining 84 patients underwent video EEG analysis. All patients (except 1) had their first 2 recorded habitual seizures analyzed. The mesial frontal group comprised 28 patients (55 seizures); the lateral frontal group, 48 patients (96 seizures); and the orbitofrontal group, 8 patients (16 seizures) (Figure 1). The digital recordings were reviewed by 3 epileptologists (H.L., K.S., and C.E.E.) blinded to the clinical information using a semiology checklist with 47 items. Each seizure episode was analyzed in the early phase (time of electrographic onset to 10 seconds) and late phase (the remainder of the seizure episode). The 10-second dividing line was chosen because frontal seizures are generally short (about 30 seconds). The interrater reliability of semiology assignment using a test semiology gave an average \( \kappa \) value of 0.78 (95% confidence interval, 0.56-0.99).

Definitions

The mesial frontal region was defined as the mesial aspect of the frontal lobe bounded posteriorly by the cingulate sulcus and the marginal ramus and inferiorly by the corpus callosum, thus encompassing the paracentral lobule, cingulate gyrus, medial frontal gyrus, and frontopolar area. The 47-item list comprised semiology that may be classified as elementary motor, automatism, nonmotor, and autonomic, with or without lateralizing (left/right) potential. They were derived from the guidelines set out by the International League Against Epilepsy. Ictal body turning along the horizontal axis was defined as truncal turning without any tonic element of the extremities for 90° or more, parallel to the body axis and horizontally (Figure 2A). The other types of body turning analyzed in this study included ictal body turning along an axis that produced “sitting up,” (Figure 2B) and ictal body turning along a vertical axis that resulted in head turned to one side and feet to another (Figure 2C).

Statistical Analysis

Semiology items with more than 10% occurrence in patients in at least 1 region (mesial frontal, lateral frontal, or orbito-
Patients were selected for \( \chi^2 \) test with Bonferroni correction. The occurrence of each semiology item was compared among the 3 frontal regions. A 2-tailed significance level was set at .05. Statistical analysis was performed using SPSS version 11.5 (SPSS Inc, Chicago, Illinois). Statistically significant localization semiology items for the mesial frontal region were further subjected to cluster analysis when more than 5 items existed.

**STUDY PART 2: ADDITIONAL STEPS TO CALCULATE THE CLINICAL USEFULNESS OF MESIAL FRONTAL SEMIOLOGY**

We reviewed 253 patients with nonfrontal epilepsy (mean age, 39 years [range, 4-70 years]; 60% male) who underwent surgery between 1997 and 2005 at the University Department of Epilepsy, Bonn, Germany. Thirty-seven patients had overlapping resection margins (and no implantation or inconclusive implantation results), 9 patients were lost to follow-up, and 63 patients had a non–Class I outcome. The remaining 144 patients had their first 2 recorded habitual seizures analyzed. The temporal group comprised 127 patients (254 seizures); the occipital group, 4 patients (8 seizures); and the parietal group, 13 patients (26 seizures) (Figure 3). The same 3 epileptologists screened the statistically significant localization semiology items from the first part of study (limited to early phase of seizure) to evaluate the clinical utility of semiology of mesial frontal epilepsy.

### RESULTS

**SEMILOGY IN THE EARLY PHASE OF SEIZURES**

Thirty-five of 47 semiology items satisfied the inclusion criteria for statistical analysis. The statistically significant localization semiology items for the mesial frontal region were ictal body turning along the horizontal axis (58.2% of seizures; 57% of patients), crawling (58.2% of seizures; 57% of patients), restlessness (56.4% of seizures; 64.3% of patients), facial expressions of anxiety (41.8% of seizures; 42.9% of patients) and fear (36.4% of seizures; 35.7% of patients), grimacing produced by bilateral facial contraction (34.5% of seizures; 42.9% of patients), barking (30.9% of seizures; 32.1% of patients), head shaking (23.6% of seizures; 25% of patients), and pelvic raising (23.6% of seizures; 25% of patients) (all \( P < .001 \)) (Table 1). Ictal body turning along an axis that produced sitting up (27.3% of seizures; 28.6% of patients), and hyperkinetic lower limb movement (25.5% of seizures; 25% of patients) were prevalent in mesial frontal seizures without localizing value. All statistically significant items belonged to the automatism category.

**SEMILOGY IN THE LATE PHASE OF SEIZURES**

Thirty-one of 47 semiology items satisfied the inclusion criteria for statistical analysis. The statistically significant localization semiology items for the mesial frontal region were facial expressions of fear (43.6% of seizures; 42.9% of patients) and anxiety (40% of seizures; 39.3% of patients), crawling (27.3% of seizures; 32.1% of patients), and recurrent utterances (16.4% of seizures; 21.4% of patients) (all \( P < .002 \)) (Table 2). By contrast, bimanual bimanual automatism (61.8% of seizures; 60.7% of patients), restlessness (52.7% of seizures; 53.6% of patients), dystonic limb posture (45% of seizures; 46.4% of patients), hyperkinetic upper limb movement (41.8% of seizures; 42.9% of patients), clonic limb jerks (38% of seizures; 39.3% of patients), ictal body turning along an axis that produced sitting up (27.3% of seizures; 28.6% of patients), and hyperkinetic lower limb movement (25.5% of seizures; 25% of patients) were prevalent in mesial frontal seizures but without localizing value. All statistically significant items belonged to the automatism category.

**CONSISTENCY OF SEIZURE DEMONSTRATION**

Each patient may demonstrate a particular semiology in 0, 1, or 2 seizure episodes. When considering semiology items with more than 10% occurrence in patients, the ratio of seizure episodes to number of patients gives an estimate of the consistency of seizure demonstration (the number ranges from 1-2). The average ratio in the early phase was 1.85 (95% confidence interval, 1.79-1.92) and in the late phase, 1.82 (95% confidence interval, 1.75-1.88).

**CLUSTER ANALYSIS OF MESIAL FRONTAL LOBE EPILEPSY SYNDROME**

In the early phase, the most strongly clustered syndrome consisted of ictal body turning along the horizontal axis, restlessness, facial expressions of anxiety and fear, and barking. The statistically significant semiology items from the late phase did not satisfy the criteria for cluster analysis (Figure 4).
Ictal body turning along the horizontal axis is a novel semiology capable of distinguishing the 3 frontal anatomical regions (Figure 5). It occurred in 16 patients among 28 patients with mesial frontal epilepsy but it only occurred in 13 patients among 200 patients with nonmesial frontal epilepsy (lateral frontal epilepsy; 3 of 48; orbitofrontal epilepsy; 0 of 8, temporal epilepsy; 10 of 127; occipital epilepsy, 0 of 4; and parietal epilepsy 0 of 13). The sensitivity of ictal body turning along the horizontal axis was 57% (16 of 28); the positive predictive value, 55.2% (16 of 29); the specificity, 93.5% (187 of 200); and the positive likelihood ratio, 8.8 (Table 3).

Limiting the analysis to a cohort of frontal epilepsy only would improve this positive predictive value to 84.2% (Table 3). More importantly, if we use the clinical cluster of ictal body turning along the horizontal axis, restlessness, facial expressions of anxiety and fear, and barking, the positive predictive value remains at 85.7%, even for the entire cohort of patients (Table 3).

**CLINICAL UTILITY OF ICTAL BODY TURNING ALONG THE HORIZONTAL BODY AXIS**

Among the patients with mesial frontal epilepsy and ictal body turning along the horizontal axis, the direction of turn during The Early Phase of Seizures According to Number of Patients

**LATERALIZING VALUE OF ICTAL BODY TURNING ALONG THE HORIZONTAL AXIS**

Among the patients with mesial frontal epilepsy and ictal body turning along the horizontal axis, the direction of turn...
was ipsilateral in 7 patients, contralateral in 7 patients, and neither in 2 patients (both directions occurred).

Our study confirmed that many semiology items may be prevalent in mesial frontal epilepsy but the one that is truly of localizing nature would be the physiological movement, a term preferred by us because such clinical manifestations are often akin to stereotyped motor behavior under voluntary control.

In previous studies adopting the gold standard method, rich descriptions of frontal semiology were given but localizing items may not have been sought, the definitions of the localizing items were diverse, or certain anatomical areas were excluded during study. In studies using only intracranial exploration, focal motor and complex partial seizures were found in a mixture of lateral frontal and fron-

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**Table 2. Semiology Items With More Than 10% Occurrence in at Least 1 Frontal Anatomical Region During the Late Phase of Seizures According to Number of Patients**

<table>
<thead>
<tr>
<th>Semiology</th>
<th>Mesial Frontal</th>
<th>Lateral Frontal</th>
<th>Orbitofrontal</th>
<th>$P$ Value Based on No. of Patients (Unadjusted)</th>
<th>$P$ Value Based on Seizure Episodes (Unadjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bimanual bipedal automatism</td>
<td>34 (61.8)</td>
<td>17 (60.7)</td>
<td>55 (57.3)</td>
<td>.07</td>
<td>.07</td>
</tr>
<tr>
<td>Restlessness</td>
<td>29 (52.7)</td>
<td>15 (53.6)</td>
<td>22 (22.9)</td>
<td>.02</td>
<td>&lt; .001c</td>
</tr>
<tr>
<td>Late dystonic limb posture</td>
<td>25 (45)</td>
<td>13 (46.4)</td>
<td>40 (42)</td>
<td>.86</td>
<td>.78</td>
</tr>
<tr>
<td>Facial expressions of fear</td>
<td>24 (43.6)</td>
<td>12 (42.9)</td>
<td>6 (6.3)</td>
<td>.001c</td>
<td>.001c</td>
</tr>
<tr>
<td>Hyperkinetic upper limb movement</td>
<td>22 (41.8)</td>
<td>12 (42.9)</td>
<td>21 (21.9)</td>
<td>.18</td>
<td>.03</td>
</tr>
<tr>
<td>Facial expressions of anxiety</td>
<td>22 (40)</td>
<td>11 (39.3)</td>
<td>6 (6.3)</td>
<td>.002</td>
<td>.001c</td>
</tr>
<tr>
<td>Limb clonic jerks</td>
<td>21 (38)</td>
<td>11 (39.3)</td>
<td>36 (37.5)</td>
<td>.99</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Ictal body turning along an axis that produced sitting up</td>
<td>15 (27.3)</td>
<td>8 (28.6)</td>
<td>13 (13.5)</td>
<td>.32</td>
<td>.10</td>
</tr>
<tr>
<td>Head shaking</td>
<td>15 (27.3)</td>
<td>8 (28.6)</td>
<td>1 (1)</td>
<td>.003</td>
<td>&lt; .001c</td>
</tr>
<tr>
<td>Crawling with tetrapod progression</td>
<td>15 (27.3)</td>
<td>9 (32.1)</td>
<td>4 (4.2)</td>
<td>.001c</td>
<td>&lt; .001c</td>
</tr>
<tr>
<td>Hyperkinetic lower limb movement</td>
<td>14 (25.5)</td>
<td>7 (25)</td>
<td>5 (5.2)</td>
<td>.05</td>
<td>.001c</td>
</tr>
<tr>
<td>Seizure during sleep</td>
<td>13 (23.6)</td>
<td>7 (25)</td>
<td>5 (5.2)</td>
<td>.05</td>
<td>.002</td>
</tr>
<tr>
<td>Simple vocalization</td>
<td>12 (21.8)</td>
<td>6 (21.4)</td>
<td>19 (19.8)</td>
<td>.96</td>
<td>.88</td>
</tr>
<tr>
<td>Facial clonic activity</td>
<td>10 (18)</td>
<td>5 (17.9)</td>
<td>33 (34)</td>
<td>.26</td>
<td>.07</td>
</tr>
<tr>
<td>Recurrent utterances</td>
<td>9 (16.4)</td>
<td>6 (21.4)</td>
<td>0</td>
<td>.002c</td>
<td>&lt; .001c</td>
</tr>
<tr>
<td>Escape reaction</td>
<td>8 (14.5)</td>
<td>4 (14.3)</td>
<td>4 (4.2)</td>
<td>.18</td>
<td>.03</td>
</tr>
<tr>
<td>Grimacing produced by bilateral facial contraction</td>
<td>7 (12.7)</td>
<td>4 (14.3)</td>
<td>7 (7.3)</td>
<td>.71</td>
<td>.49</td>
</tr>
</tbody>
</table>

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$a$ Thirty-one of 47 semiology items analyzed.

$b$ Four of 5 statistically significant items pointed to a mesial frontal localization.

$c$ Statistically significant items after $\chi^2$ and Bonferroni correction according to number of patients.

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**Dendrogram using average linkage (between groups)**

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Rescaled Distance Cluster Combine
Label
Anxiety
Fear
Barking
Body turning
Restlessness
Head shaking
Pelvic raising
Grimacing
Crawling
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**Figure 4. Cluster analysis of statistically significant localization semiology items for mesial frontal epilepsy during the early phase.**

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topolar seizures,\textsuperscript{13} bimanual bipedal automatism was localized to dorsolateral and mesial frontal regions,\textsuperscript{14} and complex motor automatism with bilateral coordinated leg movements were localized to mesial frontal or orbitofrontal onset.\textsuperscript{10} When considering studies based on scalp EEG, psychomotor seizures were identified in a frontobasal cingulate subgroup\textsuperscript{19} and motor agitation,\textsuperscript{16} vocalization, hyperventilation, truncal flexion, and complex gestural automatism\textsuperscript{11} were localized to frontopolar and orbitofrontal regions. Bilaterally coordinated limb movements, axial movements, vocalization, and nonmasticatory oral activity were attributed to the mesial frontal lobe.\textsuperscript{15}

In the literature, 1 study identified 13 patients demonstrating unidirectional whole-body turning\textsuperscript{20} and the direction of turn was contralateral to the epileptogenic focus. No definite localizing value was confirmed, although in 9 patients ictal onset was thought to originate from the temporal lobe based on surface EEG. Follow-up data were available in 6 of 13 patients. Ictal body turning with head/eye version or dystonic limb posture preceding turning were also included.\textsuperscript{20} In another study, gyratory seizures were identified in 12 patients.\textsuperscript{21} They occurred in 8 of 47 patients with frontal lobe epilepsy but only 4 of 169 patients with temporal lobe epilepsy. Using surface EEG localization in combination with imaging, the authors suggested a lateralizing value for gyratory seizures depending on whether the turn was preceded by forced head turning. Gyratory movement may

<table>
<thead>
<tr>
<th>No. of Patients (No. of Seizures)</th>
<th>Mesial Frontal Epilepsy</th>
<th>Nonmesial Frontal Epilepsy</th>
<th>Mesial and Nonmesial Frontal Epilepsy Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ictal body turning along the horizontal axis</td>
<td>16 (32)</td>
<td>13\textsuperscript{b} (26)</td>
<td>29 (58)</td>
<td>57 (16/28)</td>
<td>93.5 (187/200)</td>
<td>55.2 (16/29)</td>
<td>93.5 (187/199)</td>
<td>8.8 (57%/[1%−93.5%])</td>
</tr>
<tr>
<td>Present</td>
<td>12 (23)</td>
<td>187 (374)</td>
<td>199 (397)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>28 (55)</td>
<td>200\textsuperscript{c} (400)</td>
<td>228 (455)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6 (12)</td>
<td>1 (2)</td>
<td>7 (14)</td>
<td>21.4 (6/28)</td>
<td>99.5 (199/200)</td>
<td>85.7 (6/7)</td>
<td>90 (199/221)</td>
<td>42.8 (21.4%/[1%−99.5%])</td>
</tr>
<tr>
<td>Ictal body turning along the horizontal axis, restlessness, facial expressions of anxiety and fear, and barking</td>
<td>22 (43)</td>
<td>199 (398)</td>
<td>221 (441)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td></td>
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<tr>
<td>Total</td>
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</tr>
</tbody>
</table>

Abbreviations: NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

\textsuperscript{a}Includes lateral frontal, orbitofrontal, temporal, occipital, and parietal epilepsy.

\textsuperscript{b}Three patients with lateral frontal, 0 patients with orbitofrontal, 10 patients with temporal, 0 patients with occipital, and 0 patients with parietal epilepsy.

\textsuperscript{c}Forty-eight patients with lateral frontal, 8 patients with orbitofrontal, 127 patients with temporal, 4 patients with occipital, and 13 patients with parietal epilepsy.

\textsuperscript{d}Three patients with lateral frontal and 0 patients with orbitofrontal epilepsy.

\textsuperscript{e}Forty-eight patients with lateral frontal and 8 patients with orbitofrontal epilepsy.
take place in either the supine or standing position. Four patients operated on became seizure free. In our current study, a contralateral predictive value was not found, although we limited our analysis to patients with mesial frontal epilepsy and the definition of ictal body turning along the horizontal axis excluded coexisting tonic elements at onset. The lateralizing issue among all patients with ictal body turning along the horizontal axis will be explored in a separate study.

Motor expressions of genetically determined neuronal aggregates in the mesencephalon, pons, and spinal cord subserve innate behavior for survival. Such behavior bears the quality of physiological movement and may be hyperkinetic in nature, and it is related to the central pattern generator. Tassinari et al. proposed that in seizure conditions epileptic discharges may act as a trigger for the appearance of such behavior. Nocturnal frontal lobe epilepsy, a syndromic entity usually with no lesions and unremarkable electrophysiology results, also demonstrates such behavior.

A useful comparison can be made between ictal body turning and oromotor automatism, which is a semiology with physiological movement and localizing value to the mesial temporal region. The sensitivity of oromotor automatism is expected to be 68.8%, but the positive predictive value may be as low as 21%.27

The issue of epileptic discharge spreading early on during seizures may limit the analysis of semiology. The symptomaticogenic zone can be different from the epileptogenic zone. Analysis of how seizures spread by intracranial exploration may provide answers, although this was not carried out in the current study. Moreover, surgical results may be due to an effect of disconnection rather than resection, which is a drawback of the gold standard method. It has been suggested that semiology derived from video EEG studies of patients from tertiary referral centers may not be truly representative. Moreover, some patients were only followed up for 1 year, which may not be sufficient to judge whether seizures would recur. Finally, although the finding of semiology described in this study may aid seizure localization, clinicians are reminded to include psychogenic seizure as part of the differential diagnosis owing to the resemblance between semiology with physiological movement and pseudoseizure.

CONCLUSION

We have demonstrated that in the early phase of seizures ictal body turning along the horizontal body axis and physiological movement are not the only prevalent semiology items of mesial frontal lobe epilepsy but they can distinguish mesial frontal epilepsy from other frontal epilepsy entities.

Accepted for Publication: January 23, 2007.

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Financial Disclosure: None reported.

Funding/Support: Dr Leung was supported by the Henry C. H. Leung Scholarship of Hong Kong. Dr Schindler was supported by a scholarship of the Schweizerische Stiftung fur Medizinisch Biologische Stipendien (SSMBS) donated by Roche.

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