Nocturnal frontal lobe epilepsy is often misdiagnosed as sleep disorders in children: a case series

Silvia Miano, Rosa Peraita-Adrados

Introduction. We present a series of children who underwent a video-polysomnographic recording at our Sleep and Epilepsy Unit, who received a diagnosis of nocturnal frontal lobe epilepsy (NFLE).

Aims. To describe electroclinical and video polygraphic features of paediatric NFLE that differentiate this condition from other sleep disorders that overlap and mimic the sleep motor and autonomic events of NFLE.

Patients and methods. The inclusion criterion was that the patients have their first video-EEG-PSG recording in our laboratory.

Results. Twenty-four out of 190 children were diagnosed with NFLE (group 1); while 166 had other sleep disorders (group 2). Among children diagnosed with NFLE, seven were referred for sleep-disordered breathing, seven for parasomnias, two for insomnia, two for hypersomnia, and one for periodic limb movements, while five were referred for epilepsy. In group 1, perinatal history was normal in most cases (21 out of 24) and a familiar history of epilepsy was found in four cases. Sleep-disordered breathing was diagnosed as a comorbid condition in four children. Standard EEG was normal in 21 cases. Interictal EEG showed epileptic discharges in four cases, while ictal EEG was expressed by a rhythmic theta activity preceded by an arousal and/or a short background desynchronization, movement artifacts, and autonomic changes. All seizures, repeated highly stereotyped motor events, were followed by stage shifts and/or a postural change and by short awakenings.

Conclusions. We found a high percentage of children with NFLE, often misdiagnosed or associated with other sleep disorders, which may be a trigger for nocturnal seizures.

Key words. Children. Nocturnal frontal lobe epilepsy. Parasomnia. Pediatric sleep disorders. Seizures. Video-polysomnographic recording.

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Accepted:
22.01.13.

How to cite this article:
Miano S, Peraita-Adrados R. Nocturnal frontal lobe epilepsy is often misdiagnosed as sleep disorders in children: a case series. Rev Neurol 2013; 56: 257-67.

Versión española disponible en www.neurologia.com

Introduction

Nocturnal frontal lobe epilepsy (NFLE), which is characterized by bizarre motor behavior and autonomic activation, appears during sleep. Although accepted criteria for the diagnosis of NFLE are lacking, and even ictal scalp EEG recording could fail to disclose paroxysmal abnormalities, the main differentiating features characterizing nocturnal frontal seizures are onset at any age, several attacks per night at any time during the night, brief duration, and stereotypic motor pattern. Video-polysomnographic recording of the attack remains the gold standard for diagnosis, even if it is expensive and not universally available [1]. The Frontal Lobe Epilepsy and Parasomnias Scale (FLEPS) could prove a valid instrument to identify children with NFLE; however, its use is limited to the case referred for parasomnia, while in cases referred for other sleep disorders, video-PSG remains the gold standard [2,3].

Certain types of familial cases with an autosomal-dominant inheritance have been named autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE) [4,5]. In the past, the absence of clearly epileptic abnormalities on the scalp EEG was thought to indicate that episodes were parasomnias, even if they occurred in epileptic patients, especially in children with motor attacks during sleep [6]. Provini et al [7] found NFLE in 13% of a sample of patients referred for nocturnal motor disorder (mean age at onset, 14 ± 10 years); 72% of the sample were not aware of their nocturnal attacks. Onset in the first year of life was described in a Japanese family with ADNFLE [8]. A mean age at onset of 6.2 years was reported in a group of patients with treatment refractory NFLE [9]. We recently reported the presence of epilepsy in 4 out of 25 children who underwent video-PSG for suspected sleep breathing disorder and one of them was diagnosed as NFLE [10]. The differential diagnosis between NFLE and sleep-related non-epileptic paroxysmal motor phenomena remains arduous, particularly in the cases of parasomnias and the diagnosis of NFLE may be more frequent than

expected especially if they are investigated using video-PSG [11].

Given the lack of data in the literature, the broad spectrum of sleep disorders in childhood, and the possibility that epileptic seizures can be exclusively nocturnal, a differential diagnosis with parasomnias such as enuresis, nightmares, confusional arousals, night terrors, somnambulism, rhythmic movements during sleep, and bruxism is of major importance. NFLE is often misdiagnosed as a sleep disorder or a psychiatric problem [12,13].

We present a series of children and adolescents who underwent full-night video-EEG-PSG for suspected nocturnal paroxysmal events, sleep-disordered breathing, parasomnias, or other sleep disorders, who received a final diagnosis of NFLE. The aim of our study was to describe the specific electroclinical and video sleep polygraphic semiological features of childhood-onset NFLE that may differentiate this condition from other sleep disorders that overlap and mimic the sleep motor and autonomic events of NFLE.

Patients and methods

The study was conducted at the Sleep Disorders and Epilepsy Unit of Gregorio Marañón University Hospital in Madrid. The clinical and laboratory data of children with NFLE were collected from the clinical general sleep laboratory and video-recordings databases of patients affected by sleep disorders who were diagnosed at the unit. All patients were referred either from specialists (children's ENT, neurologists, pulmonologists) and from primary care pediatricians. We did not exclude patients with a history of epilepsy or seizures or with a history of previous treatment of obstructive sleep apnea syndrome (including tonsillectomy and adenoidectomy), acute or chronic cardiorespiratory or neuromuscular diseases, dysmorphism, major craniofacial abnormalities or associated chromosomal syndromes, because our aim was to investigate the presence of NFLE in the entire sample. Data between January and December 2010 were retrospectively analyzed. The only inclusion criterion was that the patients have their first video-EEG-PSG recording in our laboratory, after the clinical assessment collected by the clinical neurophysiologist expert in sleep disorders and epilepsy in children (R.P.A.).

A personal and family history was obtained from the database. Patients routinely underwent a full-night video-EEG-PSG recording, from 10 pm to 8 am, which is the rule in the pediatric patients referred to our sleep unit. The children's parents gave their informed consent, and the institution's research ethics committee approved the study.

Polysomnography and sleep stages scoring

Standard overnight video-EEG-PSG recordings were obtained with a computerized sleep recorder (Deltamed System). The video was analog and was synchronized with the digital recording. Patients underwent the following recordings: a 13-channel EEG –Fp (pre-frontal), Fz (frontal), C (central), T (mid-temporal), O (occipital), Pz (parietal), and Cz (vertex)– with bipolar montages following the International '10-20' system to place electrodes in standardized scalp locations, an electro-oculogram (EOG) (1 channel), a submental electromyogram (EMG), and an electrocardiogram. Thoracic and abdominal movements were recorded by inductance plethysmography (in most cases a bipolar montage which showed the sum of both movements in 1 channel), and airflow pressure by an oronasal cannula. Oxygen saturation was recorded continuously from a transcutaneous sensor (pulse-oximetry). A tibialis anterior electromyogram and/or deltoid electromyogram were also recorded.

Sleep was subdivided into 30-second epochs, and sleep stages were scored according to the standard criteria of Rechtschaffen and Kales [14]. We evaluated the following parameters of sleep architecture:

- *Sleep period time (SPT):* defined as time from sleep onset to the end of the final sleep epoch minus wake time during sleep.
- *Sleep efficiency:* defined as the percentage ratio between time from sleep onset to the end of the final sleep and time in bed.
- *Sleep-onset latency:* time from lights out to sleep onset, which was further defined as the first of 2 consecutive epochs of stage 1 sleep or 1 epoch of any other stage, in minutes.
- *REM latency:* time from sleep onset to the first epoch of REM sleep.
- *Wakefulness after sleep onset (WASO):* time spent awake between sleep onset and end of sleep, in minutes.
- *Percentage of SPT in stage 1, stage 2, and slow wave sleep:* defined as the sum of the stage 3 and stage 4 percentages.
- *Percentage of REM sleep.*
- *Number of stage shifts per hour.*

All parameters were scored by one of the investigators (R.P.A.). The EEG was reviewed by one of the

authors (R.P.A.), and each screen contained 15 s of recording. The presence of spikes (transient, clearly distinguishable from background activity, lasting 20-70 ms) and sharp waves (same as spikes, but lasting 70-200 ms), either alone or accompanied by slow waves (the slow wave being of a higher amplitude than the spike or the sharp wave) occurring in isolation or in bursts was considered to represent interictal epileptiform discharges (IEDs), according to the definitions of the International Federation of Societies for Clinical Neurophysiology [15].

Criteria for diagnosis of NFLE

The diagnosis of NFLE was made according to the criteria described by Montagna et al [16], Sforza et al [17], Oldani et al [18], Ambrosetto [19], Provini et al [7], and Tinuper et al [1]. The main differentiating features characterizing nocturnal frontal seizures from non-epileptic motor phenomena during sleep, are onset at any age, several attacks per night at any time during the night, and brief duration with stereotypic motor pattern [1]. Based on the specific intensity, duration, and features of the motor pattern, we classified epileptic seizures into 4 groups according to Oldani et al [18]:

- *Minimal motor events (MMEs):* are the briefest episodes (2-4 s) in the form of stereotypic movements involving the limbs, the axial musculature, and/or the head.
- *Minor events (ME):* accompanied by arousals and stereotypic movements (usually lasting 5-10 s) in which patients suddenly opened their eyes, raised their heads, or sat up in bed with a dystonic posture of the limbs, staring around with a frightened or surprised expression and sometimes vocalization or screaming, before going back to sleep.
- *Major motor attacks (MMA):* lasting 20-30 s, they showed a more complex behavior characterized by wide, often violent, sometimes ballistic movements, with dystonic posturing of the head, trunk, and limbs (eg, head rotation, torsion of the trunk, and choreoathetoid movements of the arms and legs with vocalization).
- *Prolonged attacks:* lasting more than 30 s.

Moreover, we take into account the recent revision criteria to differentiate parasomnia from NFLE events: features strongly favoring a diagnosis of parasomnias included a prolonged duration of the episode, crying or sobbing, waxing and waning quality, physical or verbal interaction with the environment, modification of the event by individuals present, coherent speech in sentences, and 'normal' arousal behaviors such as scratching and face rubbing [3]. In contrast, bicycling movements, thrashing, grunting, moaning, grimacing, and dystonic posturing with autonomic changes clearly favored NFLE.

Statistical analysis

Data are expressed as mean ± standard deviation. The Mann-Whitney or χ^2 test was used as appropriate to compare data. P values < 0.05 were considered statistically significant.

Results

Twenty-four out of 190 children were diagnosed with NFLE because of repeated recorded motor seizures after being referred for sleep-disordered breathing, parasomnias or paroxysmal events at night (group 1), while 166 had other sleep disorders (group 2). Children in group 1 were older (9.8 ± 4.2 vs 6.2 ± 3.6 years; $p < 0.01$), and suspected diagnosis changed after video-EEG-PSG recordings in 19/24 (79.2%) patients in group 1 and in 11/166 (6%) patients in group 2 ($p < 0.01$). There were no gender differences between the groups (70.8% males in group 1 vs 62.6% males in group 2). Among children diagnosed with NFLE, 7 were referred for sleep-disordered breathing, 7 for parasomnias (5 for somnambulism, 1 for sleep terrors, and 1 for sleep talking), 2 for insomnia, 2 for hypersomnia, and 1 for periodic limb movements, while 5 were referred for epilepsy. Snoring was recorded during sleep and diagnosed as a comorbid condition in 4 children, while parasomnia events during sleep were detected in one child and diagnosed as comorbid condition.

The clinical history of children with NFLE is described in table I. Most patients had a history of parasomnia (with agitated somnambulism and multiple trauma after an episode in 1 case) and sleep-disordered breathing. Previous episodes of seizures were found in 1 case (generalized epilepsy) and febrile convulsions in another case. Neuroimaging showed post-traumatic lesions in 2 cases and malformation in 1 (craniosynostosis and Arnold-Chiari type I malformation), normal findings in another case. Perinatal history was normal in most cases (21 out of 24), and a familiar history of epilepsy was found in 4 cases (NFLE in 1, maternal inheritance in 3 cases), sleep-disordered breathing or respiratory allergy in 4 cases, excessive daytime sleepiness

Table I. Clinical and EEG characteristics of children with nocturnal frontal lobe epilepsy.

	Sex	Age (years)	Clinical history	Perinatal history	Family history	Parasomnias	Treatment at PSG	Standard EEG
Case 1	Female	6.9	Nocturnal generalized epilepsy treated with lamotrigine and levetiracetam	Normal	NS	No	Lamotrigine, levetiracetam	Generalized IEDs
Case 2	Female	5	Parasomnias	Normal	Sister with encephalopathic epilepsy	Sleep talking, sleep agitation, tremors	No	Normal
Case 3	Female	8.8	Drepanocytosis, snoring	Normal	NS	Enuresis	Penicillin	Normal
Case 4	Female	3.5	Oxygen therapy at night, craniosynostosis, macrocephalia, OSAS, von Willebrand disease, type I Arnold-Chiari, hydrocephalus, GER, duplication of the gastric fundus	Normal	NS	No	Budesonide, montelukast	Asymmetry, background activity
Case 5	Female	11.4	Tonsillar hypertrophy, hypersomnolence	Normal	NS	No	No	Normal
Case 6	Female	17	Febrile convulsions treated with Phenobarbital until 5 years of age	Normal	NS	Somnambulism	Paroxetine	Normal
Case 7	Female	4	Hypersomnolence, hyperactivity, agitation during sleep, snoring	Normal	NS	Enuresis, sleep talking	No	Normal
Case 8	Male	17	Multiple trauma after an episode of somnambulism, at 16 years of age (pneumothorax, seizures, and psychomotor agitation), snoring. CT: right frontal and temporal hemorrhagic contusion, subarachnoid hemorrhage	Normal	NS	Somnambulism	No	Normal
Case 9	Male	11.4	Hypersomnolence, LD, sleep terrors	Normal	Father: somnambulism	Sleep terrors	No	Normal
Case 10	Male	9.5	Tonsillar hypertrophy, hypersomnolence	Normal	NS	No	No	Normal
Case 11	Male	13	Post-traumatic dorso-cervical syringomyelia, hypersomnolence	Normal	NS	No	No	Normal
Case 12	Male	4.7	OSAS, adenotonsillar hypertrophy, hyperactivity, LD, inguinal hernia, GER, dermatitis	Normal, low birth weight	Respiratory allergy	No	No	Normal
Case 13	Male	3.8	Snoring, adenotonsillar hypertrophy, dysphagia, hypersomnolence,	Dystocic delivery, hypoglycemia, respiratory distress	Mother: snoring	No	No	Normal
Case 14	Male	14	Emotional lability, apathy, hypersomnolence, anorexia for 1 week before PSG, same symptoms lasting 1 week 9 times from October 2008, anemia treated with iron supplement, adeno-tonsillectomy, tics, psychological trauma at 6 years and psychotherapy, normal cranial MRI	Normal	Mother: post-partum depression	No	No	Normal
Case 15	Male	9.6	OSAS. Episodes of rash and facial angioedema	Normal	Respiratory allergy	No	No	Normal
Case 16	Male	16	Somnambulism, respiratory allergy	Normal	Epilepsy (paternal uncle)	Somnambulism	No	Normal

Table I. Clinical and EEG characteristics of children with nocturnal frontal lobe epilepsy *(cont.)*.

	Sex	Age (years)	Clinical history	Perinatal history	Family history	Parasomnias	Treatment at PSG	Standard EEG
Case 17	Male	4.2	Somnambulism, sleep respiratory effort, and hyperhidrosis	Sepsis post partum	Kleine-Levin syndrome (cousins), mother with epilepsy, others with hypersomnolence	No	No	Normal
Case 18	Male	12	Sleep agitation, sits up and looks around, diurnal irritability, adenotonsillectomy, pyelonephritis, facial palsy, respiratory allergy, and obesity since 5 years of age	Normal	NS	No	No	Theta activity over the right central region
Case 19	Male	11.3	Tics, anxiety, respiratory allergy, sleep agitation, low ferritin level	Normal	Mother: tics	No	Sertraline	Normal
Case 20	Male	8.8	NS	Normal	NS	No	No	Normal
Case 21	Male	8.4	OSAS, dermatitis, cow- milk intolerance	Normal	Respiratory allergy	No	No	Normal
Case 22	Male	15	Nightmares, screaming, sleep talking, nuresis at 4 years of age, growth delay	Normal	Mother's uncle: suspected NFLE, with same symptoms	Sleep talking	Clonazepam	Normal
Case 23	Male	11.1	Somnambulism	Normal	Mother's uncle: epilepsy	No	No	Normal
Case 24	Male	9	Academic difficulties, somnambulism, and sleep talking	Normal	NS	Somnambulism, sleep talking	Atomoxetine	Normal

CT: cranial computed tomography; GER: gastroesophageal reflux; LD: learning disability; MRI: magnetic resonance imaging; OSAS: obstructive sleep apnea syndrome; NS: not significant.

in 1 case, maternal depression in another case, and a mother with tics in the remaining case. Standard EEG was normal in most cases (21 out of 24), with mild abnormalities in 2 cases (mild asymmetry and slow occipital rhythm in one, theta activity over frontal region in the other) and generalized spike and wave discharges in the children with a history of epilepsy (Table II).

Table II shows EEG abnormalities and clinical semiology of seizures recorded in children with NFLE. Most cases had repeated (more than 2 seizures) and mostly identical ME accompanied by stereotypic movements (usually lasting 5-10 s) (n = 14), while 10 cases had longer episodes (MMA), lasting no more than 30 seconds. Interictal EEG showed IEDs in 4 cases (case numbers 1, 2, 3 and 19), while ictal EEG was mostly expressed by a rhythmic theta activity preceded by an arousal (K complex) and/or a short background desynchronization after a K complex, superimposed movement artifacts, and autonomic changes such as tachycardia and tachypnea. All stereotyped ME were followed by arousals, stage shifts (to a lighter stage) and/or a postural change and, more rarely and mostly the longer episodes, by short awakenings. Five patients were treated with antiepileptic drugs: valproic acid in 3 cases, levetiracetam in 1, and oxcarbazepine in 1, with attenuation or resolution of ME at follow-up, as demonstrated by EEG.

Table III shows the sleep architecture of children with NFLE. The mean sleep efficiency was low (85.30 ± 10.41), and the number of stage shifts/hour (12.37 ± 3.81) was high, while the mean number of ME or MMA was 17.48 ± 16.30 (range: 2-46). There were not statistically correlation between the number of motor events and the sleep parameters: total sleep time, REM latency, sleep efficiency, stage shift/hour and number of awakenings. The closer correlation

Table II. Interictal /ictal activity and types of seizures characteristic of children with nocturnal frontal lobe epilepsy.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Ictal/ interictal EEG	Interictal: ShW Ictal: RA	Interictal: central SW. Ictal: RA	Interictal: SW Ictal: TA	Ictal: TA	Ictal: MA	Ictal: RA, MA
Video	Nose and head grasping, hypertonia, bilateral arm jerks Babinski, postural change	Nose or head grasping, jerky movements, hypertonia oral automatisms,	Leg extension, dystonic movements, bilateral Babinski with right leg triple flexion	Nose grasping, leg extension, dystonic posture, Babinski, postural change, periodic breathing	Dystonic right foot movement and Babinski, oral automatisms, postural change, tachycardia e tachypnea	Head grasping, hypertonia, bilateral Babinski, tachycardia, and tachypnea
Mean duration	20 s	< 20 s	> 5 s	< 20 s	< 30 s	5 s
PSG follow up	No	No	No	SaO_2 desaturation, paroxysmal arousal, periodic breathing	No	No
Therapy	No	No	No	Valproic acid	No	No
	Case 7	**Case 8**	**Case 9**	**Case 10**	**Case 11**	**Case 12**
Ictal/ interictal EEG	Ictal: RA	Ictal: DA	Ictal: RA, frontal TA	Ictal: TA	Interictal: ShW. Ictal: RA, TA	Ictal: TA, tachycardia, central apneas
Video	Nose and head grasping hypermotor activity, jerky movements, tachycardia, tachypnea, oral automatisms	Dystonic posture, bruxism	Nose grasping, leg extension, dystonic movements, Babinski, postural changes	Snoring, dystonic movements of hands, Babinski, oral automatisms, bruxism, hyperextension of legs, postural changes, vocalizations	Nose grasping, leg extension, dystonic movements, Babinski, postural changes	Dystonic movements, axial hyperextension
Mean duration	< 5 s	< 5 s	> 30 s		20 s	< 30 s
PSG follow up	No seizures, some arousals, and sleep talking	Increase of sleep efficiency index, persistence of paroxysmal arousals	Reduction in paroxysmal arousal and of SaO_2 97%	No	No	Not available
Therapy	Valproic acid	Levetiracetam	Oxcarbazepine	No	No	No

found between ME and REM latency was not significant (p = 0.34). We found a significant negative correlation between the number of awakenings (= 1 min) and the sleep efficiency index (p = 0.01).

Figure 1 shows a ME and figure 2 shows a MMA of the case number 5.

Discussion

Our pediatric case series confirmed that NFLE is characterized by brief, repeated, stereotypic, nocturnal and frequent seizures, rarely associated with interictal or even ictal EEG, and magnetic resonance imaging are usually normal. In our case series, NFLE was found in 24 out of 190 children consecutively admitted for video-EEG-PSG recording to evaluate sleep disorders (12.6% of sample). The children were older than those without NFLE, although no sex differences were observed. The percentage of children with NFLE is relatively high, but results may be affected by the admission of children to a tertiary care hospital with a sleep unit, where epilepsy is often diagnosed, and the percentage reported has not obviously an epidemiological value.

Most cases were referred for various sleep disorders, rather than suspected nocturnal seizures, such as sleep-disordered breathing, parasomnias (mostly somnambulism), and hypersomnia in a few cases. None of them had a previous homemade video re-

Table II. Interictal /ictal activity and types of seizures characteristic of children with nocturnal frontal lobe epilepsy *(cont.)*.

	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18
Ictal/interictal EEG	Ictal: TA	Ictal: RA, MA	Ictal: TA	Ictal: RA, MA	Ictal: MA	Ictal: MA
Video	Dystonic movements, axial hyperextension, vocalizations, Babinski, postural changes	Postural changes, dystonic movements, Babinski, legs hyperextension, oral automatisms, vocalizations, tachycardia, tachypnea	Extension of legs and arms, dystonic movements, moaning, vocalizations, postural changes	Sitting up and looking around, mild complain, dystonic movements, postural changes	Respiratory effort followed by dystonic movements of arms, Babinski, hyperextension of legs, moaning and postural changes, central apnea and tachycardia	After a respiratory effort, hyperextension arms, nose grasping, dystonic movements, bilateral Babinski, vocalizations and postural change
Mean duration	< 20 s	< 15 s	< 30 s	< 20 s	< 20 s	< 30 s
PSG follow up	No	ME	No	No	No	PSG 1: decreased number of PA, increased AHI and decreased sleep efficiency index. PSG 2 (with treatment): no apneas, only snoring, decreased number of PAs, increased sleep efficiency index
Therapy	No	No	No	No	No	Valproic acid
	Case 19	**Case 20**	**Case 21**	**Case 22**	**Case 23**	**Case 24**
Ictal/ interictal EEG	Interictal: frontal SW. Ictal: MA	Ictal: MA	Ictal: RA, MA	Ictal: MA	Ictal: MA	Ictal: MA
Video	Dystonic movements, axial hyperextension, Babinski, vocalization, tachypnea and tachycardia	Dystonic movements	Sitting up and looking around, painful expression, dystonic arm movements, postural change, tachycardia, and central apnea	Dystonic leg movement, grasping head and nose, sitting up and looking around, tachycardia	Dystonic movements, head and nose grasping, sitting up and looking around, postural changes	Dystonic movements, Babinski, nose grasping, sitting up and looking around
Mean duration	< 10 s	< 10 s	< 20 s	< 30 s	< 60 s	< 30 s
PSG follow up	No	No	Increased sleep efficiency index, decreased number of PAs	No	No	No
Therapy	No	No	No	No	No	No

AHI: apnea-hypopnea index; MA: movement artifact; PA: parosysmal arousal; PSG: polysomnography; RA: rapid activity; ShW: complex of sharp and wave; SW: complex of spike and wave; TA, theta activity.

cordings probably because of the unawareness of parents and pediatricians about this important tool, and some of them may not apparently had a wrong reason to employ a VPSG [20]. Moreover, the revision of a sleep specialist in these cases is important in order to increase the capability of a correct diagnosis, especially in a pediatric population. The extended EEG montage, routinely in our Unit, and video PSG made it possible to distinguish between MMEs, MEs, and MMAs, and between sleep attacks and non-epileptic arousals [1,17-19]. This is particularly relevant, considering that a scalp EEG was normal in most cases (both in wakefulness and during sleep). We suggest using video-PSG with extended EEG montage in children with suspected sleep-disordered breathing in whom standard and simplified PSG do not confirm diagnosis, or if they complain of frequent awakenings during sleep and

Table III. Sleep architecture of children with nocturnal frontal lobe epilepsy.

	Sleep latency (min)	Total sleep time (min)	REM latency (min)	SWS (%)	Stage 2 NREM (%)	Stage 1 NREM (%)	Stage REM (%)	Sleep efficiency index	Stage shift/hour	N/aw	WASO (min)	Seizures (n. per night)	AHI	SaO_2 (%)
Case 1	19	430	148	46	29	7	16.6	90	15	6	20	16	0	96
Case 2	1	448	166	49	21	7	20	94	15	10	13	16	0	93
Case 3	38	440	146	23.5	55	7	14.4	89	15	12	20	10	0	88
Case 4	9	429	203	38	49	12	10	93	7	4	15	40	0	95
Case 5	13	361	339	28	38	22	11	76	15	21	78	2	0	100
Case 6	25	405	241	36	28	12	13	86	22	20	22	70	0	94
Case 7	1	473	65	36	29	4	28	98	8	1	2	3	0	96
Case 8	27	426	130	39	30	7	23	87	13	8	29	3	1.5	95
Case 9	6	428	132	35.7	31.5	5	28	98	15.5	11	14	46	0	95
Case 10	16	433	162	36	36.5	4	23.5	93	6	3	7	7	0	92
Case 11	3	409	113	26	45	7	22	95	14	4	6	22	0.15	94
Case 12	3	422	187	42	33	9	16	94	10	9	20	15	0	94
Case 13	15	426	73	40	33	9	18	92	13	3	6	22	0.84	96
Case 14	16	432	184	36	35	12	17	91	10	5	12	15	0	97
Case 15	13	314	87	41	22	14	23	68	7.5	10	130	13	0	95
Case 16	20	320	77	39	33	11	15.6	68	13	18	125	25	0	99
Case 17	35	421	130	31	41	5.5	22	86.8	11	6	11	3	0	96
Case 18	16	275	30	31	29	28	11	58	18.5	35	171	5	5.6	95
Case 20	36	403	205	60.5	21.4	5.6	12.5	85	14	8	12	30	0	99
Case 21	39	397	74	50.5	22	9	18.6	82	11	13	36	7	0	96
Case 22	28	366	69	26	46	12	15	75	12	7	82	6	0	99
Case 23	20	371	121	40	40	4	15.5	81	9	10	57	14	0	99
Case 24	29	398	62	41.6	19	6	32	82	10	3	44	12	0	99
Mean	18.61	401.17	136.70	37.90	33.32	9.53	18.51	85.30	12.37	9.87	40.52	17.48	0.37	95.83
SD	11.93	48.28	70.38	8.56	9.55	5.77	5.90	10.41	3.81	7.68	46.19	16.30	1.22	2.79

AHI: apnea/hypopnea index; N/aw: number of awakenings per hour of sleep; SaO_2: mean overnight oxygen saturation; SD: standard deviation; WASO: wakefulness after sleep onset.

Figure 1. Minor motor event during stage 2-NREM after a K complex; duration 11 s (epoch of 30 s, 10 μV). The patient touches her head with the right hand. Tachycardia and irregular respiration are present. Artifacts are visible on the EEG; tonic activation is visible on the EMG 2 recording taken from the right deltoid muscle.

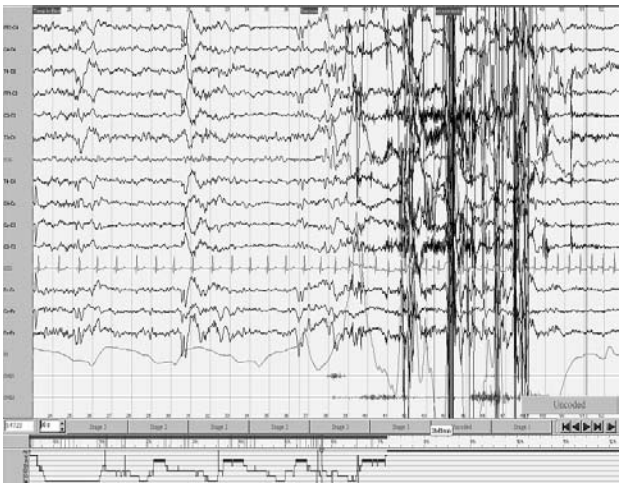
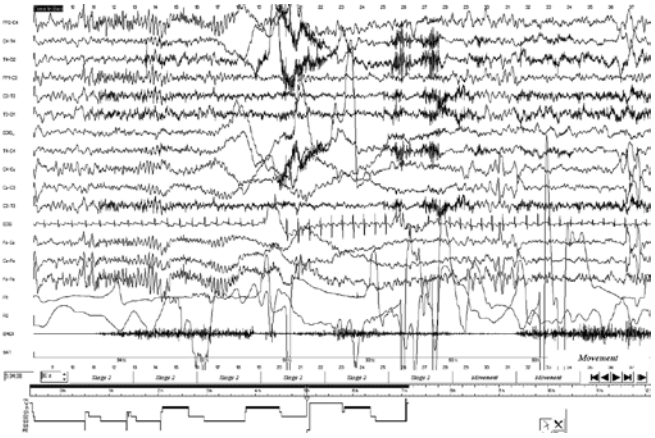


Figure 2. Major motor attack during stage 2-NREM after a K complex, lasting 30 s (epoch of 30 s, 10 μV). The patient experiences dystonic movement of the right foot and Babinski, oral automatisms, postural change, tachycardia, and irregular respiration. A rhythmic generalized theta activity is visible on the EEG followed by artifacts as well as a bruxism activity.



excessive daytime somnolence. Interestingly, children with a diagnosis of NFLE were older than children who received other types of diagnosis. At this time, we are unable to say whether our results are due to a delay in diagnosis because NFLE is misdiagnosed in children or if they represent the natural history of NFLE.

VPSG alone cannot be always considered the definitive 'gold' standard, but only one of the tools in the diagnostic process [3]. In fact, the differential diagnosis, based on VPSG, between epilepsy and parasomnias can be extremely difficult when the recorded episodes are brief, although stereotyped. Indeed, minor motor episodes in NFLE patients can be very similar to physiologic movements occurring during sleep [16,21]. Although the epileptic nature of minimal or minor motor phenomena in NFLE cannot be established on the clinical phenomenology of the event [21], in subjects in whom a clinical suspicion of NFLE clearly exists, the finding of an extremely high frequency of minor motor phenomena and the association with clinical symptoms (such as hypersomnolence, familiar history of epilepsy) may help to a final diagnosis of epilepsy. The children diagnosed as having NFLE showed nocturnal seizures characterized by tonic posturing of extremities or limb elevation (associated with clonic movements, vocalization, fencing posture) with preservation of consciousness, the interictal EEG was often normal and ictal EEG showed diffuse theta rhythmic high-voltage activity, and/or rapid activity and/or movements artifacts. A recent stereo-EEG study demonstrated that some sleep-related paroxysmal motor behaviors are the manifestation of insular-opercular seizures rather than the sleep-related complex motor attacks of NFLE, at this time we are not able to distinguish these cases from NFLE [22].

In children with NFLE we found a high comorbidity with other sleep disorders, such as sleep-disordered breathing, and we found sleep architecture alterations as indicated by an increased number of stage shifts and arousals, a higher percentage of light sleep stages, decreased percentages of slow-wave sleep and REM sleep, and diminished sleep efficiency.

We can argue that a history of sleep disorders could imply a risk of developing NFLE, since it has been reported that cortico-subcortical networks, which regulate arousal from sleep, play a central role in seizures precipitating in ADNFLE. Increased frequency of arousal disorders in patients with a family history of NFLE suggests a link between parasomnias and NFLE that may be associated with

an abnormal cholinergic arousal system [23]. Signs of nocturnal seizure may overlap with sleep respiratory events, and sleep respiratory events can trigger motor paroxysmal events. We recently reported a case of NFLE in a child with sleep-disordered breathing [10], and a higher percentage of paroxysmal EEG activity that was found in an Italian series of children with obstructive sleep apnea syndrome [24]. NFLE was also found in an obese child with severe obstructive sleep apnea syndrome in whom NFLE developed within a week after therapy with continuous positive airway pressure, and neuroimaging disclosed frontal dysplasia [25]. Arousal fluctuations play an important role in triggering MME during sleep in NFLE; the epileptic discharge acts as a trigger for the appearance of behaviors which are the expression of inborn motor patterns, related to central pattern generators (CPG), mainly located outside the cerebral cortex. According to Tassinari et al, the concept may be extended to parasomnias, whose motor expressions is the same as in epileptic seizures since they result from the activity of the same CPG [26]. Recent findings indicate that, in a single epileptic patient, highly stereotyped MME can occur in either the presence or absence of an epileptiform discharge [21].

In conclusion, we found a high percentage of children with NFLE, often misdiagnosed and associated with sleep disruption and comorbidity with other sleep disorders. We can hypothesize that epileptic seizures provoke nocturnal sleep disruption with high fragmentation, and the presence of other sleep disorders may be a trigger for nocturnal seizures. Moreover, chronic sleep deprivation may be the main cause of excessive daytime hypersomnolence and cognitive and behavioral disturbances, frequently associated with NFLE.

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Epilepsia nocturna frontal infradiagnosticada en la infancia como un trastorno del sueño: estudio de una serie

Introducción. Presentamos una serie de niños a los que se les realizó un registro videopoligráfico de sueño en nuestra unidad de sueño y epilepsia, y se les diagnosticó una epilepsia nocturna frontal (ENF).

Objetivos. Describir las características electroclínicas y videopolisomnográficas de la ENF en edad pediátrica y establecer las diferencias con otros trastornos de sueño que pueden enmascarar o mimetizar los eventos motores y autónomos típicos de la ENF.

Pacientes y métodos. Los criterios de inclusión fueron que los pacientes tuvieran su primer registro de videoelectroencefalograma (video-EEG) poligráfico de sueño en nuestra unidad.

Resultados. Se diagnosticaron 24 niños de ENF de un total de 190 (grupo 1); los 166 restantes presentaban otros trastornos del sueño (grupo 2). Entre los niños diagnosticados de ENF, siete fueron remitidos por trastornos respiratorios del sueño, siete por parasomnias, dos por insomnio, dos por hipersomnia, uno por movimientos periódicos de las extremidades y los cinco restantes por epilepsia. La historia perinatal fue normal en la mayoría de los casos del grupo 1 (21 de 24) y cuatro casos tenían historia familiar de epilepsia. Encontramos comorbilidad con un trastorno de la respiración durante el sueño en cuatro casos. El EEG estándar fue normal en 21 casos. El EEG intercrítico mostró descargas paroxísticas en cuatro casos, mientras que el EEG crítico consistió en una actividad theta rítmica precedida por un *arousal* o una breve desincronización de la actividad de fondo, artefactos de movimiento y cambios autónomos. Todas las crisis consistieron en eventos motores muy estereotipados, repetidos y seguidos por un cambio de fase de sueño y/o un cambio postural, o por un breve despertar.

Conclusiones. Se ha hallado un porcentaje elevado de niños con ENF, no diagnosticada previamente y asociada con otros trastornos del sueño, que podrían ser los desencadenantes de las crisis nocturnas.

Palabras clave. Crisis. Epilepsia nocturna frontal. Niños. Parasomnias. Registros poligráficos de sueño nocturno. Trastornos de sueño pediátricos.