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Status epilepticus in epileptic patients Related syndromes, precipitating factors, treatment and outcome in a video-EEG population-based study

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Summary

Introduction: Status epilepticus (SE) is frequently observed in epileptic patients. We reviewed a series of video-EEG documented SE to define the characteristics of SE in this population.
Materials and methods: Retrospective evaluation of 50 epileptic patients with SE, revision of the electro-clinical data and therapies, and definition of the semeiological subtypes, aetiology, outcome and related epileptic syndromes.
Results: We identified 28 convulsive (19 focal and 9 generalized) and 22 non-convulsive (8 focal and 14 generalized) SE patients. In 13 patients, SE was situation-related (poor compliance, AED reduction, worsening seizures).

In the remaining 37 patients, SE was related to the natural history of epilepsy (progression of underlying pathologies or intrinsic expression of epileptic syndromes); in these last cases, our results show a higher occurrence in cryptogenic frontal epilepsy ($p = 0.01$). We identified two subgroups according to the duration of the event, i.e. SE lasting <12 h and SE lasting >12 h. Our results showed a worse response to therapy in SE lasting >12 h ($p = 0.01$), a better response to therapy in non-convulsive SE than in convulsive SE ($p < 0.05$) and a relationship at statistical

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significance limit between a poor response to therapy/worse outcome and symptomatic epileptic syndromes ($p = 0.06$).
Conclusion: SE in epileptic patients has a wide spectrum of electro-clinical features. It may be related to the withdrawal or reduction of AEDs, or may even be the expression of the evolution of epileptic syndromes. Response to therapy is dependent on early diagnosis and therapy.

Introduction

Status epilepticus (SE) is a neurological emergency characterized by the occurrence of a ''prolonged seizure or many seizures which present so repetitively as to create a fixed or enduring epileptic condition''.[1] SE may be the expression of an acute neurological pathology; however, in many cases (up to 50%) it may occur in cases of defined epilepsy,[2] either as the first ictal manifestation or as a complication in non-compliant patients. Data on the clinical and EEG features in either case are often lacking because a targeted assessment of this condition in the emergency department (ER) setting, which is where SE is usually observed, is considered to be either of little use or too complicated.[3–6] Although SE in epileptic patients is often precipitated by specific factors (poor compliance, AED withdrawal/reduction, gastroenteral malfunctioning, and multiple other factors such as fever or intoxications with proconvulsant substances), it may even occur for no apparent reason. In this study we reviewed the clinical and EEG data of 50 epileptic patients with a video-EEG recorded SE in an attempt to define the SE semeiological subtypes, aetiology, outcome as well as any related epileptic syndromes.

Materials and methods

We performed a retrospective study of 50 consecutive epileptic patients with SE who had been referred to the video-EEG laboratory of our Epilepsy Unit between 1996 and 2004. The patients' video-EEG studies were selected from a total of 6749 recordings performed in our laboratory during the period we considered (average of 750 examinations per year). As our video-EEG laboratory is located within the neurological ward, hospitalised patients promptly undergo, in case of epileptological emergencies, a video-EEG recording to assess electro-clinical findings and to monitor the response to therapy. Our outpatients, especially those suffering from drug-resistant seizures, are usually advised to come directly to our laboratory in case of prolonged seizures. Of the 50 patients we selected, 20 had been referred to our laboratory directly by the ward, 17 by our outpatient service and only 13 by the ER.

Inclusion criteria

The inclusion criteria were: (1) a video-EEG documented SE; according to Gastaut's definition,[7] SE was defined as any prolonged seizure/cluster of recurrent seizures lasting $\geq$30 min without intervening recovery of consciousness; (2) a previous, documented diagnosis of epilepsy accompanied by complete clinical data (including general characteristics, seizure type, syndromic classification).

Exclusion criteria

The exclusion criteria were: (1) SE in patients with acute neurological disease or with no previous history of epilepsy; (2) incomplete clinical data, including lack of previous documentation, inability to identify the SE time of onset, its temporal evolution and therapy before our clinical and video-EEG assessment.

Main clinical and EEG findings

In accordance with previous documentation, the clinical characteristics (age at seizure onset, seizure type, risk factors, neurological examination, neuroimaging and interictal EEG) were defined and a epilepsy syndromic classification was drawn up. In the syndromic context, lobar definition was defined according to ictal semeiology, interictal and ictal EEG and neuroimaging features. According to the ILAE classification,[8] epileptic syndromes not clearly defined as generalized or partial were considered as undetermined. On the basis of the video-EEG documentation, SE semeiological features, EEG findings, temporal evolution, therapeutic management (drug used, route and timing of its administration, loading and maintenance dose) and short-term outcome were analyzed. According

to the inclusion criteria, SE duration was defined as the interval between the onset of symptoms (identified on the basis of the information reported by the patients' relatives or by medical staff) and video-EEG-documented SE resolution (established according to the disappearance of or significant reduction in epileptiform abnormalities).

Although several SE classifications have been proposed in the past[7,9,10] we decided to use a classification proposed more recently[11] (revised according to specific concepts regarding different subtypes of CSE, with particular attention being paid to focal motor SE, which is usually difficult to classify[12]) because we deemed it more suitable for the purposes of the present work (it envisages both clinical and instrumental findings).

As regards SE aetiology we adopted a clinically oriented classification with the aim to avoid any terminological confusion between SE and epilepsy aetiology.

Given the retrospective design of the study, only short-term outcome (defined as the patients' condition in the 30 days following the SE resolution) was evaluated.

Statistical analysis

The statistical analyses were performed by means of χ^2-test, with Fisher's correction when required. The values of $p \leq 0.05$ were considered statistically significant. All analyses were performed with SPSS (Version 12.0).

Results

General characteristics of the patients

This study included 50 patients, 23 men and 27 women, aged 6—79 years (mean age 36.9 years). The mean age at seizure onset was 15 years, the mean age at first recorded SE was 37 years. The clinical, neurophysiologic and neuroimaging findings of the patients included in the present study are shown in Table 1.

SE clinical features and semeiological classification

According to the classification,[11,12] SE was subdivided in convulsive and non-convulsive (CSE and NCSE), with both groups including focal and generalized subtypes. The specific semeiological subtypes are shown in Fig. 1.

SE aetiologies

Definite precipitating factors or conditions were identified in 13 patients. This group, referred to as patients with situation-related SE, included poor compliance in three cases, planned AEDs reduction in eight cases and AED-related seizure worsening in two cases. In the remaining 37 patients, SE was related to epileptic syndrome evolution: a progression of the underlying cerebral pathologies was documented in 4 cases (high grade glioma in 1 case, undetermined encephalopathy in 1 case and late-

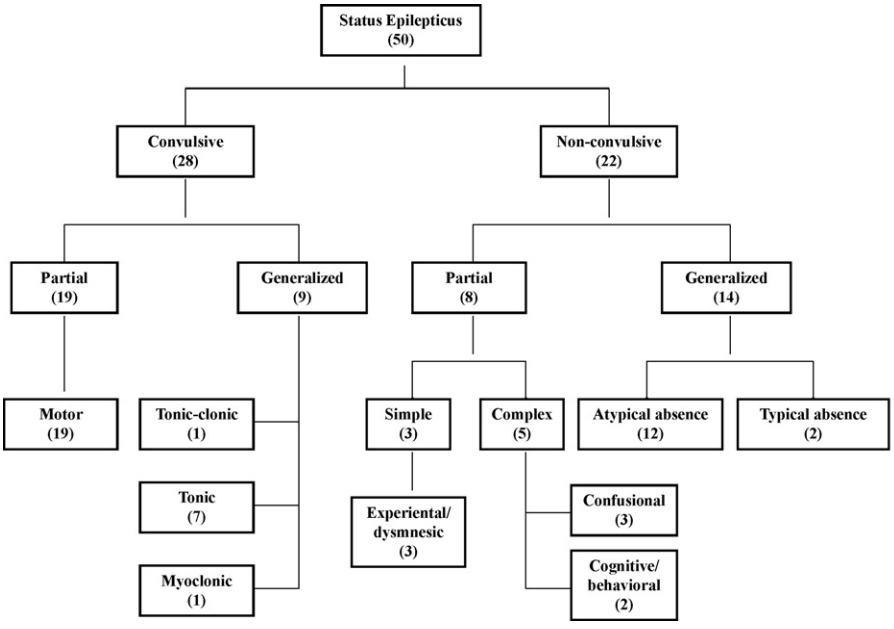

Figure 1 Classification of SE population according to a recently published proposal.[11]

Table 1 General characteristics of the patients and SE electro-clinical, aetiological and therapeutical findings

Pt	Seizure type	Epilepsy syndrome	MRI	Interictal EEG	SE semeiological subtypes	SE aetiology	SE EEG findings	SE clinical pattern
1	SPS, CPS	Cryptogenic FLE	Normal	L Frontal spikes, 4 Hz generalized SW-PSW discharges	Simple partial NCSE (experiential)	Epilepsy evolution	4 Hz generalized SW-PSW activity	Slight confusional state, sensation of ''feeling cold, a thrill inside'', bil subtle perioral myoclonic jerks
2	SPS, SGS	Cryptogenic FLE	Normal	1.5–2 Hz generalized SW-PSW discharges	Generalized CSE	Epilepsy evolution	Bilateral (>R) fronto-central LVFA → bil PS → 1.5 Hz SW-PSW activity	Staring, slight oral automatisms followed by upper limbs and axial tonic postural modification
3	SPS, SGS	Cryptogenic FLE	Normal	Bil frontal slow waves	Partial CSE	Epilepsy evolution	L frontal LVFA → bil rhythmic slow wave activity	Asymmetric axial tonic posturing (fencing-like)
4	CPS, SGS	Cryptogenic FLE	Normal	R 4–5 Hz slow waves	Complex partial NCSE (cognitive-behavioural)	Epilepsy evolution	R Fronto-central 2.5 Hz SW activity	Confusional state, gestural automatism, motor and vocal perseveration
5	SPS, SGS	Cryptogenic FLE	Normal	R 4–5 Hz slow waves	Partial CSE	Epilepsy evolution	Diffuse LVFA → R hemispheric rhythmic slow wave activity	Sensation of ''something painful in the throat'' → a bilateral postural modification
6	SPS, SGS	Cryptogenic FLE	Normal	L fronto-central slow wave	Partial CSE	Epilepsy evolution	L central rhythmic slow wave and spikes activity	Paresthesias and clonic movements involving R upper and lower limbs

7	SP, CPS, SGS	Cryptogenic FLE	Normal	Diffuse 2.5 Hz generalized SW-PSW complexes	Generalized CSE	Epilepsy evolution	GPFA (with doubt L frontal onset)	Bilateral upper limbs tonic posture, vocal automatisms
8	SPS, CPS	Cryptogenic FLE	Normal	L Frontal theta SW	Complex partial SE (cognitive-behavioural)	Epilepsy evolution	L frontal 2.5 Hz sharp waves rhythmic activity	Slight confusional state, disinhibition and euphoria state
9	CPS, SGS	Cryptogenic FLE	Normal	Bil Frontal slow wave and L frontal spikes	Generalized NCSE	Epilepsy evolution	2—3 Hz generalized SW and PSW activity with L predominance	Confusional state, psychomotor slowiness
10	CPS, SGS	Cryptogenic FLE	Normal	Bil frontal 3—4 Hz slow wave and R fronto-central sharp waves	Generalized NCSE	Epilepsy evolution	1.5 Hz generalized sharps waves and SW activity	Confusional state, subtle myoclonic jerks
11	Pseudoabsence, GTCS	Cryptogenic FLE	Normal	R frontal spikes + SBS (2—3 Hz generalized SW-PSW discharges)	Generalized NCSE	Epilepsy evolution	2—3 Hz generalized SW activity with R predominance	Confusional state
12	CPS, SGS	Cryptogenic FLE	Normal	L frontal spikes + SBS (bil frontal 2,5 Hz SW)	Generalized NCSE	Epilepsy evolution	1.5—2 Hz generalized SW activity	Confusional state, oral automatism, motor and verbal perseveration
13	SP, CP, SGS	Cryptogenic TLE	Normal	Asynchronous bitemporal slow waves and spikes	Complex partial NCSE (confusional)	AEDs reduction	Recurrent seizures with LVFA in L temporal lobe → rhythmic slow waves in homolateral temporo-parietal regions	Confusional state, oral, gestural and verbal automatisms

Table 1 (*Continued*)

Pt	Seizure type	Epilepsy syndrome	MRI	Interictal EEG	SE semeiological subtypes	SE aetiology	SE EEG findings	SE clinical pattern
14	SP, CPS	Cryptogenic TLE	Normal	R temporal slow wave and spikes	Complex partial NCSE (confusional)	AEDs reduction	Recurrent seizures with LVFA in R temporal lobe → spikes and slow waves in homolateral fronto-temporal regions	Confusional state, aphasia, oral and gestural automatisms
15	CPS	Cryptogenic TLE	Normal	Bil 1.5—2 Hz slow wave	Simple partial NCSE (experiential)	Epilepsy evolution	Recurrent seizures with LVFA in R temporal lobe → rhythmic slow wave activity in homolateral fronto-central regions	Sensations of ''being not myself'', slight confusional state, oral and gestural automatisms
16	SP, CPS, SGS	Cryptogenic TLE	Normal	L temporal slow wave and spike	Generalized NCSE	Epilepsy evolution	1.5′Hz generalized SW activity	Confusional state
17	SPS, CPS, SGS	Cryptogenic TLE	Normal	R Temporal 4 Hz slow wave	Complex partial NCSE (confusional)	Epilepsy evolution	SW activity and rhythmic spikes in R temporal lobe	Confusional state, oral and gestural automatisms
18	SPS, CPS	Cryptogenic TLE	Normal	R temporal slow wave and spike	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA in R centro-parietal and temporal → homolateral hemispheric rhythmic delta slow waves activity	''a pressure in my head... a dizziness...'', grimace, speech arrest, head flexion, autonomic signs
19	SPS, SGS	Cryptogenic POE	Normal	Bitemporal slow wave	Partial CSE	AEDs reduction	Recurrent seizures with LVFA in R parietal lobe → theta rhythmic slow waves in homolateral posterior regions	Sensation ''something painful under my left armpit'', left upper limb tonic postural modification

20	Pseudoabsence	Symptomatic FLE	L frontal perinatal anoxic lesion	2.5 Hz generalized SW-PSW discharges	Generalized NCSE	Worsening seizures	2,5 Hz generalized SW-PSW activity	Confusional state, slight oral automatisms
21	SPS, SGS	Symptomatic FLE	R fronto-central lesion (ischemic stroke)	R frontal slow waves	Partial CSE	Poor compliance	Recurrent seizures with LVFA in R frontal lobe → rhythmic spike activity in homolateral fronto-central regions	Leftward head and eye turning, left arm tonic posture
22	SPS, SGS	Symptomatic FLE	L frontal lesion following aneurysm rupture	L frontal slow waves	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA in L frontal lobe → rhythmic spike activity in homolateral fronto-central regions	Rightward head and eye turning, right arm tonic posture
23	SPS, CPS	Symptomatic FLE	L fronto-temporal glioma	L fronto-temporal slow wave and spikes	Partial CSE	Epilepsy evolution	L fronto-temporal 2—3 HZ continuous sharp waves activity	Oral automatism, aphasia, R upper limb dystonic posturing, slight confusional state
24	SPS, SGS	Symptomatic FLE	R frontal-temporal atrophy	R hemispheric 4—5 Hz slow wave	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA in R fronto-temporal → γrhythmic slow waves fronto-central regions	L facial myoclonic jerks, dysarthria, tongue and mouth apraxia
25	SPS, SGS	Symptomatic FLE	L frontal focal cortical dysplasia	L fronto-temporal slow waves	Partial CSE	Poor compliance	Recurrent seizures with LVFA in L frontal region → rhythmic spike activity in bil fronto-central regions	Marked dysarthria, sialorrhea, tongue and mouth praxic deficit
26	SPS, CPS, SGS	Symptomatic FLE	L frontal focal cortical dysplasia	L temporal slow waves	Partial CSE	AEDs reduction	Recurrent seizures with LVFA → rhythmic theta slow waves and spikes activity in L temporal and frontal region	''a fear.'', loss of contact, head turning, bilateral upper limbs posturing, complex motor activity

Table 1 (*Continued*)

Pt	Seizure type	Epilepsy syndrome	MRI	Interictal EEG	SE semeiological subtypes	SE aetiology	SE EEG findings	SE clinical pattern
27	CPS, SGS	Symptomatic FLE	Leucoencephalopathy	Generalized delta slow wave, R frontal spikes	Generalized NCSE	Epilepsy evolution	1.5—2 Hz generalized SW activity	Confusional state, motor perseveration, myoclonic jerks
28	SPS, SGS	Symptomatic TLE	L temporal cortical focal dysplasia	L 1—4 Hz slow waves	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA L temporal lobe → rhythmic delta slow waves in homolateral temporo-fronto-central regions	Leftward head and eye turning, L upper limb tonic posture
29	SPS, CPS	Symptomatic TLE	R temporal lobe focal atrophy	R temporal theta slow wave and spike	Simple partial SE (experiential)	AEDs reduction	Recurrent seizures with LVFA and rhythmic theta-delta slow waves in R temporal lobe	Sensation "... the head as empty, I can't speak", forced thinking and slight confusion
30	SPS, SGS	Symptomatic TLE	CNS indefinite infective disease	L temporal slow waves and spikes	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA and rhythmic theta slow waves and spikes in L temporal lobe	Clonic movements involving R face and limbs
31	SPS, CPS	Symptomatic POE	R parieto-occipital dysplasic lesion	R temporo-parieto-occipital slow waves, spikes and SW	Partial CSE	Epilepsy evolution	Recurrent seizures with LVFA → rhythmic spikes in R parietal-occipital regions	Sensation "I see all blank", slight confusional, gestural automatism, leftward head, eye turning and R upper limb tonic posture
32	SPS, CPS, SGS	Symptomatic POE	R band heterotopia and pachygyria	Bil and R temporo-parietal delta SW activity and 2 Hz SW-PSW	Generalized NCSE	Epilepsy evolution	1.5—2 Hz generalized SW-PSWD with focal onset in R temporo-parieto-occipital regions	Clouding of consciousness, apathy, accompanied by slight leftward eye and head turning and brief axial tonic posturing

33	PS, SGS	Symptomatic POE	Normal	R temporo-parieto-occipital theta slow waves and spikes	Partial CSE	AEDs reduction	Recurrent seizures with LVFA in R temporo-occipital regions → homolateral hemispheric rhythmic slow wave activity	Leftward head and eye turning, L upper limb tonic posture, L facial clonic jerks
34	Absences, GM	IGE (JAE)	Normal	Typical 3—3.5 Hz generalized SW complexes	Generalized NCSE	Epilepsy evolution	Continuous 3.5 Hz generalized SW-PSW activity	Clouding of consciousness, slight oral automatisms
35	Absences, myoclonic	IGE (JME)	Normal	Photoparoxysmal response	Generalized CSE	Worsening seizures	Continuous 3 Hz generalized PSW activity	Diffuse myoclonic positive and negative jerks (facial muscles, limbs), slight confusional state
36	Absences, GM	IGE (JAE)	Normal	Generalized SW complexes	Generalized NCSE	AEDs reduction	2.5—3 Hz generalized SW activity	Confusional state, slight automatic motor activity
37	Atypical absences, SPS, SGS	Symptomatic generalized (LGS)	Bil parieto-occipital double cortex and pachygyria	2—2.5 HZ generalized SW-PSW activity	Partial SE	Epilepsy evolution	3 Hz generalized SW activity with focal onset in R central-parietal regions	Rhythmic eye blinking, leftward eye and head turning
38	SPS, SGS	Cryptogenic generalized (LGS)	Normal	L delta slow waves	Partial CSE	Poor compliance	Recurrent seizures with LVFA in frontal lobe → L frontal-central discharge	Leftward head, eye turning, bilateral upper limbs tonic posturing
39	Atypical absences, tonic	Symptomatic generalized (LGS)	Normal	2—2.5 HZ generalized SW-PSW activity	Generalized CSE	Epilepsy evolution	Continuous generalized slow SW and GPFA	Staring, bilateral tonic posturing of axial muscles and upper limbs
40	Atypical absences, tonic	Symptomatic generalized (LGS)	Tuberous sclerosis	Bil frontal 1.5 Hz slow waves and R fronto-temporal spikes	Generalized CSE	Epilepsy evolution	Continuous generalized slow SW and GPFA	Tonic posturing of axial muscles, arms; grimace

Table 1 (*Continued*)

Pt	Seizure type	Epilepsy syndrome	MRI	Interictal EEG	SE semeiological subtypes	SE aetiology	SE EEG findings	SE clinical pattern
41	Tonic, atypical absences	Symptomatic generalized (LGS)	Normal	2—2.5 generalized SW discharges	Generalized CSE	Epilepsy evolution	Continuous generalized slow SW and GPFA	Staring, slight leftward eye and head turning, bilateral tonic posturing of upper limbs, oral and verbal automatisms
42	Pseudoabsence, SGS	Undetermined	Normal	Normal	Generalized NCSE	Epilepsy evolution	3.5 Hz generalized SW-PSW activity	Clouding of consciousness, oral automatisms and motor perseveration
43	Tonic	Undetermined	Normal	4 Hz generalized SW-PSW complexes	Generalized CSE	Epilepsy evolution	GPFA	Tonic posturing of axial muscles and upper limbs; grimace
44	Tonic, absences	Undetermined	Normal	2 Hz generalized SW-PSW complexes	Generalized CSE	Epilepsy evolution	GPFA	Tonic posturing of axial muscles and upper limbs; grimace
45	Pseudoabsence	Undetermined	Normal	Bil frontal slow wave	Generalized NCSE	Epilepsy evolution	Continuous 3 Hz generalized SW activity	Confusional state, subtle perioral myoclonic jerks
46	GTCS, myoclonic	Undetermined	Normal	Bil temporal slow waves	Generalized CSE	AEDs reduction	Generalized PSW discharges → tonic-clonic generalization	Subcontinuous myoclonic jerks, tonic-clonic seizures
47	Pseudoabsence, GTCS	Undetermined	Leucodistrophy	3 Hz generalized SW-PSW complexes	Generalized NCSE	Epilepsy evolution	3 Hz generalized SW-PSW activity	Confusional state
48	Pseudoabcense	Undetermined	Normal	4 Hz generalized SW-PSW discharges	Generalized NCSE	Epilepsy evolution	3.5—4 Hz generalized SW-PSW activity	Confusional state

49	SPS	Late-onset RE	R fronto-insular focal atrophic area	R frontal theta SW	Partial CSE	Epilepsy evolution	R fronto-temporal 1–1.5 Hz rhythmic slow waves	Sensation as "a pain in my mouth…", sialorrhea, dysarthria, dystonic posture involving left limbs
50	SP, SGS	Late-onset RE	R hemispheric atrophy	R frontal slow wave and spikes	Partial CSE	Epilepsy evolution	R frontal-central spike/sharp wave activity	Continuous left myoclonic jerks (oral, upper limb)

SPS, simple partial seizure; CPS, complex partial seizure; SGS, secondary generalized seizure; GTCS, generalized tonic-clonic seizure; GM, grand mal seizures; FLE, frontal lobe epilepsy; TLE, temporal lobe epilepsy; POE, parieto-occipital epilepsy; JME, juvenile myoclonic epilepsy; JAE, juvenile absence epilepsy; LGS, Lennox–Gastaut Syndrome; RE, Rasmussen Encephalitis; SW, spike-and-waves; PSW, polyspike-and-waves; SBS, secondary bilateral synchrony; GPFA, generalized paroxysmal fast activity; LVFA, low voltage fast activity; CSE, convulsive status epilepticus; NCSE, non-convulsive status epilepticus; BDZ, benzodiazepines; PHT, phenytoin; TPS, thiopental sodium; Bil, bilateral; R, right; L, left.

onset Rasmussen Encephalitis in 2 cases); in the other 33 cases in which no apparent precipitating factors were discovered, SE was presumed to be an intrinsic condition of the epileptic syndrome (in these cases we preferred not to use the term "cryptogenic" so as to avoid any confusion between the aetiologies of epilepsy and SE). This last group of 33 patients contained a large number of patients with a history of recurrent episodes of SE.

SE and related epileptic syndromes

Thirty-three of the 50 patients had partial epilepsy (symptomatic in 14 cases, cryptogenic in 19 cases), 8 patients had generalized epilepsy (idiopathic in 3 cases, symptomatic in 5 cases), 7 patients had undetermined syndromes (whether focal or generalized), 2 patients had a diagnosis of late-onset Rasmussen Encephalitis. Table 2 shows the main clinical characteristics of SE and the related epileptic syndromes. When assessing a possible relationship between epileptic syndromes and SE aetiology, statistical analysis revealed a statistically significant relationship between the forms of cryptogenic partial epilepsy and SE aetiology ($p = 0.01$).

SE duration and response to treatment

We divided our population in two subgroups of patients according to the duration of the SE: in 28 cases, the SE lasted less than 12 h, whereas in the remaining 22 cases it lasted more than 12 h. Our therapeutic approach included a sequential strategy with: (i) a first-line step consisting of i.v. benzodiazepines (Lorazepam 4–8 mg in bolus, maintenance dose of 16 mg/24 h) and (ii) a second-line step consisting of i.v. phenytoin (dose of 15–18 mg/kg) and of thiopental sodium in non-responders (loading dose of 100–250 mg given over 20 s until seizures are controlled, followed by a maintenance dose of 3–5 mg/kg/h); despite of the refractoriness, in two patients with late-onset Rasmussen's Encephalitis no other acute therapy was administered (immunotherapy was planned). Fig. 2 shows the specific therapies used and the relative responder ratios.

Short-term outcome

In 41 patients we did not observe any neurological deficits related to SE. In the remaining nine patients only slight sequelae were documented mainly consisting of a mild cognitive impairment and, in just two cases, a slight pyramidal hemisyndrome (both of them with late-onset Rasmussen's Encephalitis).

Table 2 SE and related epileptic syndromes

	SE type				SE aetiology		SE recurrence
	CSE		NCSE		Situation related	Syndrome evolution	
	PCSE	GCSE	PNCSE	GNCSE			
Cryptogenic partial epilepsy							
Frontal lobe (12)	3	2	3	4	—	12*	12
Temporal lobe (6)	1	—	4	1	2	4	4
Parieto-occipital lobe (1)	1	—	—	—	1	—	0
Symptomatic partial epilepsy							
Frontal lobe (8)	6	—	—	2	4	4	4
Temporal lobe (3)	2	—	1	—	1	2	2
Parieto-occipital lobe (3)	2	—	—	1	1	2	2
Idiopathic generalized epilepsy							
Juvenile myoclonic epilepsy (1)	—	1	—	—	1	—	0
Juvenile absence epilepsy (2)	—	—	—	2	1	1	0
Symptomatic/cryptogenic generalized epilepsy							
Lennox-Gastaut syndrome (5)	2	3	—	—	1	4	5
Undetermined focal or generalized (7)	—	3	—	4	1	6	5
Special syndromes							
Late onset Rasmussen Encephalitis (2)	2	—	—	—	—	2	2

CSE, convulsive status epilepticus; NCSE, non-convulsive status epilepticus; PCSE, partial convulsive status epilepticus; GCSE, generalized convulsive status epilepticus; PNCSE, partial non-convulsive status epilepticus; GNCSE, generalized non-convulsive status epilepticus. *$p = 0.01$ (χ^2-test).

Response to therapy and short-term outcome related to age, semeiological subtypes, epileptic syndrome, SE aetiology and duration

The statistical analysis showed a statistically significant correlation between a shorter SE duration and a better response to therapy ($p = 0.01$) and between CSE subtype and a worse response to the first-line therapy ($p < 0.05$); a relationship at statistical significance limit between epileptic syndromes and response to therapy ($p = 0.06$) and between epileptic syndromes and outcome ($p = 0.06$) was also observed (Table 3). Response to therapy and outcome were not influenced by SE age of onset (Table 3).

Discussion

Although SE is usually the expression of acute cerebral disease, it can be observed in 2—16% patients suffering from various epileptic syndromes.[10]

In this study, a video-EEG analysis allowed us to identify a wide spectrum of electro-clinical features in a population almost equally distributed in the two main groups of CSE and NCSE. In disagreement with previously published series and historical data,[3,4,6,13,14] in this study we observed a significant percentage of NCSE (44%) and relatively small number of CSE, especially as regards GCSE (18%). These data are amply justified by the selection criteria adopted in this study that specifically focused on SE in patients suffering from pre-existing epilepsy. In particular the evidence of a low

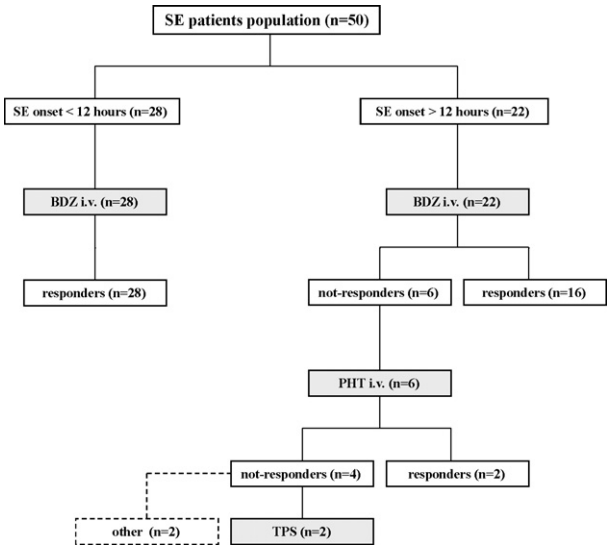

Figure 2 Algorithm showing therapeutic strategies in the patients with status epilepticus included in the study. SE, status epilepticus; BDZ, benzodiazepines; PHT, phenytoin; TPS, thiopental sodium; i.v., intravenous administration; other, in patients with a late-onset Rasmussen Encephalitis an immunotherapy was planned.

Table 3 Response to therapy and outcome related to age, semeiological subtypes, epileptic syndrome, aetiology and duration

	Response to therapy		Sequelae	
	First-line therapies	Further therapies	No	Yes
Age at SE onset				
<30 years (19)	16	3	14	5
30–60 years (24)	22	2	22	2
>60 years (7)	6	1	5	2
SE Semeiological subtypes				
CSE (28)	22	6***	23	5
NCSE (22)	22	–	18	4
Epileptic syndromes				
Cryptogenic/Idiopathic (22)	22	–**	21	1**
Symptomatic (28)	22	6	20	8
SE aetiology				
Situation related (13)	12	1	13	–
Syndrome evolution (37)	32	5	28	9
SE duration				
<12 h (28)	28	–*	24	4
>12 h (22)	16	6	17	5

*$p = 0.01$; **$p = 0.06$ (χ^2-test with Fisher's correction); ***$p < 0.05$.

proportion of GCSE is unsurprising as most of our patients had been referred to our laboratory from either a ward or outpatient service. Indeed, patients in more critical conditions, such as those with GCSE, are usually referred to emergency departments where prompt therapy is the primary aim, while the definition of the clinical and neurophysiological features becomes secondary. With respect to semeiological definition, this study confirms the central role of the ictal neurological evaluation and EEG data in classifying NCSE, especially when differentiating partial from generalized subtypes.[9,11,15]

In some conditions, a more careful electro-clinical assessment appears to be useful as a means of understanding the role of SE in different epileptic syndromes.

Although epileptic patients account for as many as 50% of the patients in SE population-based studies (predominantly performed in emergency departments), the data available on this subgroup of patients cannot be considered exhaustive because targeted clinical and neurophysiological assessments needed for a thorough definition of the syndrome are lacking.[3,4,6]

It is commonly accepted that SE, when recognized in epileptic patients, is often related to AED withdrawal due to either the medical strategy or patient non-compliance. However, the natural evolution of some epileptic syndromes, especially drug-resistant ones, has been known to be characterized by the occurrence of SE or seizure clustering.[16]

Although we found, in accordance with previous studies,[5] a number of cases of SE closely related to AED (non-compliance, planned reduction or worsening seizures), it is noteworthy that SE in a large number of patients was related to epileptic syndrome natural history (37/50 cases). Indeed, with the exception of a few cases in which progression of the underlying cerebral pathologies was documented (4/37 cases), SE, which was often found to recur in the same patient, was presumably an intrinsic condition of the cryptogenic/non-evolving symptomatic epileptic syndrome in the vast majority of the cases (33/37 cases) confirming previously published data.[17] From a syndromic point of view, this group of "unexplained" recurrent SE, which often occurred in patients with an apparently normal brain, comprised various conditions. While recurrent SE may be expected in the natural history of some of these conditions (e.g. drug-resistant partial epilepsy and Lennox-Gastaut syndrome),[15,18] it is more difficult to explain in the remainder (undetermined syndrome, whether focal or generalized, or idiopathic generalized epilepsy with secondary "lennoxization"). In this regard, the higher incidence of SE in patients with frontal lobe epilepsy, particularly in those suffering from a cryptogenic partial syndrome, is worthy of note. Further studies are warranted to shed light on this specific issue.

In the present study, the analysis of the patients' variables with respect to the patient's response to therapy and short-term outcome yielded some noteworthy findings. Symptomatic epileptic syndromes

tend to be related to a worse response to therapy and a less favourable outcome: a very interesting finding was that this group included epilepsies related not only to evolving lesions (in which it is difficult to assess the exact role SE plays in the prognosis) but also to fixed and ''remote'' conditions, in which a worsening neurological status is related to prolonged activity per se. Moreover, in accordance with published data[5,19] we found a close relationship between SE duration and the response to therapy: indeed, SE lasting less than 12 h responded promptly to therapy, whereas SE lasting longer was more likely to be therapy-resistant. As regards the relationship between SE semeiological subtypes and the response to therapy, this study seems to be in agreement with previous studies, confirming that CSE is usually more difficult to manage than NCSE,[11] especially in epileptic patients. One apparent contradiction was that a longer-lasting SE was not, as would be expected, related to a worse outcome. This last issue which in fact partially confirmed already published data[11,20] however appears to be closely related to the intrinsic limitations of this study. Indeed, the small number of patients did not yield statistically significant information on this specific topic; moreover, the retrospective design of the study allowed us to evaluate short-term outcome alone, and not the possible presence of subtle, long-term cognitive consequences, particularly in patients presenting recurrent episodes of SE.

In conclusion, though SE in epileptic patients appears to be a less critical condition than acute symptomatic SE, a long-lasting epileptic condition may reinforce its self-sustaining neurophysiological mechanism, thereby affecting the patient's response to therapy and the time of recovery. As regards the prognosis, if administered promptly, therapy may, as happens in brief, single seizures, help avoid or limit the ''cumulative damage'' in the long term.

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