■ Original article

*Epileptic Disord 2022; 24 (2): 387-396*

Epileptic Disorders

# Non-convulsive febrile status epilepticus mimicking a postictal state after a febrile seizure: an ictal electroclinical and evolutive study

Jacopo Proietti[1,2], Elena Fiorini[1,3], Lisa Meneghello[1,4], Gaetano Cantalupo[1,3,5], Elena Fontana[1,3], Tommaso Lo Barco[5,6], Bernardo Dalla Bernardina[3], Francesca Darra[1,3,5]

[1] U.O.C. di Neuropsichiatria Infantile, Dipartimento ad Attività Integrata Materno Infantile – AOUI di Verona, Verona, Italy
[2] PhD program Applied Sciences of Life and Health, University of Verona, Verona, Italy
[3] Centro Ricerca per le Epilessie in età Pediatrica (CREP), Azienda Ospedaliera Universitaria di Verona, Verona, Italy
[4] U.O.S. di Neuropsichiatria Infantile, Azienda Ulss9 Scaligera, Verona (Italy)
[5] Child Neuropsychiatry, Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, University of Verona, Verona, Italy
[6] PhD program Clinical and Experimental Medicine, University of Modena and Reggio Emilia, Modena, Italy

Received July 27, 2021; Accepted November 01, 2021

**ABSTRACT**

***Objective.*** Febrile status epilepticus evolves from a febrile seizure (FS) in 5% of cases. Its prompt recognition is challenging, especially when motor manifestations are absent or subtle. We describe the ictal electroclinical features of non-convulsive febrile status epilepticus (NCFSE) following an apparently concluded FS, initially misinterpreted as postictal obtundation and in some way mimicking the described "non-epileptic twilight state".

***Methods.*** We present an electroclinical study of 18 children, collected in our unit, who presented with NCFSE after an apparently resolved FS, longitudinally followed for one year to seven years and nine months (mean: four years and three months). The age at first NCFSE ranged between one year and two months and five years and eight months (mean: two years and six months). Patients were examined after spontaneous or rectal diazepam-induced resolution of a FS, while showing persisting impairment of awareness.

***Results.*** A lack of responsiveness to painful stimulation, abnormal posturing and aphasia were present in all cases, variably associated with perioral cyanosis, hypersalivation, automatisms, gaze deviation and other lateralizing signs; eyes were open. The EEG recording started 20 to 140 minutes after the apparent resolution of the FS and was invariably characterized by delta or theta-delta pseudorhythmic activity, mainly involving the fronto-temporal regions, with hemispheric predominance in two thirds of the cases. The electroclinical condition, lasting 25 to 210 minutes, quickly recovered after intravenous diazepam. Follow-up revealed normal neurodevelopment and EEG in almost all patients (learning disability emerged in three). In five subjects, NCSE relapsed (twice in two). None presented afebrile seizures.

***Significance.*** Our series highlights the electroclinical features of focal NCFSE. Distinctive elements are a lack of reactivity, cyanosis, lateralizing clinical and EEG signs, and resolution clearly tied to intravenous benzodiazepine administration.

**Key words:** febrile seizures, febrile status epilepticus, twilight state, ictal EEG

• **Correspondence:**
Francesca Darra
University of Verona,
AOUI Verona,
P.le A. Stefani 1,
37126 Verona, Italy
<francesca.darra@univr.it>

doi:10.1684/epd.2021.1402

Febrile seizures (FS) are the most common epileptic seizures in childhood, affecting 2-5% of children between six months and six years of age in the United States and Western Europe, with a peak incidence in the second year of life [1-3]. Of FS, 60-70% are simple, whereas 30-40% are complex, the latter defined as lasting for more than 15 minutes and/or having focal semiology and/or recurring within 24 hours [1, 4]. FS are prolonged (lasting 10 to 30 minutes) in 25-30% of cases and evolve to febrile status epilepticus (FSE) in 5-9% cases [4-6]. Since FSE is less likely to terminate spontaneously [5], it requires prompt recognition and treatment. FSE is defined as a prolonged seizure or repetitive seizures lasting for more than 30 minutes without regaining alertness, occurring in the context of a febrile illness [7]. It is generally characterized by a unilateral, or predominantly unilateral, convulsive manifestation [4, 8]. There are no descriptions in the literature of FSE with varying symptomatology without significant motor manifestations. Despite FS frequency, to date, iconographic documentation of ictal electroclinical features of FSE is lacking, and even data on immediate postictal phase is sparse [9]. The prompt recognition of FSE is challenging, especially when obvious motor manifestations are absent. As reported by the FEBSTAT study, in the emergency department, one out of three cases of FSE is unrecognized [10]. The discrimination between postictal behavioural symptoms and ongoing ictal non-convulsive status epilepticus (NCSE), which can follow a convulsive seizure, is difficult and depends mainly on EEG [11].

Some authors have reported electroclinical features of a peculiar postictal status following a FS, characterized by impaired awareness (with eyes closed and lack of cyanosis), reactivity to painful stimuli including crying, and absence of an obvious EEG paroxysmal activity (a diffuse slowing with posterior predominance is described). Importantly, the mentioned clinical signs and EEG pattern were not modified by benzodiazepine administration. Authors stressed the need to distinguish this condition, named "non-epileptic twilight state with convulsive manifestations (NECT)" [12, 13] or "prolonged non-epileptic motor status after a FS" [14], from an ongoing seizure, in order to avoid unnecessary administration of antiseizure medication (ASM).

In this study, we describe the ictal electroclinical features of FSE following an apparently concluded FS, clinically resembling a non-epileptic twilight state, which we recognized as an ongoing epileptic phenomenon. We report the electroclinical presentation of a population of 18 children, retrospectively collected in our unit, who presented with one or more episodes of non-convulsive febrile status epilepticus (NCFSE) and who were followed from their arrival at hospital at the time of their first FSE.

## Materials and methods

Eighteen subjects were included, nine males and nine females, aged between six years and 11 years and seven months, who presented, on one or more occasion, at a mean age of four years and one month (range: 1 year and 2 months - 10 years and 4 months), with long-lasting FSE following an apparently concluded FS. For all patients, urgently admitted at our Child Neuropsychiatry Unit at the University Hospital of Verona, we were able to obtain an EEG recording of the ictal event (video-EEG of 14 events; video-EEG-polygraphic in 11). All 18 subjects received a diagnosis of FS, and presented their first FSE before the age of six years. Fever was present in all cases at the time of FS presentation; detected shortly after onset in two episodes within 12 hours before onset in the remaining cases. Fever was related to infection in 24/25 episodes, in which elevated blood lymphocytes and/or clinical signs of the upper respiratory tract were recorded. In one case, the temperature increased following MMR vaccination. Body temperature exceeded 38°C in all cases, for which the exact measurement was available (individual values are reported in *table 1*). All recordings were started during emergency care with active participation of the physician, who performed the electroclinical evaluation and treatment at the bedside. The diagnosis of NCFSE was based clinically on complete impairment of awareness with unresponsiveness to painful stimuli, accompanied by lateralizing signs, and the recurrence of paroxysmal discharges and/or rhythmic and subcontinuous delta/theta activity on EEG, with dramatic EEG and clinical improvement after intravenous diazepam administration. The above-mentioned EEG parameters are congruent with the definition of NCFSE based on the Salzburg criteria [15]. Other inclusion criteria were normal motor and cognitive development at the time of FSE presentation and the exclusion of an acute cerebral pathology (based on clinical data alone in 12 cases, with support from a brain CT scan in six in whom four had a lumbar puncture). All patients were longitudinally followed at our unit, through periodic electroclinical evaluations (including neurological and psycho-diagnostic assessment and EEG recordings during wakefulness and spontaneous sleep) for a minimum of one year to a maximum of seven years and nine months (mean follow-up: four years and three months) after the first FSE. We point out that four other subjects who presented with a long-lasting FSE following an apparently concluded FS, under the age of six years, were not included in the analysis due to insufficient follow-up (less than one year).

Brain MR imaging was also performed in the five subjects who presented with recurrent FSE.

▼ **Table 1.** Electroclinical features of the study population.

| Patient | Age at 1st FS | Age at 1st FSE | Age at 2nd FSE | Age at 3rd FSE | Seizure triggering SE | | | | SE | | | | Age at last FS | Age at last visit |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Body T (°C) | Semiology | Duration | Treatment | *n* | Semiology (in addition to IA, Ap, D – always present) | Duration | EEG: side predominance | | |
| 1 | 8m | 3y | - | - | 38.7 | FNM | 15′ | N | 1 | C, ED, Au | 120′ | N | 4y6m | 6y7m |
| 2 | 4y2m | Id | - | - | 39.2 | FNM | 15′ | DZP | 1 | - | 45′ | L | Id | 6y8m |
| 3 | 1y11m | 5y8m | - | - | 38.5 | FNM→G | 5′ | N | 1 | C, ED | 64′ | R | 5y8m | 6y8m |
| 4 | 1y10m | Id | 2y1m | 2y7m | 39 / NR / 38.8 | FM→G / U / G | 5′ / 7′ / 5′ | N / DZP / DZP | 3 | ED, FSD / C, ED / - | 90′ / 50′ / 75′ | N / N / N | 2y7m | 6y9m |
| 5 | 11m | 1y6m | - | - | 39.5 | G | 5′ | N | 1 | - | 25′ | N | 1y6m | 6y |
| 6 | 1y1m | 1y2m | - | - | 39.2 | FNM | 5′ | N | 1 | ED, Au, C | 120′ | R | 2y2m | 7y |
| 7 | 1y4m | 2y2m | 2y3m | - | 39 / 38.8 | FNM→G / FNM→G | 15′ / 10′ | DZP / DZP | 2 | C, ED / C, ED | 40′ / 50′ | R / R | 2y3m | 6y1m |
| 8 | 1y7m | Id | - | - | 39 | U | 20′ | N | 1 | ED | 120′ | L | Id | 8y8m |
| 9 | 3y | 5y6m | 6y3m | 10y4m | 39.2 / 40 / 38.7 | FNM→G / FNM / FNM→G | 9′ / 5′ / 7′ | DZP / DZP / DZP | 3 | C, MD, ED / C, ED / - | 50′ / 40′ / 48′ | N | 10y4m | 11y7m |
| 10 | 11m | 3y7m | 3y9m | - | 38.5 | FNM / FNM | 20′ / 10′ | DZP / DZP | 2 | C / ED, C, HD | 40′ / 30′ | R | 3y9m | 6y5m |
| 11 | 1y10m | Id | - | - | 39.2 | U | 20′ | N | 1 | - | 80′ | N | Id | 9y7m |
| 12 | 10m | 2y1m | - | - | 38.3 | G | 3′ | N | 1 | - | 68′ | N | 2y1m | 6y3m |
| 13 | 1y11m | Id | - | - | 40.2 | FNM→G | 5′ | DZP | 1 | - | 100′ | N | Id | 6y3m |
| 14 | 2y5m | Id | - | - | 39 | FM→G | 5′ | N | 1 | C, Au | 50′ | R | Id | 6y3m |
| 15 | 1y4m | Id | 3y1m | - | 38.5 / NR | G / U | 3′ / 10′ | N / DZP | 1 | - / ED, HD, MD C | 45′ / 30′ | R / R | Id | 6y4m |
| 16 | 2y | Id | - | - | 38.8 | G | 2′ | N | 1 | ED, C, Au | 50′ | R | Id | 7y |
| 17 | 1y4m | Id | - | - | 39.5 | G | 5′ | DZP | 1 | - | 90′ | R | Id | 6y6m |
| 18 | 1y2m | 2y2m | - | - | 38.4 | FNM→G | 6′ | DZP | 1 | HD, ED, FSD | 210′ | R | 2y6m | 9y10m |

T: temperature; FM: focal motor; FNM: focal non motor; G: generalized; U: undetermined; DZP: rectal diazepam; N: none, NR: not reported; IA: impaired awareness (reduced reactivity): Ap (aphasia) and D (dystonic posturing; at rest or induced by nociceptive stimulation) present in all cases; Au: automatisms; C: perioral cyanosis; HD: head deviation; ED: eye deviation; MD: mouth deviation; FSD: focal strength deficit.

Considering both presentation and follow-up, 25 episodes of FSE were recorded. The following parameters were analysed: gender distribution, personal history, family history of FS and/or epilepsy, age at first FS, age at first FSE, semiology and duration of FS preceding and triggering the status, semiology and EEG features characterizing the FSE, treatment, and electroclinical and developmental follow-up.

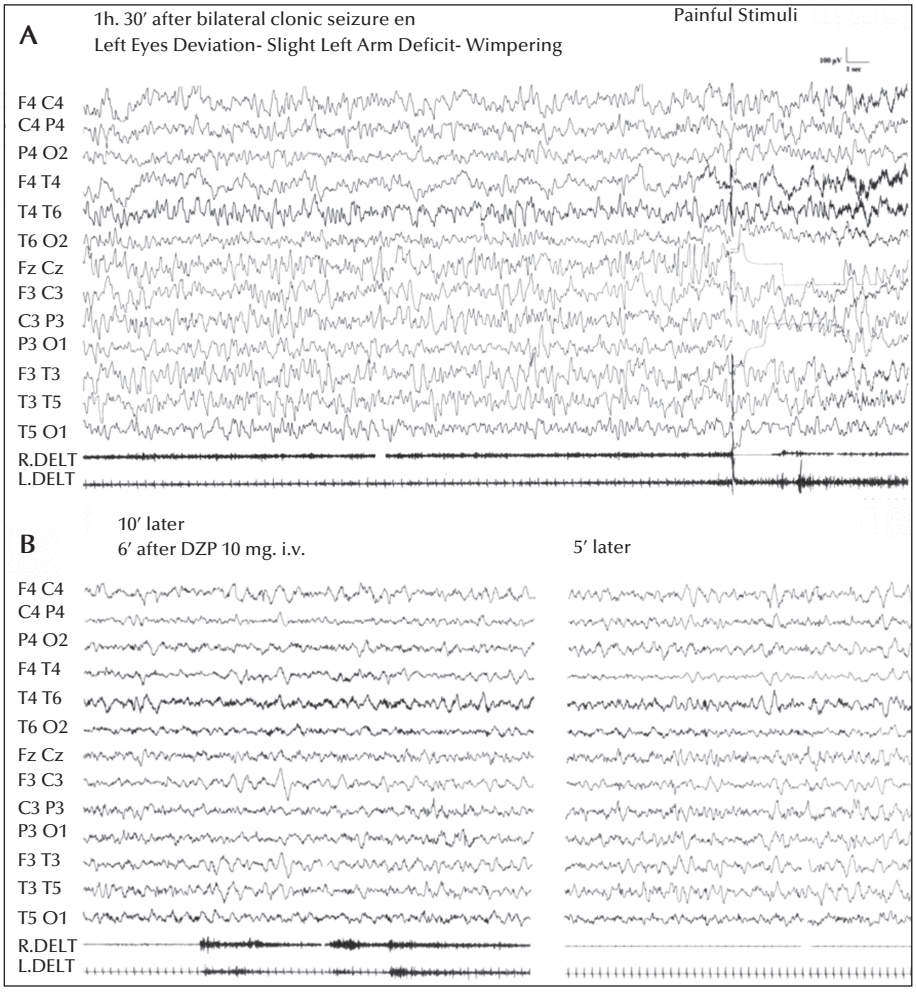
## Results

The electroclinical features of the study population are summarized in *table 1*. Males and females were equally represented. Motor and cognitive development was normal in all patients. A family history of FS and/or epilepsy (in first- or second-degree relatives) was present in 11 patients (61%): eight with a history of FS, one with epilepsy, and two with both FS and epilepsy. In nine subjects (50%), the occurrence of the FSE was preceded by one or more FS (mean: two episodes), lasting less than 10 minutes, between the age of eight months and three years (mean: one year and four months). According to the parents' descriptions, the latter were generalized in 25% of cases, focal motor or non-motor in 37%, and focal to generalized in 21%; in the remaining 17%, information was lacking. In this subpopulation, the interictal EEG, recorded between the first FS and the occurrence of FSE, was normal both during wakefulness and sleep. In nine subjects (50%), the FSE was the first ictal event.

The age at first FSE ranged between one year and two months and five years and eight months (mean: two years and six months). Since five subjects presented with more than one episode of FSE, 25 events were recorded in total. Based on parents' descriptions, the ictal event triggering the FSE was a generalized tonic-clonic seizure in six cases (24%), a unilateral to generalized motor seizure in two (8%), a focal non-motor seizure (characterized by awareness impairment, lateral gaze deviation, perioral cyanosis, and loss of muscle tone) in seven (28%), and a focal non-motor seizure followed by bilateral motor manifestations in six (24%); in four cases (16%), the ictal semiology of the FS triggering the FSE was undetermined due to insufficient information. All events seemed to resolve spontaneously within a few minutes in 11 cases (44%) and within 5 to 20 minutes after rectal administration of diazepam in the remaining 14 cases (56%). When the FS apparently ended, all patients showed persisting marked awareness impairment, with unresponsiveness to voice and touch, interpreted as a postictal condition. The clinical observation and the EEG recording started at between 20 and 140 minutes after the apparent resolution of the FS. As a first clinical observation, impaired awareness was confirmed and fluctuating dystonic posturing (with an inability to maintain the sitting position) was encountered in all subjects. Eyes were open in most cases. Lateralizing signs were present in 12 out of 18 subjects (67%) and in 15 out of 25 episodes (60%): lateral gaze deviation in 11/18 subjects (14/25 episodes) and other lateralizing signs in 5/18 subjects and 5/25 episodes (focal strength deficit in two, lateral tonic flexion of the head in three, and mouth deviation with subtle eyelid myoclonia in two). Four subjects (22%) showed simple oral and gestural automatisms; perioral cyanosis was present in 10/18 patients (56%) and 13/25 episodes (52%), and hypersalivation in 12 patients. Reactivity to manipulation and sensory stimulation was poor. Intense nociceptive stimuli induced the appearance of non-finalized abnormal movements and a global exacerbation of tonic posturing, in some cases, resulting in opisthotonos. No verbal response or cry was evoked. No patient required respiratory support. Convulsive motor manifestations were absent in all cases.

The EEG recording was invariably characterized by the absence of a physiological background activity. Two different patterns were observed. The first was characterized by continuous, diffuse, high-amplitude, theta-delta pseudorhythmic activity with irregular sharp waves intermixed mainly involving the temporal regions (*figure 1, 2B*). The second was represented by subcontinuous waxing and waning 2-4-Hz rhythmic delta activity, variable in amplitude, mainly involving the fronto-temporal regions (*figure 3*). The above featured paroxysmal activity was not modified by tactile or nociceptive stimuli. It showed a hemispheric predominance in 12 out of 18 patients (*figure 4*), while in the remaining six, it was symmetric over the two hemispheres. In all cases, clear spikes, spike-waves or recruiting fast activity were absent at the beginning of the recording. In two subjects, an electroclinical focal motor seizure (unilateral, recruiting fast poly-spikes, predominating on the fronto-temporal region, with concomitant contralateral limb stiffness and jerking) occurred during the recording; in one case, the event spontaneously resolved in 90 seconds and in the other, it was stopped by levetiracetam intravenous administration after the failure of diazepam.

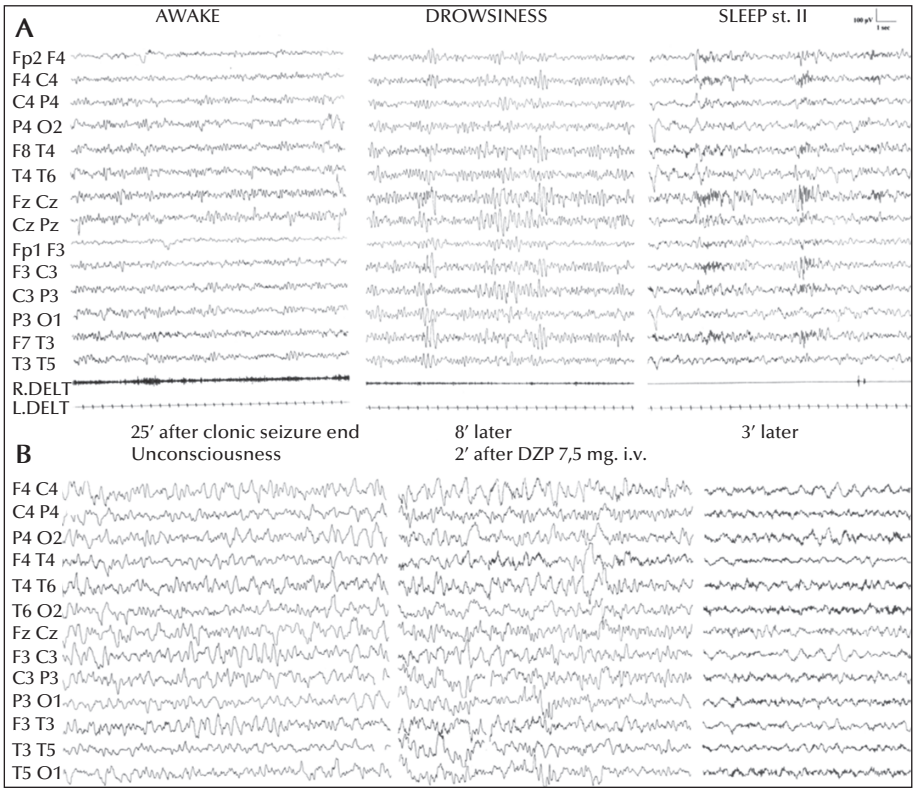
The documented NCFSE ranged in duration between 25 and 210 minutes (mean: 69 minutes). Considering the whole manifestation as a single event (the "trigger" FS and the following NCFSE), its duration was between 30 and 216 minutes (mean: 78 minutes). In all subjects, the whole electroclinical condition improved after intravenous diazepam administration (5 mg or 10 mg according to patient weight and age); abnormal posturing and movements were quickly replaced by progressive recovery of an adequate level of awareness and verbal production for age, which




■ **Figure 1.** EEG showing continuous, diffuse, high-amplitude, theta-delta pseudorhythmic activity with irregular sharp waves intermixed mainly involving the temporal regions.

was complete within 2-5 minutes after the injection, invariably followed by drowsiness or sleep. At spontaneous or induced reawakening, 15 to 30 minutes later, the clinical recovery was complete and post-ictal deficits were absent in all cases. Concomitantly with the clinical recovery, the EEG showed a clear discontinuation of the slow paroxysmal activity, replaced by pharmacological low-voltage fast activity. Later in the recording, normal background activity, both in the awake state and during sleep, was observed in all cases, together with an absence of paroxysmal abnormalities.

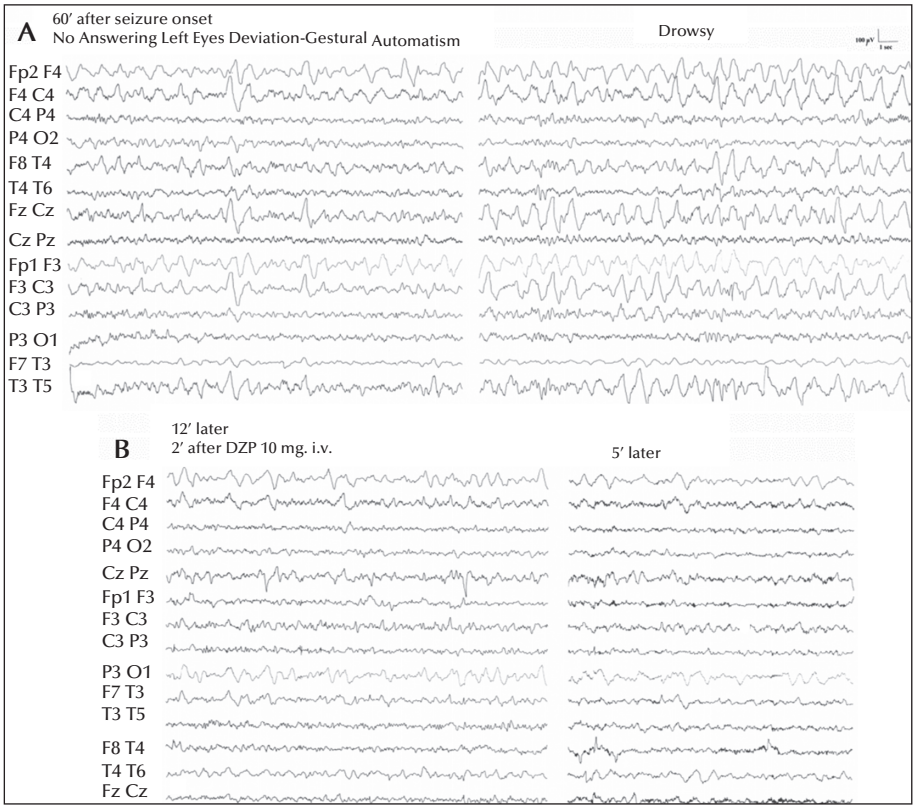
During the follow-up, in the large majority of cases, the neurological and cognitive profile remained in the normal range. Three subjects presented with learning disability, which was associated with attention deficit with hyperactivity (ADHD) in two. The interictal EEG during wakefulness and sleep was entirely normal in the majority of patients (*figure 2A*); in five cases, interictal epileptiform abnormalities were detected only during drowsiness and sleep (brief spike-and-wave discharges in three patients and focal centro-temporal spikes in two) and in one case, we recorded brief generalized poly-spike and wave discharges without clinical correlate induced by IPS. In 13 subjects (72%), the FSE remained isolated and five subjects (28%) presented with a second FSE with similar electroclinical features (*figure 2B*) between the second and sixth year of life, of whom two also presented a third episode of FSE. Brain MRI was performed in these patients with recurrent FSE and resulted normal. After the FSE, three out of 18 patients (17%) presented with one or two FS lasting for less than five minutes. No patients presented with afebrile seizures. Four out of 18 patients were treated with VPA for a variable period of time.




■ **Figure 2.** EEG showing continuous, diffuse, high-amplitude, theta-delta pseudorhythmic activity with irregular sharp waves intermixed mainly involving the temporal regions.

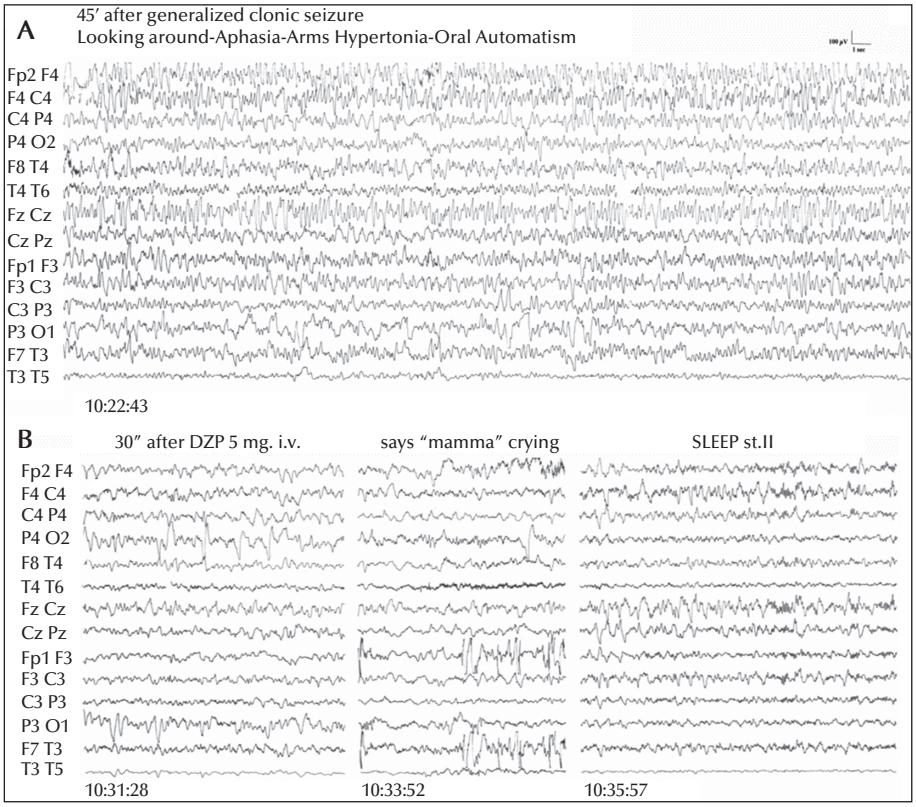
## Discussion

Although FS are usually brief ictal events that do not require intervention, they can evolve into a prolonged FS or into a FSE in 25-30% and 5% of cases, respectively [4]. FSE represents 25% of SE in the paediatric age and more than 60% of SE in the second year of life [16]. The risk of developing a FSE is higher when a prompt rescue therapy is not available, and relatively higher in patients treated with rectal benzodiazepines compared to those who receive intravenous or intranasal administrations [5, 17, 18]. When it presents as a NCSE, the FSE is often recognized late or remains unrecognized: differential diagnosis between ongoing NCFSE and postictal obtundation can be challenging and depends to a large degree on electroencephalography. In some cases, the discrimination can be difficult even with the use of EEG, since clear-cut definitions of ictal and postictal changes are not available and prolonged focal status can occur without obvious ictal scalp activity [11]. The diagnosis of NCSE is usually considered definitive when adequate administration of ASM is temporally tied to clinical and EEG improvement [19]. Our 18 subjects showed a homogeneous electroclinical picture which, in our opinion, represents an unusual type of NCFSE. Its peculiar features are the following: (1) an initial FS (focal, generalized, or focal to bilateral), which apparently terminates spontaneously or after rectal DZP administration; (2) a long-lasting status, following the "trigger" FS, characterized by impairment of awareness with eyes open and a lack of responsiveness to painful stimulation, abnormal posturing and aphasia, variably associated with lateralizing signs; (3) a concomitant EEG pattern characterized by subcontinuous delta or theta-delta pseudorhythmic activity, mainly involving the fronto-temporal regions, with a hemispheric predominance in more than half of cases, poorly modified by painful stimuli; (4) clear and quick recovery of the whole electroclinical condition after intravenous DZP administration (5 to 10 mg), followed, within a few seconds, by reappearance of interaction (with the child crying or saying some words) and simultaneous EEG improvement (slow paroxysmal abnormalities replaced by fast pharmacological activity). According to the mentioned clinical and EEG findings, this status represents a focal nonconvulsive febrile status epilepticus (NCFSE), resembling in many aspects a focal status epilepticus with impaired awareness [20] or a limbic status epilepticus




■ **Figure 3.** EEG showing subcontinuous waxing and waning 2-4-Hz rhythmic delta activity, variable in amplitude, mainly involving the fronto-temporal regions.

[21]. We considered the alternative diagnosis of Panayiotopoulos syndrome [22], however, the invariable association with the febrile trigger, occurrence in the awake state, absence of vomiting among the ictal symptoms and interictal EEG lacking local interictal abnormalities allowed us to rule out this hypothesis. In recent years, some authors observed a condition occurring after a FS and lasting between two and several minutes, with clinical and EEG features, in some way similar to those of our cases described here, which they interpreted as a postictal non-epileptic condition referred to as "non-epileptic twilight state with convulsive manifestations" (NECT) [12-14]. According to these authors, clinical findings in favour of a postictal non-epileptic condition were the presence of a cry in response to painful stimuli, the eyes closed and the absence of cyanosis and lateralizing signs. Only Yamamoto observed, among other clinical signs, a conjugate eye deviation in seven and focal clonic movements in three of 14 cases [12], which are in our opinion usual findings in a post-ictal state. Therefore, the non-epileptic interpretation of these cases, in particular, remains doubtful. Concerning the EEG, the posterior predominance of the slow abnormalities and especially the inefficacy of DZP both on the clinical and EEG state were considered evidence of the non-epileptic nature of this condition. However, only some of these patients were treated and none of the authors reported the administered dosages. Focusing on the electroclinical picture characterising our population, the clinical findings supporting the epileptic nature are the lack of verbal responsiveness (not even a cry) also to painful stimuli, the high incidence of lateralizing signs (eye deviation, asymmetrical or unilateral dystonic posturing, mouth deviation), oroalimentary automatisms, hypersalivation, cyanosis and eyes open. Persistently open or deviated eyes, in particular, are considered an indicator of ongoing seizure activity [23]. On the EEG, the clear predominance of a subcontinuous pseudorhythmic theta/delta activity over the fronto-temporal regions with suppression of the physiological background activity is evocative. Above all, the fast recovery of both clinical and EEG features after intravenous DZP administration, in spite of the long duration of the status, is suggestive of an ictal nature. The risk of immediate or late neurological impairment and/or epilepsy after a FS is generally considered




■ **Figure 4.** EEG showing hemispheric predominance (in 12 of 18 patients).

greater when it is focal and/or FSE occurs [24]. Despite the dramatic presentation of the FSE, its focal semiology and long duration, the outcome of the cases reported in our series was very favourable. In all subjects, at the mean age of four years and six months, neurological and cognitive development appeared invariably normal. Only three subjects presented with learning disability, associated with attention deficit with hyperactivity (ADHD) in two. In the follow-up period, three of our patients presented with isolated brief FS, which resolved spontaneously or after DZP administration before the age of four years and six months. Five subjects presented with one or two more episodes of FSE, with analogous clinical and EEG presentation between the age of two years and one month and ten years and four months. The large majority of our patients experienced NCFSE within an age range typical of FS. Patient 9 was the only patient in the series who experienced seizures associated with fever beyond the age of six years. His clinical picture might be interpreted as a GEFS-plus phenotype [25], however, *SCN1A* genetic testing resulted negative in this patient.

Brain MRI was performed in the five subjects who presented with recurrent FSE, with the main aim of excluding an underlying structural intracranial disease. The examination was performed within 48 hours following the second episode of FSE and was normal in all the cases examined. Neither acute T2 hyperintensity nor hippocampal malrotation, encountered in 15.6% and 8.8% of patients, respectively, in the FEBSTAT study population [26, 27], were detected in our series. Nonetheless, in the majority of our patients, brain MRI was not considered to be clinically indicated and thus was not performed, and this represents a limitation regarding the comparison with previously published neuroimaging data.

It is well documented in the literature that children with prolonged seizures have a risk or recurrence similar to that of children with brief seizures [28]; at the same time, when a child with a prolonged FS experiences another FS, the latter is more likely to be prolonged. Earlier studies on unprovoked seizures in children suggested that, according to seizure duration, two groups can be identified: one with brief seizures and one with prolonged seizures [10, 29]. The cases reported in our study probably belong to the subpopulation of those predisposed to prolonged FS, not adequately treated at onset. Although continuous ASM was established only in four out of 18 patients and discontinued during the follow-up, none of the patients in our series presented with afebrile seizures.

Further evidence supporting this hypothesis is based on the observation that the vast majority of our cases were observed between 1992 and 2006. In the last 15 years, with the introduction of first-aid practitioners routinely treating children at home, in the ambulance or in the emergency room, more often with buccal, intranasal or intravenous benzodiazepines which are more effective in interrupting seizures than rectal DZP [17, 30, 31], we have observed only four cases.

In conclusion, we would like to focus the reader's attention on the possibility that an apparently concluded FS may evolve into focal non-convulsive status epilepticus, characterized by impaired awareness, aphasia, unresponsiveness to painful stimulation, cyanosis, tonic-dystonic posturing and often lateralizing signs. From a practical perspective, when approaching such a clinical situation, if the EEG recording is not rapidly available or otherwise not showing a clear paroxysmal activity, the prompt administration of intravenous benzodiazepines is advisable ■

**Supplementary material.**
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

**Disclosures.**
None of the author have any conflict of interest to declare.

## References


1. Provisional Committee on Quality Improvement, Subcommittee on Febrile Seizures. Practice parameter: the neurodiagnostic evaluation of the child with a first simple febrile seizure. *Pediatrics* 1996; 97(5): 769-75.

2. Verity CM, Butler NR, Golding J. Febrile convulsions in a national cohort followed up from birth. I–Prevalence and recurrence in the first five years of life. *Br Med J* 1985; 290 (6478): 1307-10.

3. Hauser WA. The prevalence and incidence of convulsive disorders in children. *Epilepsia* 1994; 35(Suppl 2): S1-6.

4. Berg AT, Shinnar S. Complex febrile seizures. *Epilepsia* 1996; 37(2): 126-33.

5. Shinnar S, Hesdorffer DC, Nordli Jr DR, Pellock JM, O'Dell C, Lewis DV, *et al*. Phenomenology of prolonged febrile seizures: results of the FEBSTAT study. *Neurology* 2008; 71(3): 170-6.

6. Hesdorffer D, Beghi E. ILAE epidemiology commission report: introduction to the supplement. *Epilepsia* 2011; 52 (Suppl 7): 1.

7. Weiss EF, Masur D, Shinnar S, Hesdorffer DC, Hinton VJ, Bonner M, *et al*. Cognitive functioning one month and one year following febrile status epilepticus. *Epilepsy Behav* 2016; 64(Pt A): 283-8.

8. Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. *Pediatrics* 1978; 61(5): 720-7.

9. Maytal J, Steele R, Eviatar L, Novak G. The value of early postictal EEG in children with complex febrile seizures. *Epilepsia* 2000; 41(2): 219-21.

10. Hesdorffer DC, Shinnar S, Lewis DV, Moshé SL, Nordli Jr DR, Pellock JM, *et al*. Design and phenomenology of the FEBSTAT study. *Epilepsia* 2012; 53(9): 1471-80.

11. Shorvon S, Trinka E. Nonconvulsive status epilepticus and the postictal state. *Epilepsy Behav* 2010; 19(2): 172-5.

12. Yamamoto N. Prolonged nonepileptic twilight state with convulsive manifestations after febrile convulsions: a clinical and electroencephalographic study. *Epilepsia* 1996; 37(1): 31-5.

13. Miyahara H, Akiyama T, Waki K, Arakaki Y. Differential diagnosis of nonepileptic twilight state with convulsive manifestations after febrile seizures. *Brain Dev* 2018; 40(9): 781-5.

14. Specchio N, Cusmai R, Volkov J, Montaldo P, Vigevano F. Occurrence of a prolonged nonepileptic motor status after a febrile seizure. *Epilepsia* 2006; 47(6): 1079-81.

15. Leitinger M, Beniczky S, Rohracher A, Gardella E, Kalss G, Qerama E, *et al*. Salzburg consensus criteria for non-convulsive status epilepticus–approach to clinical application. *Epilepsy Behav* 2015; 49: 158-63.

16. Shinnar S, Pellock JM, Moshé SL, Maytal J, O'Dell C, Driscoll SM, *et al*. In whom does status epilepticus occur: age-related differences in children. *Epilepsia* 1997; 38(8): 907-14.

17. Bassan H, Barzilay M, Shinnar S, Shorer Z, Matoth I, Gross-Tsur V. Prolonged febrile seizures, clinical characteristics, and acute management. *Epilepsia* 2013; 54(6): 1092-8.

18. Kimura M, Taketani T, Kurozawa Y. High incidence of status epilepticus and ongoing seizures on arrival to the hospital due to high prevalence of febrile seizures in Izumo, Japan: a questionnaire-based study. *Brain Dev* 2019; 41(10): 848-53.

19. Privitera M, Hoffman M, Moore JL, Jester D. EEG detection of nontonic-clonic status epilepticus in patients with altered consciousness. *Epilepsy Res* 1994; 18(2): 155-66.

20. Kikumoto K, Yoshinaga H, Kobayashi K, Oka M, Ohtsuka Y. Complex partial status epilepticus in children with epilepsy. *Brain Dev* 2009; 31(2): 148-57.

21. Sutter R, Kaplan PW. Electroencephalographic criteria for nonconvulsive status epilepticus: synopsis and comprehensive survey. *Epilepsia* 2012; 53(Suppl 3): 1-51.

22. Panayiotopoulos CP. Benign childhood epilepsy with occipital paroxysms: a 15-year prospective study. *Ann Neurol* 1989; 26: 51-6.

23. Steering Committee on Quality Improvement, Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics* 2008; 121(6): 1281-6.

24. Pavlidou E, Panteliadis C. Prognostic factors for subsequent epilepsy in children with febrile seizures. *Epilepsia* 2013; 54(12): 2101-7.

25. Scheffer IE, Berkovic SF. Generalized epilepsy with febrile seizures plus. A genetic disorder with heterogeneous clinical phenotypes. *Brain* 1997; 120(Pt 3): 479-90.

26. Gallentine WB, Shinnar S, Hesdorffer DC, Epstein L, Nordli Jr DR, Lewis DV, *et al*. Plasma cytokines associated with febrile status epilepticus in children: a potential biomarker for acute hippocampal injury. *Epilepsia* 2017; 58(6): 1102-11.

27. Chan S, Bello JA, Shinnar S, Hesdorffer DC, Lewis DV, MacFall J, *et al*. Hippocampal malrotation is associated with prolonged febrile seizures: results of the FEBSTAT study. *Am J Roentgenol* 2015; 205(5): 1068-74.

28. Shinnar RC, Shinnar S, Hesdorffer DC, O'Hara K, Conklin T, Cornett KM, *et al*. Parental stress, pediatric quality of life, and behavior at baseline and one-year follow-up: results from the FEBSTAT study. *Epilepsy Behav* 2017; 69: 95-9.

29. Shinnar S, Pellock JM, Berg AT, O'Dell C, Driscoll SM, Maytal J, *et al*. Short-term outcomes of children with febrile status epilepticus. *Epilepsia* 2001; 42(1): 47-53.

30. Lahat E, Goldman M, Barr J, Bistritzer T, Berkovitch M. Comparison of intranasal midazolam with intravenous diazepam for treating febrile seizures in children: prospective randomised study. *BMJ* 2000; 321(7253): 83-6.

31. Jain S, Santhosh A. Febrile seizures: evidence for evolution of an operational strategy from an armed forces referral hospital. *Pediatric Health Med Ther* 2021; 12: 151-9.

## TEST YOURSELF

**(1) Which of the following clinical findings support the epileptic nature of NCFSE?**

A. Impaired awareness with a lack of responsiveness to painful stimulation and aphasia
B. A high incidence of lateralizing signs
C. Hypersalivation, cyanosis and eyes open
D. All of the above

**(2) Which of the following electroencephalographic features are commonly observed in this condition?**

A. Asubcontinuous theta/delta pseudorhythmic activity, mainly involving the fronto-temporal regions, often with a hemispheric predominance
B. The concomitant suppression of the physiological background activity
C. The discontinuation of the slow paroxysmal activity, replaced by pharmacological low-voltage fast activity, after intravenous benzodiazepine administration
D. All of the above

**(3) The follow-up of patients with NCFSE after an apparently concluded FS reveals:**

A. Moderate-to-severe developmental delay
B. Normal neurodevelopment and EEG in almost all patients
C. Recurrence of afebrile seizures
D. MRI evidence of progressive brain atrophy

*Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.*