

SUPPLEMENT - MANAGEMENT OF A FIRST SEIZURE

Is the first seizure truly epileptic?

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SUMMARY

Transient loss of consciousness (T-LOC) with abnormal posture or movements reflects a temporary dysfunction of the brain, either primary or secondary. In a period of high technological medical access, patients with T-LOC constitute a challenge to improve the medical “art of listening.” The difficulty in dealing with isolated paroxysmal phenomena is associated with the probability of

the occurrence of a second event and therefore the entrance of the patient into a chronic disorder. We present a detailed analysis of symptoms that should help the general practitioner in the differential diagnosis among three main entities in the adult populations: syncope, epileptic seizure, and psychogenic seizure (dissociative convulsion).

KEY WORDS: First seizure, Diagnosis, Syncope, Dissociation convulsion, Parasomnia.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. An *epileptic seizure* is a transient occurrence of signs and/or symptoms due to abnormal excessive or enhanced synchronous neuronal activity in the brain. It is specified by its mode of onset and termination and its clinical manifestations. In some cases, anticipatory signs may be even detected in the scalp EEG several minutes before seizure onset (Aksenova et al., 2007). Following the recent tendency to define epilepsy after the occurrence of at least one epileptic seizure, it is mandatory to confirm the epileptic origin of the seizure (Fisher et al., 2005). A *syncope* is defined as a transient loss of “consciousness” (T-LOC) usually leading to loss of postural tone. The onset is relatively rapid, and the subsequent recovery is spontaneous, complete, and relatively prompt. The underlying mechanism is transient global cerebral hypoperfusion (Brignole et al., 2001). A *psychogenic seizure* is a transient behavioral disturbance without any organic basis. In the DSM-IV (American Psychiatric Association, 1994) such attack is classified as a somatoform disorder, while under the ICD-10 classification (World Health Organisation, 1992) it is classified as dissociative convulsion in the group of conversion disorders. This paper deals with different seizure mechanisms, thus we will adopt the more illustrative term of *dissociative convulsion*.

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EPIDEMIOLOGY

The lifetime incidence of an afebrile epileptic seizure is 5% (Hauser et al., 1993; Forsgren et al., 1996) while that of a reflex syncope is 50%. Among patients presenting at an Emergency Department (ED) with a T-LOC, 51% of events are represented by syncope and only 8% by epileptic seizures (Day et al., 1982; Eagle et al., 1985; Kapoor, 1990). The prevalence of active epilepsy is 0.5–1% while syncope is thought to affect 15% of children and middle age men and women (Smith et al., 1999). A first epileptic seizure is reported only in 0.2–0.3% of all the adults who present to the ED (Krumholz et al., 1989; Huff et al., 2001) while syncope represents 1.2% of all ED visits (Quinn et al., 2006).

IS THE FIRST SEIZURE TRULY EPILEPTIC?

The diagnosis of an epileptic seizure is a clinical act depending on a precise history reported by the patient and the eyewitnesses. There is a plethora of events affecting primarily or secondarily the brain known as “imitators” of epilepsy. Typically, imitators like the loss of postural tone in atonic seizures and cataplexia have misleading clinical similarities. It is estimated that 20–30% of cases are indeed misdiagnosed as epileptic seizures (Scheepers et al., 1998; Chadwick & Smith, 2002). It is only after the second event that a correct classification becomes possible.

Syncope is a common clinical condition mimicking an epileptic seizure and in some cases its incorrect diagnosis can lead to premature death. Therefore, some medical

societies recommend that patients with a suspected diagnosis of epileptic seizure should be seen by a neurologist or an epilepsy specialist before the diagnosis is made (Scottish Intercollegiate Guidelines Network, 2003).

CAN WE EASILY RECOGNIZE AN EPILEPTIC SEIZURE?

Reports by the patient and the witnesses may be inaccurate and misleading or simply insufficient when there is a suspicion of an epileptic seizure. Search for additional information is time-consuming in an ED but it should be mandatory and organized as follows.

Before the event

Information should be provided to decide whether the epileptic seizure was provoked by sleep deprivation, alcohol withdrawal, drug misuse, or unusual stimuli (flickering lights), etc.

During the event

For a witness the seizure onset usually corresponds to the beginning of the tonic-clonic (TC) phase of a primary or secondary generalized seizure. Nevertheless, direct questions on what happened at the onset (strange behavior, focal rhythmic movement, automatisms of the face or extremities, etc.) may contribute to reveal a partial onset. Expiratory groan or cry with tonic movements of the extremities, falling in a stiffening posture with traumatic impact, then rhythmic followed by arrhythmic slower jerking of extremities, facial contraction with clenched teeth, purple lips (cyanosis) with froth or blood in the mouth, incontinence are all symptoms that strongly suggest a TC seizure. The duration of the symptoms is important because we know that the TC phase usually lasts less than 2 min (Theodore et al., 1994). Sometimes it is useful to ask the witness to imitate the seizure; we can thus better appreciate the characteristics of the clonic movements as opposed to the more complex movements of hypermotor seizure. The behavior during the convulsion is important since a recent study showed that having the eyes closed during the TC phase predicted a dissociative seizure with a sensitivity of 96% and a specificity of 98% (Chung et al., 2006).

After the event

The patient is unconscious with noisy respiration (sterthorous breathing is a combination of postapneic hyperventilation with snoring-like sound related to upper airway hypotonia, hypersalivation and sometime blood in the mouth). Then the patient becomes stuporous, wanting to be left alone, searching for a position to sleep, and being confused for several minutes, with a slow return of orientation and collaboration. This postictal confusion reported by the eyewitness is a strong marker of an epileptic seizure (Hoefnagels et al., 1991).

Physical and neurological status

Head injury, shoulder dislocation, and severe lateral tongue biting are suggestive of an epileptic seizure (Manford, 2001). Bilateral Babinski sign can be seen in the immediate postictal phase when the patient is still stuporous.

EEG

It is useful in children and young adults, in whom paroxysmal abnormalities are seen in 34% of cases after a first seizure, and in up to 50–70% of cases when performed within 24–48 h (King et al., 1998; Schreiner & Pohlmann-Eden, 2003). When standard EEG is negative, sleep deprived EEG will detect spike discharges in an additional 13–31% of cases. Because of its low sensitivity, EEG should not be used to exclude the diagnosis of epilepsy but should be done to classify epileptic seizures. Over interpretation of minor EEG abnormalities encourages misdiagnosis, as 2.8% of children and 0.4% of adults have paroxysmal discharges in the absence of epileptic seizures (Walczak & Jayakar, 1997). Thus, the EEG should better be asked by a specialist (where available). A British study about EEG use in a district hospital without a neurologist indicated that 56% of the EEG requests were considered inappropriate (Smith et al., 2001).

Brain imaging

The CT-scan is the fastest available imaging technique but its sensitivity is low (4–6%) in the absence of abnormal neurological signs (Ramirez-Lasepas et al., 1984; Breen et al., 2005). MRI (T₂-weighted and FLAIR fast spin echo slices) is the best-suited method for structural imaging but it should only be planned by a specialist. In a series of 166 adults with a first unprovoked epileptic seizure, MRI was abnormal in 47% of patients (Pohlmann-Eden & Schreiner, 1998).

Laboratory tests

Routine blood testing (glucose, serum electrolytes, calcium, and full blood count) is expected to reveal only a small proportion of patients with significant metabolic abnormalities (Turnbull et al., 1990; Dunn et al., 2005). Additional blood tests should be done only when clinically indicated (e.g., alcohol or drug levels).

IF NOT EPILEPTIC, WHAT IS THIS PAROXYSMAL EVENT?

In patients experiencing collapse with T-LOC and hyper/hypotonia or abnormal movements, the principal “imitators” are syncope and dissociative convulsion.

Anoxic/hypoxic paroxysmal event (syncope)

Syncope is almost ten times commoner than epilepsy (Soteriades et al., 2002) in particular when considering the elderly population. It was reported that 23% of people aged over 70 years experience a syncope over a 10-year period

(Sarasin et al., 2001). The basic investigation of syncope should comprise a 12-lead ECG; echocardiography is useful only at the presence of a positive cardiac history or an abnormal ECG (Sarasin et al., 2002). According to the guidelines from the European Society of Cardiology, the tilt-table testing is recommended only with atypical histories of T-LOC (Brignole et al., 2004).

Syncope is often mistaken for an epileptic seizure, especially when accompanied by jerking movements. This seems to occur quite frequently, according to a video recording of self-induced syncope in 56 medical students (Lempert et al., 1994). In this sample, myoclonic jerking occurred in 90% of cases. There is usually a characteristic prodromal phase with lightheadedness, visual and auditory surroundings fading away, blurred vision, generalized weakness. The patient is pale (in contrast with the cyanosis sometimes seen during a generalized TC seizure), with nausea, epigastric discomfort (without ascending sensation), and diaphoresis. (S)he then loses of postural tone with T-LOC and little or no wounding. If there are a few tonic movements or clonic jerks, they always happen after a few seconds and never during the fall. According to the Lempert's study on intentionally provoked syncope, clonic jerks are multifocal, arrhythmic and are probably less frequent than those observed in "spontaneous" syncope. Jerking movements range from 12% (Lin et al., 1982) to 46% (Newman & Graves, 2001) among blood donors who faint.

Some vocalizations (40%) and automatisms like lip-licking or chewing, fumbling or righting movement (45%) can be confused with partial seizures. The duration of the episode is in seconds. If cortical hypoxia persists, hypertonia with either "decortication" posture or "opisthotonus" will appear. Urinary incontinence is not uncommon. In the postictal phase, recovery is rapid (eye-contact re-established in few seconds) without neurological deficits, with fatigue, nausea, pallor, and persisting diaphoresis (Table 1).

A detailed history of precipitating factors is mandatory, looking for "emotional" stress, prolonged standing or dehydration, low salt intake, raised intrathoracic pressure (e.g., during coughing), and carotid sinus stimulation. The commonest causes of syncope are listed in Table 2 being classified as benign (the most common being neurocardiogenic, carotid sinus syndrome, situational, and postural hypotension) and malignant (generally cardiogenic). If T-LOC has occurred after exercise, it could suggest a reflex syncope, and if during exercise, a cardiomyopathy or an intracardiac conduction defect.

It is worth noting that a transient ischemic attack (TIA) in the vertebrobasilar territory can affect the ascending reticular activating system (ARAS) and cause T-LOC. A TIA may also cause signs of brainstem dysfunction such as vertigo, diplopia, dysarthria, ataxia, or hemiparesis and about 75% of TIAs last longer than 5 min, which is con-

Table 1. Comparative clinical features of epileptic seizure and syncope

Syncope	Epileptic seizure
Provocation by prolonged standing, hunger, heat, pain, micturition, cough, etc.	In the context of sleep deprivation, drugs or alcohol withdrawal, intermittent flashes, etc.
Prodrome: visual and/or auditory progressive fading, pallor, diaphoresis	Aura: olfactory, gustatory hallucination, epigastric rising sensation, dysmnestic phenomena ("déjà-vu," etc.). Auditory, visual positive hallucination (noise, music, flash, colors, figures, etc.)
No automatism	Oro-alimentary, manual automatism, complex behavior
Flaccidity, with or without brief myoclonus, opisthotonus (rare)	Strained cry, tonic-clonic jerks, severe tongue biting, incontinence, limb posturing
Duration: 10–30 s	Duration: 1–2 min
Postictal phase: minimal (few seconds)	Postictal phase: several minutes

siderably longer than the duration of a syncope or seizure (Warlow et al., 2001).

Psychogenic paroxysmal event

Dissociative convulsion and psychogenic pseudosyncope represent a diagnostic challenge for the general practitioner and the specialist. These events are present in about 30% of patients seen in syncope clinics and up to 25% of patients presenting with "refractory seizures" at a video-EEG monitoring unit in university hospitals (Mattson, 1980; Gates et al., 1985; Benbadis et al., 2004).

Psychogenic paroxysmal events usually begin in a particular context sometimes represented by external (place, time, witness) or internal triggers (flash backs, emotions).

Table 2. Classification of syncope^a

Insufficient pumping action of the heart
-Arrhythmia (paroxysmal supraventricular and ventricular tachycardia, long QT syndrome)
-Structural cardiac disease (valvular disease, obstructive cardiomyopathy)
Insufficient vascular tone, leading to orthostatic hypotension
-Autonomic failure
Primary (MSA, pure autonomic failure)
Secondary (diabetic and other neuropathies)
Drugs (antidepressants, beta-blockers)
Insufficient circulatory volume
-Hypovolemia (Addison's disease, diuretics, hemorrhage)
Inappropriate neural control over the circulation
-Reflex syncope (vasovagal syncope, carotid sinus syndrome, micturition syncope)
^a Thijs et al., 2004. MSA, multiple system atrophy.

Table 3. Some clinical semiological features of epileptic and dissociative seizure^a

	Dissociative seizure	Epileptic seizure
Duration >2 min	Common	Very rare
Motor features		
-Gradual onset	Common	Rare
-Fluctuating course	Common	Very rare
-Thrashing, violent movements	Common	Rare
-Side to side head movements	Common	Rare
-Asynchronous movements	Common	Very rare
-Eyes closed	Very common	Very rare
-Pelvic thrusting	Occasional	Rare
-Opisthotonus	Occasional	Very rare
Weeping	Occasional	Very rare
Incontinence	Occasional	Common
Injury		
-Severe tongue biting	Very rare	Common
-Scalp, face wounds	Very rare	Common
Recall for period of unresponsiveness	Common	Very rare

^aAdapted from Mellers, 2005.

The prodromal phase may be characterized by neurovegetative symptoms (tachycardia, tachypnea, difficulty taking a deep breath, epigastric discomfort), “neurologic” features (tremor, weakness, paresthesia, headache), or “psychiatric” features (unreality sensation, depersonalization, dream-like state, distortion of visual or auditory perception, freighting sensation, imminent death sensation).

The patient can stare blankly and enter a trance state followed by a slow fall without severe wounding. Then, a T-LOC follows for several (up to 10) minutes. In some cases, it can evolve into pseudo–status epilepticus. There can be either asynchronous demonstrative movements, beginning with slight shaking and intermittent motor activity, with out-of-phase limb activity, vocalization in the middle of the seizure, pelvic thrusting, and rhythmic side-to-side head motion with eyes shut and resistance to passive eye-

lid opening. Intense truncal opisthotonus-like arching (*la grande courbure* of Charcot) is now rarely seen.

The postictal phase has variable features with either immediate return of consciousness or a passive, areactive state progressing to wakefulness. There can be partial amnesia during the seizure; complete amnesia is rare (Bowman, 2006) (Table 3).

The term “psychogenic nonepileptic seizure” has been coined by the epileptologists. American psychiatrists classify them in the conversion disorders group (seizure type) of the DSM-IV somatoform section (American Psychiatric Association, 1994). However, the most suitable clinical terminology should be dissociative convulsion. The ICD-10 classification states that “the common theme shared by dissociation disorders is a partial or complete loss of the normal integration between memories of the past, awareness of identity and immediate sensations and control of bodily movements” (World Health Organization, 1992). According to Bowman & Markand (1996), who studied 45 patients, dissociation convulsions begin in the young adulthood (20–30 years of age) and are preferably observed in women (78%). A past traumatic event is reported by 84% of subjects (sexual abuse 67%, physical abuse 67%, other trauma 73%). A psychiatric comorbidity is common and includes somatoform disorders (89%), dissociative disorders (91%), affective disorders (64%), personality disorders (62%), posttraumatic stress disorders (49%), and other anxiety disorders (47%) (Bowman & Markand, 1996).

Paroxysmal events occurring during sleep

Repetitive sleep starts, known as hypnagogic or hypnic myoclonus, are brief body jerks that coincide with sleep onset. Other sleep-wake transition disorders comprise body rocking, head banging, head rolling (International Classification of Sleep Disorders, 2001). REM-sleep behavior disorders are seen in adults older than 50 years. Some of these conditions can be quite difficult to differentiate from nocturnal frontal lobe seizures (Table 4).

Table 4. Distinguishing sleep disorders from seizures^a

	NFLE	NREM parasomnia
Age at onset	Variable	Pediatric age
Duration of event	Less than 1 min	Several minutes
Clustering (>2)	Frequent	Infrequent
Timing	Stage 2 sleep (soon after falling asleep)	Stage 3–4 sleep (1 or 2 h after falling asleep)
Symptoms	Dystonic or tonic posturing; wandering rare (usually confined to the bedroom)	Sleepwalking (wandering around or even outside the home) Performing complex tasks (dressing, driving)
Stereotypy	High degree of stereotypy	Variability
Recall	Lucid recall relatively common	Vague recollection
Vocalization	Simple words or complex speech, reflection of retained awareness, usually remembered	Complex speech when the patient is not fully conscious, not remembered

^aAdapted from Derry et al., 2006.

Table 5. Paroxysmal nonepileptic and epileptic events during sleep

Sleep disorder	Epilepsy
NREM arousal parasomnia	Nocturnal frontal lobe epilepsy (NFLE)
a) Confusional arousal	a) Paroxysmal arousal
b) Sleepwalking	b) Episodic nocturnal wandering
c) Sleep terror	c) Nocturnal paroxysmal dystonia
REM behavior disorder	
Nocturnal panic attack	

NREM arousal disorders (parasomnia), such as confusional arousals, sleep terrors, and sleepwalking, are frequent in the pediatric population. Some motor behaviors of partial seizures (frontal or temporal) have some similarities with parasomnia (Table 5). One explanation could be the functional “release” by the cortex or basal ganglia of central pattern generators and the emergence of stereotyped inborn fixed action patterns (Tassinari et al., 2005). Night terror happens during the first 3 h of sleep, in stage 3 or 4. There is a sudden sitting up with screaming, the child appearing terrified and unresponsive for about 10 min. Sleepwalking is seen in older children (5–10 years of age) during the first 3 h of sleep. The child walks around with his/her eyes open, in a trance-state, sometimes mumbling, usually leaving the room and then returning back to bed.

Several other conditions could have been included in a differential diagnosis of epilepsy, including: transient global amnesia, excessive daytime sleep, migraine, paroxysmal choreoathetosis and other movement disorders, and the manifestations of hypoglycemia. However, the discussion of these entities is outside the scope of this chapter because, with few exceptions, they tend to come to medical attention only after recurrence.

DISCUSSION

To differentiate an epileptic from a nonepileptic seizure, the clinician has to rely on his “art of listening.” This is time-consuming and remains a challenge during a time-limited consultation. The suggestibility of the questions asked by the clinician is also usually underestimated. If a dissociative convulsion is suspected, the clinician should take time to ask about dissociative symptoms such as depersonalization and derealization. Symptoms of panic and dissociation are common in the prodromal phase, although patients may be sometimes reluctant to provide a detailed description (Stone et al., 2005).

Ideally all patients suspected of having a first epileptic seizure should be examined by a neurologist or an epileptologist, whose sensitivity for the identification of an epileptic seizure is high (96%) (Deacon et al., 2003). Patients should not be treated if there is uncertainty about the diagnosis and the wisdom would be to “wait and see” for

the next event. If further events are frequent and the diagnosis is still doubtful, then video-EEG monitoring is helpful when trying to reproduce a T-LOC (Grubb et al., 1991).

Zaidi et al. (2000) performed a head-up tilt test and carotid sinus massage under EEG in 38 patients with uncertain diagnosis and in 47% a diagnosis could be established. If a dissociative convulsion is suspected, a 48-h video-EEG monitoring may be sufficient to document an episode (Lobello et al., 2006). Provocation of the event by an experienced senior physician under video-EEG is ethically acceptable if the patient is correctly informed. If a sleep disorder is suspected, video-polysomnography should be organized.

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