# Sequential Tonic Motor Phenomena of Generalized Seizures

Warren T. Blume [1] • Mashael Al. Khateeb [2] • Salah Baz [3]

[1] London Health Science center, London, Ontario, Canada
[2] Department of Neurosciences. King Faisal Specialist Hospital, PO Box 3354, Riyadh 11211.Kingdom of Saudi Arabia
[3] King Faisal specialty hospital & Research center, Riyadh, Kingdom of Saudi Arabia
kmashael@kfshrc.edu.sa

## ABSTRACT

**Objective**: To demonstrate that the semiology of human bilateral tonic motor seizures evolves intra-ictally and that their full description should comprise this evolution.

**Method**: We scrutinized sequential tonic phenomena of bilateral motor seizures as recorded by video-EEG telemetry among 15 adult patients investigated because of intractable epilepsy. Seizures were divided into sequential stages, each defined as a tonic motor posture maintained for at least three seconds. As posture reflects joint involvement and its principally flexor or extension contour, results are expressed by joints as opposed to patients. Only the first seizure of each patient meeting all criteria are included. All four limbs had to be involved for three consecutive stages for inclusion. Two authors (SB, WB) each independently assessed ictal evolution, rare discordances (rare werer esolved by mutual review.

**Results**: The tonic motor component of each of 15 seizures evolved intra-ictally. More joints were involved in seizure stages two and three than in stage one, except cephalic version, which occurred principally in, stage one. Involvement of joints became more bilaterally symmetrical as seizures evolved. Joint flexion evolved to extension far more commonly than conversely**.**

**Significance**: Our data suggest that any study describing tonic motor semiology must indicate at what point in seizure evolution the observations were made. Its findings will sharpen ictal history taking: lay persons' observations may better reflect ictal evolution if sequence is emphasized. We interpret these findings as reflecting increasing reticulospinal tract involvement as the seizure proceeds.

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**Keywords**: Seizures, Motor, Sequence.

## 1. Introduction:

Relatively few semiological descriptions of bilateral motor seizures have charted their intra-ictal evolution; most of these have detailed the sequential appearance of clonic and tonic events (Theodore et al., 1994; Niaz et al., 1999; Jobst et al., 2001) We are unaware of any study of sequential tonic events in bilateral motor seizures since the classical descriptions by Gastaut and Broughton (Gastaut, et al. 1972); scrutiny of such phenomena during video-EEG telemetry constitutes this report. Spontaneous or metrazol-induced supplementary motor area seizures were described by Penfield and Jasper (1954) and by Ajmone Marsan and Ralston (1957) as contralateral shoulder tonic external rotation and abduction producing a posture. However, neither report describes intra-ictal evolution of this and other joints.

Although cephalic version (McLachlan, 1987) and the "figure four" sign of Kotagal et al. (2000), correctly indicate laterality of secondarily generalised seizure origin in many cases, their reliability apparently diminishes as a seizure progresses (Williamson et al., 1992). Moreover,, the evolution of tonic extension postures (implying greater excitation) and tonic flexion (lesser excitation) has not been systemically studied.

Herein we report the semiological progression of 15 epilepsy monitoring unit patients in whom the ictal tonic component was completely video-recorded from onset to termination. Therefore, to attain our purpose of describing ictal semiology, our principal focus must be joints.

To study evolution of tonic components we demarcated seizures into one or more stages. A stage was defined as maintenance of tonic flexion or extension in one or more joints, thus a posture, for at least 3 seconds.

We sought to answer the following: 1) Do tonic components of seizures evolve? 2) How many phases appear? And 3) Do certain patterns of evolution predominate? Our findings will suggest that sequential phase semiology must be included to fully describe and categorise a seizure.

**2. Methods:**

Among patients admitted to our Epilepsy Unit over a three year period for

investigation of intractable seizures, we studied one focal seizure in each of 15 consecutive patients whose EEG-video recordings satisfied the following criteria: 1) bilateral tonic motor activity of limbs at any seizure stage (see further), 2) clear video appearance of all limbs and head throughout a clinical event, and 3) adequate scalp or subdural EEG recording to identify the event as an epileptic seizure (Blume et al., 1984).

Seizures were depicted by 24/7 video EEG monitoring using XLTEK Systems. Mandibular notch electrodes supplemented the Ten Twenty System for scalp EEG (Sadler, & Goodwin, 1989). Subdural recordings (Adtech) consisted of 6-10 lines totaling 42-70 electrode positions, placed according to seizure localizing requirements in patients whose non-invasive data failed to firmly identify ictal origin (Blume et al., 2001). The patient or observers identified epochs of seizure activity by push-button. Automated seizure detection was not employed.

We clinically identified episodes as generalised tonic seizures when such events involved at least one limb on each side (see further). Neither symmetries nor asymmetries of tonic events were selection criteria.

The sequential events were divided into stages. A seizure stage was defined as a distinct postural change in any newly involved or on-going tonically involved joint toward flexion or extension, each posture(s) lasting at least 3 seconds. Thus, change would include unilateral or bilateral symmetrical or asymmetrical tonic activity of limbs maintained at one or more of limb joints as flexion and/or extension lasting three or more seconds. Such activity must have simultaneously involved left and right limbs for at least one stage. As a seizure phase was defined as maintenance of a position for ⩾ 3 seconds, transitional postures were not analysed. The first seizure of each patient with bilateral tonic phenomena clearly visible on video was evaluated. Sequential, evolving ictal scalp or subdural EEG potentials and accompanying clinical events were requisite for seizure identification (Blume et al., 1984). Our setup did not allow simultaneous clinical-EEG comparison at each seizure instant.

When such change appeared, videos were paused and a detailed description of all joint postures (neck, shoulder, elbow, wrist, hip, knee, ankle) were made independently by SB and WTB and its data collected to a spreadsheet by these authors who remained blind to patient identity and seizure type assessed clinically. Comparison of spreadsheet data of these authors disclosed no discrepancies of pattern of sequential involvement. Small differences of timing of stage onset and termination in two patients were resolved by mutual observation.

Proportions and symmetry of extensor-flexor positions were analysed by the Chi-Square (Fisher's exact) test.

**3. Results:**

Three ictal phases could be analysed in all 15 patients; of these only eight patients proceeded to a fourth stage. . More joints were involved in seizure stages two and three than appeared in stage one; cephalic version occurred principally in stage one (Table 1).

*Table 1. Involvement of Body Part by Seizure Stage*

| STAGE ⇨<br>BODY PART ⇩ | 1 | 2 | 3 |
|---|---|---|---|
| HEAD (VERSION) | 13 | 9 | 3 |
| NECK | 6 | 11 | 10 |
| FACE | 2 | 2 | 2 |
| SHOULDERS | 2 | 20 | 15 |
| ELBOWS | 11 | 15 | 15 |
| WRISTS | 4 | 9 | 14 |
| DIGITS | 5 | 9 | 12 |
| HIPS | 9 | 14 | 12 |
| KNEES | 9 | 14 | 13 |
| ANKLES | 2 | 4 | 4 |
| TOTALS | 63 | 107 | 100 |

Note. Numbers are joints

Joint flexion evolved to extension far more commonly than the converse or than other sequences Among 60 joints (15 patients) for which flexion or extension positions of elbows, hips, or knees were visibly involved for two phases or more, flexion progressing to extension occurred in 39 (65%) joints, extension to flexion in two (3%) while flexion and extension were each sustained in five (8%) and nine(15%) joints respectively. Flexion / extension alternated in five joints (8%). A shift from flexor-dominated semiology to extensor-dominated semiology occurred principally between phases 2 and 3 (Table 2).

Involvement of joints became more bilaterally symmetrical as seizures evolved (Table 3). Among 90 involved joints in phase 2 the symmetrical: asymmetrical ratio was 30:60 whereas this shifted to 65:35 for 100 joints in phase 3 ($p= 0.0001$). Similarly, the proportion of patients in whom a majority of joints exhibited symmetrical features (flexion or extension) was greater in later phases (3 and 4) than in early phases (1 and 2) (Table 3).

*Table 2. Limb Flexion/Extension & Phase*

| Limb | Phase | Flexion | Extension |
|---|---|---|---|
| **Elbow** | | | |
| | 2 | 19 | 8 |
| | 3 | 7 | 23 |
| **Hips/Knees** | | | |
| | 2 | 18 | 8 |
| | 3 | 9 | 19 |
| **Total** | | | |
| | 2 | 37 | 16 |
| | 3 | 16 | 42 |

Numbers are joints. A shift from flexor-dominated to extensor-dominated semiology occurred from phase 2 to 3, compared by Chi-Square (Fisher's Exact) for: elbows,$P < 0.001$( very significant); hips/knees, $P=0.013$ (significant); total, $P<0.0001$(extremely significant).

*Table 3. Symmetry of Tonic Postures & Phase*

| **PHASE ⇨ SYMMETRY ⇩** | **1** | **2** | **3** | **4** |
|---|---|---|---|---|
| **SYMMETRICAL** | **6** | **4** | **12** | **6** |
| **ASYMMETRICAL** | **9** | **11** | **3** | **2** |

Numbers = patients in whom majority of joints were bilaterally symmetrical or asymmetrical. Table shows increasing bilateral symmetry of limb joints (shoulders, elbows, hips, knees, ankles) as seizures proceed. Chi square (Fisher's exact test) for symmetry: phases 1, 2 versus 3, 4: $P= 0.002$ (very significant).

## 4. Discussion:

Similar to the classic description by Gastaut and Broughton4,our data indicate that tonic motor ictal events progress from joint flexion to extension far more commonly than the converse (Table 2) and that this sequence applies to both the elbows and hips/knees. Additionally, postures became more bilaterally symmetrical as the seizure proceeds (Table 3).

What system(s) mediates these phenomena in seizures whose generation involves principally the cortex and thalamus? In mammals only a restricted portion of the frontal cortex projects directly to the spinal cord; other regions project to the cord via the primary motor cortex or medullary reticular formation (RF) (Wiesendanger & Wise, 1992). Of brain stem-originating descending tracts, the reticulospinal tract (RST) is likely the principal conveyer of motor seizures as the vestibulospinal tract has no cortical afferents, the tectospinal tract descends only to the cervical area and the rubrospinal tract is small in humans. The RST originates from the pons and medulla, which are also the termini of cortico-reticular fibres. Cortically originating afferents to the RST arise from area 6, the rostral portion of area 4, the prefrontal cortex and the supplementary motor area (Wiesendanger & Wise, 1992; Catsman-Berrevoets & Kuypers,1976; Keizer, & Kuypers, 1984; Kuypers, 2011; Newman et al., 1989).

Strongest excitatory effects upon spinal motor neurons likely originate from the nucleus reticularis (NR) pontis caudalis and NR gigantocellularis in the medulla and conveyed by the RST.

Thus, the RST, the considered conveyer of tonic seizures, originates at the termini of cortico-reticular fibres. However, the complexity of RF anatomy and physiology is well-described by the Scheibels, (1958): " The fine structure of the brainstem core is such that given the proper physiologic conditions an impulse pattern can probably describe any conceivable path within the reticular formation, so extensive is the interconnectivity of the elements." Thus, close juxtaposition exists for excitation and inhibition (Newman, 1995). Additionally, pontine-originating RST tracts facilitate axial and limb extension while medulla-orignating RST facilitates flexors and inhibits extensors (Brooks, 1986; Mori et al., 1995). As the Scheibels suggested, other than area of stimulus may influence an elicited motor phenomenon. Burnham, (1987) evoked the following motor semiologies with increasing mAmp stimulation to the same pontine RF area of the rat: forelimb clonus, hind limb clonus, forelimb tonic flexion, hind limb tonic flexion, forelimb and hind limb tonic extension. The medullary RST may have greater connexions with extremities than the pontine RST (Brodal, 2004). These anatomo-physiological data together suggest that, as a tonic seizure progresses, a more intense and widespread reticular system activation occurs to tonically extend the limbs, increase symmetry of motor effects and to increasingly involve wrists and digits (Table 1).

Although ancillary features may help distinguish primary from secondarily generalized tonic seizures22 both asymmetrical and symmetrical features may appear in each group (Lüders, 2000; Chatrian, 1982; Gastaut et al., 1962)."Hemispheric epilepsy", patients with symmetrical motor seizures and one-hemisphere-predominant spike-wave discharges, exemplify this gradation (Terra et al., 2010) as does "one sided generalised epilepsy" described by Gastaut et al 1962.

## 5. Statistical Methods:

Proportions and symmetry of extensor-flexor positions were analysed by the Chi-Square (Fisher's exact) test.

## 6. Key Point Box:

At least 3 distinct phases of ictal motor involvement could be identified in all 15 patients. More joints become involved as a seizure progresses. Joint flexion evolved to extension more commonly than other motor sequences Motor involvement became more symmetrical as the seizure progressed. The foregoing sequences suggest greater involvement of the reticulospinal tract as a motor seizure progresses.

**Conflict of Interest Statement**

Neither of the authors has any conflict of interest to disclose.

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**Involvement**

Both authors have been significantly involved in all phases of this project.

**Corresponding Author:**

Mashael Al. Khateeb, MD.

Department of Neurosciences. King Faisal Specialist Hospital, PO Box 3354, Riyadh 11211.Kingdom of Saudi Arabia

E-mail: kmashael@kfshrc.edu.sa

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