

## Analysis of ictal semiology: contralateral tonic activity associated with ipsilateral automotor seizure in temporal lobe epilepsy

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### Abstract

Ictal semiology is essential for the pre-operative evaluation of candidates for epilepsy surgery. We propose an ictal sign of temporal lobe epilepsy (TLE) termed tonic-automotor (TA), defined as contralateral tonic spasm of upper limb associated with ipsilateral hand automotor seizure and often accompanied ipsilateral head turning. We assessed the occurrence and lateralizing/localizing value of TA in TLE, we analyzed 129 seizures in 41 patients with TLE: 90 seizures in 30 patients with TLE of hippocampal sclerosis (TLE/HS) and 39 seizures in 11 patients with TLE of other lesions (TLE/non-HS). When compared with unilateral automotor seizure and unilateral tonic spasm, TA occurred more frequently in TLE/HS patients (40% vs 10% and 16.7%). In addition, 24 seizures in 12 patients with TA were observed only in TLE/HS patients and contralateral to the seizure focus based on the side of tonic spasm. However, there was no significant difference in the TLE/HS between dominant side and nondominant side. In addition, TA sign occurred relatively early in the ictal phase. Thus, TA may be a more reliable lateralizing sign of epileptogenic zone and a semiologic marker of TLE/HS patients.

### INTRODUCTION

The gold standard of successful epilepsy surgery is seizure free after resection of epileptogenic zone.<sup>1</sup> A comprehensive pre-operative evaluation of epilepsy, including video electroencephalogram (EEG) monitoring, and neuro-imaging and neuropsychological assessment, is crucial for the localization of epileptogenic zone. The importance of seizure semiology and clinical lateralizing signs has recently been increasingly recognized. Ictal semiology can improve the lateralization and localization of epileptogenic zone and provide additional information for the pre-operative evaluation.<sup>2-4</sup>

Temporal lobe epilepsy (TLE) is a common type of epilepsy in both adults and children. Useful ictal lateralizing signs in TLE patients include abdominal auras, unilateral dystonia, orolimentary automatism, hand automotor seizure, automatism with preserved responsiveness, versive seizure, unilateral tonic spasm, ictal vomiting, ictal verbalization/vocalization, postictal aphasia, and postictal nosewiping.<sup>5-8</sup>

On the basis of our analysis of video-EEG documented seizures in TLE, a clinical sign, a combination of contralateral tonic spasm and ipsilateral automotor seizure, was more frequently observed in TLE patients. The majority of previous studies investigated the lateralizing value of single motor sign. Investigations on the combined symptoms are rarely reported. Dupont *et al* reported that the combination of contralateral dystonic posturing and ipsilateral automatism was observed only in patients with mesial temporal lobe epilepsy (MTLE).<sup>9</sup> Asymmetric tonic limb posturing (ATLP, “figure-of-4 sign”) is also a combined symptom with bilateral tonic arm posture representing a “4”. Jobst *et al* found contralateral ATLP in 94% of patients with TLE.<sup>10,11</sup> To our knowledge, no study has reported the combination of contralateral tonic spasm and ipsilateral automotor seizure in TLE. The present study aimed to determine the lateralizing and/or localizing value of this sign in TLE.

## METHODS

### Patients

The study was approved by the local ethics committee. All the patients in this study gave informed consent prior to study. All the patients with TLE operated before July 2009, with outcome of Engel I for at least 2 years after surgery from the Department of Neurosurgery were recruited in this study. There were 41 patients (total 129 seizures) with refractory TLE, including 31 men and 10 women. They consisted of 90 seizures in 30 patients with TLE of hippocampal sclerosis (TLE/HS) and 39 seizures in 11 patients with TLE of non-HS (TLE/non-HS). The mean age was  $24 \pm 9.2$  years (range: 7-51 years). The mean number of seizures per patient was  $3.2 \pm 2.5$  (range: 1-10).

All patients completed comprehensive pre-operative evaluation, including medical history assessment, video-EEG monitoring, high-resolution magnetic resonance imaging/spectroscopy (MRI/MRS), neuropsychological assessment, and positron emission computed tomography (PET).

All patients were classified as Engel I in the 2-year follow-up. Histopathological examination revealed either hippocampal sclerosis (TLE/HS group,  $n=30$ ) or other lesions (TLE/non-HS group,  $n=11$ ). In the TLE/HS group, one patient had both hippocampal sclerosis and focal cortical dysplasia (FCD) in the neocortical temporal lobe. Of the 11 patients in the TLE/non-HS group, 3 (27.3%) had subarachnoid cysts; 4 (36.4%) had cavernomas; 2 (18.2%) had nonspecific gliosis;

and 2 (18.2%) had no specific lesions. We defined clinical seizure based on the semiological seizure classification developed by Luders *et al.*<sup>12</sup> In each seizure, the ictal signs were analyzed according to the chronological sequence of their occurrence. The analysis was performed by two independent observers, and only signs with consensus by both observers were included.

### Statistical analysis

Statistical analysis was performed with chi-square test and Fisher's exact test. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

### Occurrence of ictal motor signs in all patients

The following ictal sign was observed: contralateral tonic spasm of upper limb associated with ipsilateral hand automotor seizure, often accompanied by ipsilateral head turning (tonic-automotor [TA]). In one of these seizures, a progressive movement of left hand (including scratching and fumbling) and flexible tonic spasm of right upper limb were observed (Figure 1, picture 1-4). In another seizure, the patient manifested tonic spasm of right upper limb accompanied by automotor seizure of left hand and head turning left (Figure 1, picture 5-8). We observed TA sign in 12/41 (29.3%) patients and 24/129 (18.6%) seizures (Table 1). Unilateral automotor seizure was observed in 6/41 (14.6%) patients and 10/129 (7.8%) seizures. Unilateral tonic spasm was noted in 7/41 (17.1%) patients and 18/129 (14.0%) seizures.



**Figure 1** Picture 1-4 showed the progressive movement of left hand (including scratching and fumbling) and flexible tonic spasm of right upper limb in a patient. Picture 5-8 showed left-TLE/HS in another patient. Tonic spasm of right upper limb and fumbling of left hand was accompanied by left head turning.

**Table 1: Occurrence of three ictal motor signs in all patients with TLE**

<b>Ictal sign</b>	<b>Patient (n=41)</b>	<b>Seizure (n=129)</b>
Unilateral automotor seizure	6 (14.6%)	10 (7.8%)
Unilateral tonic spasm	7 (17.1 %)	18 (14.0%)
Tonic-automotor (TA)*	12 (29.3%)	24 (18.6%)

\*contralateral tonic spasm of upper limbs associated with ipsilateral automotor seizure and often accompanied by ipsilateral head turning.

There was no statistically significant difference in the occurrence of three signs in the whole group of patients (P=0.211) and in seizures (P=0.037) of the TLE patients.

#### *Lateralizing value of three ictal motor signs*

Table 2 outlines the lateralization of all observed signs. In patients with unilateral automotor seizures, 83.3% of patients and 70.0% of seizures were related to the ipsilateral onset seizures. Unilateral tonic spasm occurred more frequently in contralateral onset seizure (85.7% of patients and 72.2% of seizures).

We determined the lateralizing value of TA based on the side of tonic spasm. This sign was correlated with the contralateral onset seizure in all 12 patients (100%) and in all 24 seizures (P<0.0001). However, there was no significant difference in TLE/HS between dominant side and nondominant side (Table 3).

#### *Differences between the TLE/HS and TLE/non-HS groups*

Table 4 shows the differences in the ipsilateral automotor seizure, contralateral tonic spasm and TA sign between TLE/HS group and TLE/non-HS group. TA sign in 12 patients was observed only in the TLE/HS group. There was significant difference in the occurrence of TA between two groups (P<0.0001).

In the TLE/HS group, TA was more frequently noted when compared with ipsilateral automotor seizure and contralateral tonic spasm (P=0.015).

#### *TA in the chronological sequence of seizure*

Analysis of the chronological sequence of TA revealed that the sign was more often noted as a second sign, but less seen as the first and third sign, and never occurred in the later phase of seizures (Table 5). There was significant difference in the chronological sequence of seizures (P=0.001).

**Table 2: Lateralizing value of three ictal motor signs**

<b>Ictal sign</b>	<b>Ipsilateral</b>		<b>Contralateral</b>	
	<b>Patient</b>	<b>Seizure</b>	<b>Patient</b>	<b>Seizure</b>
Unilateral automotor seizure	5/6 (83.3%)	7/10 (70.0%)	1/6 (16.7%)	3/10 (30%)
Unilateral tonic spasm	1/7 (14.3%)	5/13 (16.1%)	6/7 (85.7%)	13/18 (72.2%)
Tonic-automotor (TA)*	0	0	12/12 (100%)	24/24 (100%)

\*lateralization of TA was base on the side of tonic spasm.

**Table 3: Frequency of TA in dominant/nondominant side in TLE/HS**

<b>Side of seizure</b>	<b>Patient (n=12)</b>	<b>Seizure (n=24)</b>
Left	6	12
Right	6	12
Total	12	24

**Table 4: Occurrence of three ictal motor signs in two groups of TLE patients**

Ictal sign	Patient (n=41)		Seizure (n=129)	
	TLE/HS (n=30)	TLE/non-HS (n=11)	TLE/HS (n=90)	TLE/non-HS (n=39)
Ipsilateral automotor seizure	3 (10.0%)	2 (18.2%)	5(5.6%)	2(5.1%)
Contralateral tonic spasm	5 (16.7%)	1 (9.1%)	7(7.8%)	6(15.4%)
Tonic-automotor (TA)	12 (40.0%)	0 (0%)	24(26.7%)	0(0%)

## DISCUSSION

Ictal semiology is essential for the evaluation of epilepsy surgery. It also provides additional information on the lesioned site in seizure, and is especially important for the selection of patients for noninvasive pre-operative evaluation. In most motor signs, single ictal sign has been described to be crucial for TLE and these signs include unilateral hand automotor seizure, unilateral tonic spasm, versive movement, and oro-alimentary automatism. However, the ictal signs are complex in the chronological sequence of seizure. The combination of different signs has been observed in the ictal phase, but the combined signs were not systematically investigated in previous studies.

In the present study, an ictal sign was observed and termed TA, defined as contralateral tonic spasm of upper limb associated with ipsilateral hand automotor seizure and often accompanied by ipsilateral head turning. In addition, the occurrence and lateralizing/localizing value of TA sign was compared with the unilateral automotor seizure and unilateral tonic spasm, which corresponded well to several earlier reports. Bleasel *et al* reported that tonic limb posturing occurred in 17.7% of patients with TLE<sup>13</sup>, which was consistent with our findings (17.1%). The frequency of occurrence of unilateral automotor seizure and correlation was not reported earlier. Our results showed that there was no significant difference in the occurrence of the three signs in all patients with TLE, but TA was only significantly found in the TLE/HS

group. Thus, TA may be a strong indicator of TLE/HS epileptogenic focus.

The lateralizing value of single ictal motor symptoms – unilateral tonic spasm and unilateral automotor seizure – has been investigated in previous reports. Dupont *et al* reported that unilateral motor automatism was predominantly ipsilateral to the seizure focus in patients with medial temporal lobe epilepsy (MTLE) and exclusively contralateral in patients with neocortical temporal lobe epilepsy (NTLE).<sup>9</sup> Mirzadjanova *et al* described that predominantly ipsilateral upper limb automatisms were more common than predominantly contralateral ones.<sup>14</sup> Our findings showed that 83.3% of patients (70.0% of seizures) with unilateral automotor seizures were correlated with ipsilateral focus of seizure. Unilateral tonic spasm was observed in contralateral seizure in 89% of frontal lobe epilepsy.<sup>15</sup> Werhahn *et al*<sup>16</sup> found that unilateral tonic spasm correctly lateralized the epilepsy syndrome to the contralateral hemisphere. In the present study, unilateral tonic spasm was observed more frequently in the contralateral side (85.7% of patients and 72.2% of seizures), which was consistent with previous reports. Thus, it is probable that the unilateral tonic spasm and unilateral automotor seizure have lateralizing significance.

The lateralizing value of TA was determined based on the side of tonic spasm. All patients and seizures with TA occurred in the contralateral

**Table 5: Tonic-automotor (TA) in the chronological sequence of seizures**

Tonic-automotor (TA)	Seizure (n=24)
As initial ictal sign	6
As the second ictal sign	12
As the third ictal sign	6
As the fourth ictal sign	0

hemisphere with temporal lobe lesion. Thus, TA may be a more reliable lateralizing sign in TLE. Nevertheless, our findings clearly showed that TA occurred early in the seizure. In addition, the underlying mechanism of this sign was further investigated. Automotor seizure with loss of consciousness has been observed as stimulation of mesiotemporal structures in the intracranial stereoelectroencephalography<sup>17</sup>, and unilateral tonic spasm most likely result from the activation of supplementary motor area (SMA).<sup>17</sup> When the ictal discharge influences the temporal structures and synchronously spreads to SMA, TA is present. Thus, TA is impossible as the first feature of seizure in TLE, which was also consistent with our findings that TA was the second ictal sign in seizure.

In conclusion, TA has lateralizing significance of contralateral hemisphere and is beneficial to differentiate TLE/HS from TLE/non-HS, so TA may be a reliable semiologic marker of TLE/HS. Our study still had some limitations: the number of patients was relatively small, and the frequency of TA occurrence was higher than what stated in our study. Certainly, the semiology is only a part of pre-operative epilepsy evaluation, and should be combined with other examinations such as video-EEG and neuro-imaging assessment to more precisely localize the epileptogenic zone.

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