Original article

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Myoclonic jerks are commonly associated with absence seizures in early-onset absence epilepsy

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ABSTRACT – *Aim*. Typical absence seizures are observed in various epilepsy syndromes, however, few series have focused on early-onset absence epilepsy (EOAE). We aimed to evaluate the occurrence of this seizure type in children under 4 years of age in order to evaluate their electroclinical characteristics and outcome.
Methods. We retrospectively studied (2006-2014) the electroclinical features of children with normal development and typical absence seizures starting before the age of 4 (with available pre-treatment video-EEG).
Results. Nine patients were included. Among them, eight patients had rhythmic myoclonic jerks involving the muscles of the upper face (eyebrows and eyelids) or neck, present from the onset to the end of the typical absence discharge. The myoclonia were synchronous with spike-wave complexes. One patient with GLUT-1 deficiency was refractory to antiepileptic polytherapy. The other eight became seizure-free; five with one antiepileptic drug and three with a combination of two drugs. The treatment was successfully withdrawn in five of the six patients who achieved two years of seizure freedom. None of them exhibited any other seizure type. Four of the eight patients with normal schooling required some support. We observed a positive correlation between the duration of absence seizure and the age of the patient at examination.
Conclusion. Most of the patients under four years with only typical absence seizures had EOAE, and the motor symptoms may represent a distinctive age-related feature of EOAE. Further investigations are required to better correlate the role of brain maturation with the duration of the absence. [*Published with video sequence on www.epilepticdisorders.com*]

Key words: typical absence seizure, early-onset absence epilepsy, childhood absence epilepsy, myoclonus, paediatric epilepsy syndrome

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Typical absences (TAbs) are generalized seizures clinically defined by a transient impairment of consciousness of sudden onset and termination, lasting for seconds, with a concomitant bilateral, generalized, regular and symmetric spike-wave (SW) or polyspike-wave EEG discharge of 2.5 to 4 Hz (Panayiotopoulos, 2008). TAbs have mainly been described in epileptic syndromes that mostly affect children from 4 years of age to adolescence, formerly defined as idiopathic generalized epilepsy; childhood absence epilepsy (CAE), juvenile absence epilepsy, and juvenile myoclonic epilepsy (Panayiotopoulos, 2008). TAbs have also been described in eyelid myoclonia with absences, also called Jeavons syndrome, or perioral myoclonia with absences (Panayiotopoulos, 2008). Nonetheless, early-onset TAbs have also been reported in early-onset absence epilepsy (EOAE), an epileptic syndrome affecting children under the age of 4 in whom typical absences are the only seizure type. EOAE is rare, representing 0.7 to 1% of epilepsy cases before the age of 4 (Chaix *et al*., 2003; Caraballo *et al*., 2011). The first reports in the 80s were isolated cases (De Marco, 1980; Cavazzuti *et al*., 1989) while more recently, series of cases have been reported (Chaix *et al*., 2003; Shahar *et al*., 2007; Caraballo *et al*., 2011; Verrotti *et al*., 2011a, 2011b; Giordano *et al*., 2013). For certain authors, EOAE should be seen as a distinct entity (Shahar *et al*., 2007; Verrotti *et al*., 2011a), whereas others suggest that it lies within a continuum with other syndromes, such as CAE (Verrotti *et al*., 2011b; Giordano *et al*., 2013). However, some authors consider early-onset TAbs as a probable exclusion criterion for CAE (Panayiotopoulos, 2008). EOAE is often regarded as a severe condition with a high rate of refractoriness (Chaix *et al*., 2003). More recently, it has been shown that early-onset TAbs can also be a symptom of glucose transporter type 1 (GLUT-1) deficiency syndrome (DS) (Leary *et al*., 2003) and some authors have reported mutations in the *SLC2A1* gene, which encodes GLUT-1, in up to 10% of children with TAbs with an onset before the age of 4 (Suls *et al*., 2009; Arsov *et al*., 2012; Muhle *et al*., 2013).

In this study, we analysed a series of patients with TAbs starting before the age of 4, with the aim of better defining their electroclinical characteristics and outcome.

Patients and methods

Study design and patients

In this retrospective study, we included children first referred to Robert-Debré University Hospital, Paris, France, between January 2006 and June 2014.

The inclusion criteria were repetitive transient loss of consciousness with an onset before the age of 4, normal development, normal neurological examination, and pre-treatment video-EEG documentation of TAbs according to the Panayiotopoulos definition of 2008; clinical symptoms associated with generalized high-amplitude spikes and double or, at most, triple rhythmic SW complexes, at a frequency of 2.5-4 Hz, with gradual and regular slowing down from the initial to the terminal phase of the discharge (Panayiotopoulos, 2008).

We reviewed all first pre-treatment video-EEG records, analysed the clinical and electrographic characteristics of the absences, and reviewed clinical records to obtain information about the patient's sex, age at seizure onset, history of febrile seizures, presence of other seizure types, family history of epilepsy, treatment, investigations including lumbar puncture, MRI and neuropsychological assessments, and outcome.

Measurements and procedures

Video-EEG was performed during wakefulness and, depending on the child's cooperation, sleep, photic stimulation, and hyperventilation conditions. EEG recordings were carried out using Ag-AgCl scalp electrodes positioned according to the international 10-20 system, as well as electrocardiographic, respiration-rate, and electromyographic electrodes. Signals were acquired by computerized systems and recorded using montages with a common reference electrode.

Children were defined as responsive to treatment when they were seizure-free. Seizure freedom was defined as an absence of seizures reported by the family, consistent with an absence of seizures during the video-EEG recording.

We evaluated the frequency (number per hour) and the mean duration (in seconds) of absence seizures during the first video-EEG recording. Using a Pearson correlation test (Prism software, GraphPad), we evaluated the correlation between age (in months) at recording and these two parameters.

Results

Of the 656 patients who underwent EEG in our unit for investigation of a repetitive transient loss of consciousness during the study period, electroclinical absences were documented in 194 children. Absence seizures started before the age of 4 in 16 patients, of whom seven had atypical absences. Nine patients fulfilled the criteria for TAbs starting before the age of 4.

These nine patients included four girls and five boys, none of whom had a past medical history of epilepsy or febrile seizures. Their main clinical characteristics are summarized in *table 1*.

Table 1. Clinical features of nine patients with early-onset absence epilepsy.

Patient ID	Sex	Age	Past medical history	Family history of epilepsy	Absence onset (months)	First AED	Second AED	Seizure free (effective AED)	Additional seizure types	AED duration (months)	Follow-up duration (months)	Glycorrhachia	Schooling	Cognitive assessment
1	F	6 years, 9 months	-	Symptomatic (brother)	7	VPA	ETH	Yes (ETH)	0	12	63	ND	Normal grades	N
2	M	4 years, 5 months	-	"Seizures" (Cousin)	11	ETH	-	Yes (ETH)	0	27	31	ND	Preschool	N
3	F	2 years	Hypoaldosteronism	Symptomatic (mother and father)	12	VPA	LTG	Yes (LTG)	0	Ongoing	11	Normal	Preschool	N
4	M	4 years, 9 months	Paludism	-	24	VPA	ETH	Yes (VPA + LTG)	0	Ongoing	30	Normal	Preschool	N
5	F	6 years, 10 months	Perinatal	-	24	ETH	-	Yes (ETH)	0	31	39	ND	Normal grades with assistance	Hyperkinesia
6	M	6 years, 9 months	-	IGE (grandmother)	30	ETH	VPA	Yes (VPA + LTG)	0	25	39	ND	Normal grades with assistance	Attention deficit
7	M	4 years, 7 months	-	-	30	ETH	-	Yes (ETH)	0	Ongoing	13	ND	Preschool	Attention deficit (methylphenidate)

Table 1. Clinical features of nine patients with early-onset absence epilepsy (*continued*).

Patient ID	Sex	Age	Past medical history	Family history of epilepsy	Absence onset (months)	First AED	Second AED	Seizure free (effective AED)	Additional seizure types	AED duration (months)	Follow-up duration (months)	Glycorrhachia	Schooling	Cognitive assessment
8	F	5 years, 7 months	-	IGE (mother)	36	VPA	ETH	No (LTG + VPA + KD)	0	Ongoing	18	Hypoglycorrshachia (*SLC2A1* mutation - GLUT1 DS)	Preschool; assistance will be provided on school admission	Borderline intellectual ability
9	M	8 years, 4 months	-	IGE (father)	38	VPA	ETH	Yes (VPA + ETH)	0	54	57	Normal	Normal grades with assistance	Dysphasia

AED: antiepileptic drug; ETH: ethosuximide; IGE: idiopathic generalized epilepsy; KD: ketogenic diet; LTG: lamotrigine; N: normal; ND: not done; VPA: valproate.

Case 3 had pseudo-hypoaldosteronism with a mutation of the mineraloglucocorticoid receptor. Case 4 had a history of malaria. A perinatal history was present in one patient (Case 5) with intrauterine growth retardation and premature birth at 27 weeks within a context of toxaemia. A first or second-degree family history of epilepsy was found in six cases with either symptomatic epilepsy (Case 1: post-meningitis epilepsy in a brother; and Case 3: post-encephalitis epilepsy in the mother and epilepsy within a context of congenital hemiplegia in the father), idiopathic generalized epilepsy with full remission without treatment in adulthood (Cases 8 and 9), or with ongoing antiepileptic treatment (Case 6). A cousin of Case 2 had seizures but no further details were available. No child had delayed milestones at the onset of TAbs. The mean follow-up time was 33.4 months (range: 11-63).

Polygraphic semiology

The mean age at onset of absences was 23.5 months (range: 7-38) (*table 1*). All patients had at least one absence during video-EEG recording. Eight patients out of nine had rhythmic myoclonic jerks of the eyebrows, eyelids or neck during absence seizures (*table 2 and video sequence*).
The mean age at first EEG was 33 months (range: 13-46). The mean diagnostic delay was 10 months (range: 1-19 months). Polygraphic features, including video-EEG and surface EMG, are summarized in *table 2*. Background activity was normal in all. Among the eight patients who slept during the EEG recording, seven had diffuse paroxysmal abnormalities. Ictal EEG showed generalized symmetric SW discharges of 2.5-3 Hz. The mean duration of absences was 7.5 seconds (range: 2-14 seconds). Polygraphy of patients with myoclonia showed that the jerks were rhythmic, lasting from the onset to the end of the EEG discharge and were synchronous with each SW complex, without any tonic or hypotonic manifestations (*figure 1 and video sequence*). Out of the nine patients, seven underwent photic stimulation without any significant effect. Hyperventilation was difficult to induce at this age; four patients underwent spontaneous hyperventilation while crying, which activated absences in one of them.
We found a correlation between the duration of the seizure and the age at EEG recording (*figure 2*) without any change in the seizure frequency (absences/hour) (*figure 2; upper part*).

Diagnosis

Brain MRI was performed in four children, and was normal. Four patients underwent lumbar puncture; one (Case 8) had hypoglycorrhachia and was then screened for mutations in *SLC2A1*, which confirmed the diagnosis of GLUT-1 DS (*table 1*).
According to their electroclinical features, the nine patients in our series may be considered a homogeneous group with onset of TAbs before the age of 4, with normal development at onset, and a predominance of rhythmic myoclonic jerks that accompanied the absence seizure.

Treatment

Five patients received valproate and four received ethosuximide as a first-line treatment. All five patients who first received valproate either displayed no seizure control with treatment (Cases 1, 4, 8 and 9) or had side effects (Case 3; vomiting), and had to be switched to ethosuximide or lamotrigine. Only one of the four patients who first received ethosuximide displayed no seizure control and was switched to valproate (Case 6). Of the nine patients in our series, four required bitherapy for symptoms to be controlled; valproate and ethosuximide (Case 9), valproate and lamotrigine (Cases 4 and 6), or valproate and lamotrigine associated with a ketogenic diet (Case 8; GLUT-1 DS). All patients except one (Case 8; GLUT-1 DS) reached seizure freedom. One patient relapsed under bitherapy (Case 4).

Outcome

No patient in our series experienced any other type of seizure. Among the eight patients who were followed for more than two years, six were seizure-free for two years or more and could stop their treatment without any relapse over a mean follow-up period of 33 months (range: 16-72).
Cognitive outcomes are summarized in *table 1*. Eight patients were school-aged. All benefited from normal schooling, but four required some support at school; two for attention deficit, one for dysphasia, and one for borderline intellectual function within the context of GLUT-1 DS.

Discussion

In our study, we found a homogeneous electroclinical group of nine patients with TAbs as the only seizure type, starting before the age of 4, and with normal neurodevelopment at onset. This homogeneous group was diagnosed as having EOAE. We observed a high frequency of rhythmic myoclonic features involving the eyebrows, eyelids or neck, observed from the beginning to the end of the EEG discharge.

Table 2. Polygraphic features of nine patients with early-onset absence epilepsy.

Patient ID	Age at first video-EEG (months)	Video-EEG duration (minutes)	Number of electro-clinical absences	Range of absence duration (seconds)	Ictal pattern (frequency)	Motor symptoms	EMG analysis of myoclonic jerks
1	17	30	3	3 - 7	SW (3 Hz)	Rhythmic myoclonic jerks (eyebrows)	Regular, synchronous with SW from onset to termination of discharge
2	23	45	13	2 - 5	SW (3 Hz)	Rhythmic myoclonic jerks (neck)	Regular, synchronous with SW from onset to termination of discharge
3	13	81	3	3 - 6	SW (3 Hz)	Rhythmic myoclonic jerks (eyebrows)	Regular, synchronous with SW from onset to termination of discharge
4	27	36	7	3 - 10	SW (3 Hz)	Rhythmic myoclonic jerks (eyebrows)	Regular, synchronous with SW from onset to termination of discharge
5	43	37	4	8	SW (3 Hz)	None	-
6	43	39	1	6 - 10	SW (3 Hz)	Rhythmic myoclonic jerks (eyeballs or neck)	Regular, synchronous with SW from onset to termination of discharge
7	42	34	4	6 - 14	SW (3 Hz)	Rhythmic myoclonic jerks (neck)	Regular, synchronous with SW from onset to termination of discharge
8	48	32	6	5 - 12	SW (3 Hz)	Rhythmic myoclonic jerks (eyelids)	Regular, synchronous with SW from onset to termination of discharge
9	40	36	1	14	SW(2.5 Hz)	Rhythmic myoclonic jerks (eyelids)	Regular, synchronous with SW from onset to termination of discharge

S: spike; SW: spike-wave.

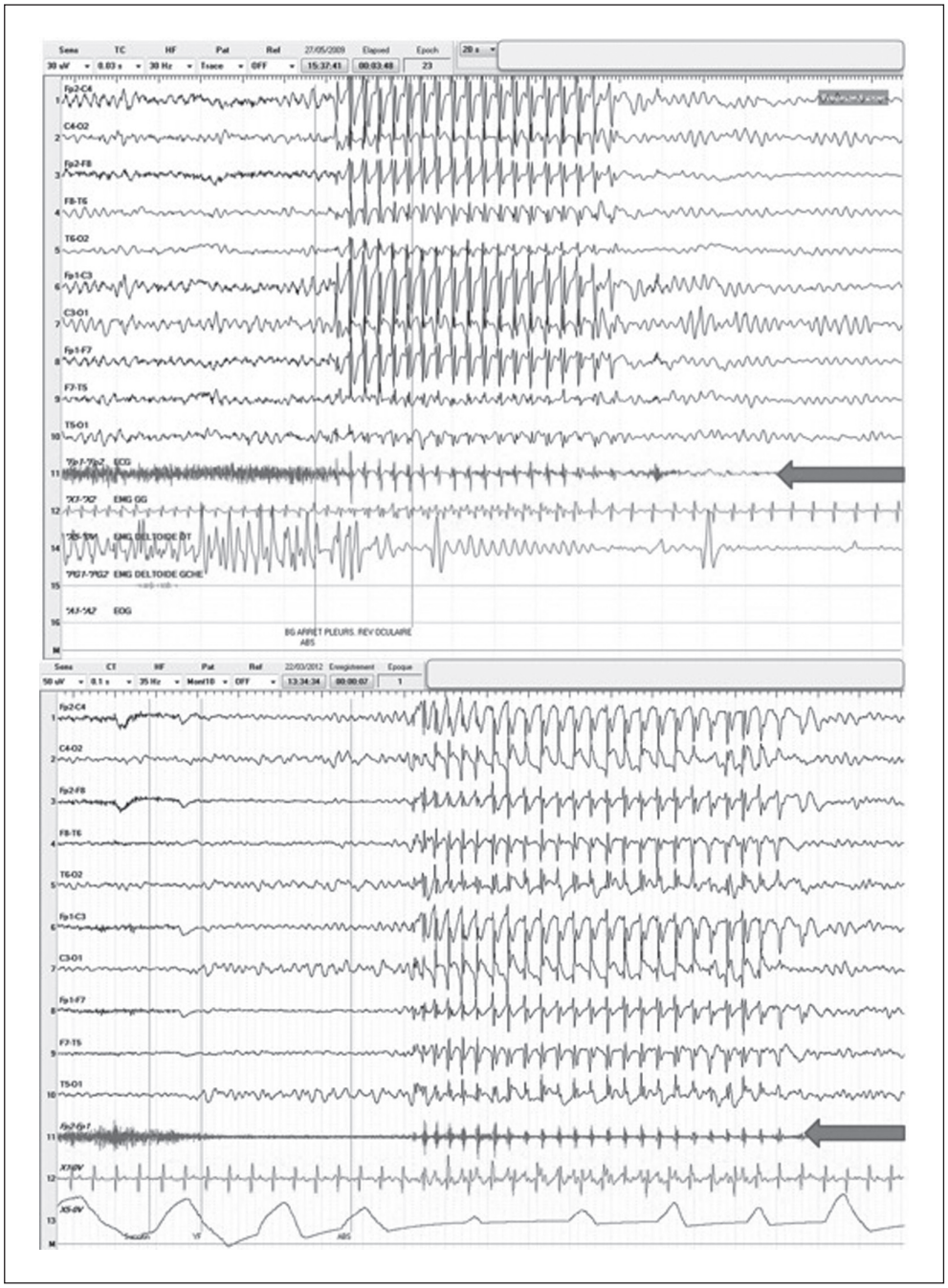

Figure 1. Polygraphic recordings of Patient 1 (upper part) and Patient 4 (lower part) showing rhythmic myoclonic jerks of frontal muscles on EMG (arrows), occurring synchronously with SW discharges of the absence seizures on EEG.

The duration of the absence seizure seemed to correlate with the age at recording.

All patients diagnosed after 2009 (based on the description of GLUT1-DS in the case of early-onset Tabs) (Suls *et al*., 2009) were systematically investigated for hypoglycorrhachia. Before 2009, a lumbar puncture was performed when the patients did not meet the Panayiotopoulos criteria for CAE (Agostinelli *et al*., 2013). This led to the diagnosis of GLUT1-DS in one of our nine patients. This patient required a combination of three antiepileptic drugs and a ketogenic diet and did not achieve full seizure control. The frequency of

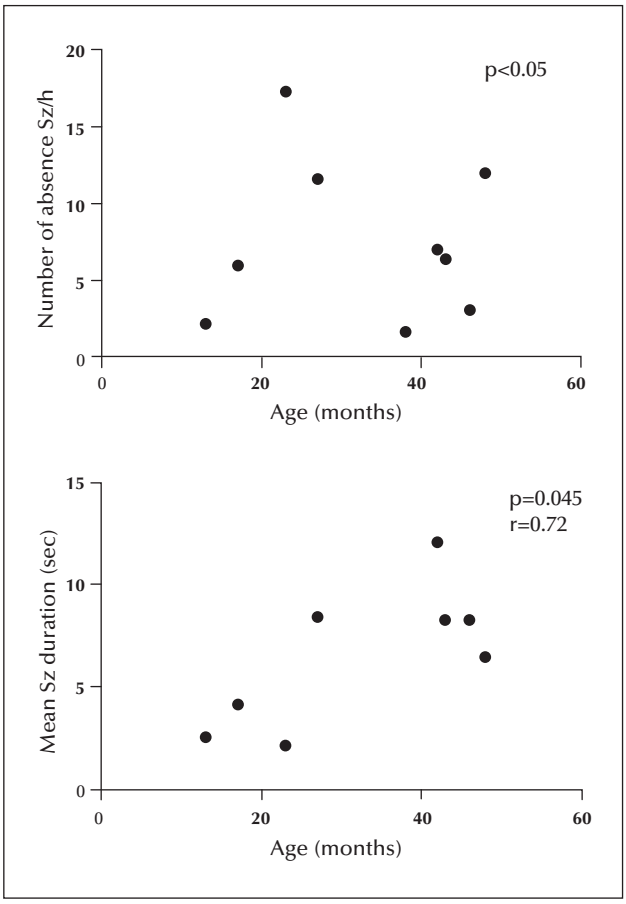

Figure 2. Correlation of the number of absence seizures (upper part) and the mean duration of recorded absence seizures (lower part) with age at the time of EEG recording (Pearson correlation test). Sz: seizure.

GLUT-1 DS in our series was consistent with the literature in which mutations in the *SLC2A1* gene are found in up to 10% of patients with EOAE (Suls *et al.*, 2009; Arsov *et al.*, 2012; Muhle *et al.*, 2013). Although the number of patients in our series was limited, the response to treatment was not as good as for CAE (Glauser *et al.*, 2010); three required bitherapy to be seizure-free, including one who relapsed. Valproate was withdrawn due to a lack of efficacy or side effects in five of the nine patients, as described by others (Belcastro *et al.*, 2013). Mild cognitive or behavioural abnormalities were also more frequent than in CAE (D'Agati *et al.*, 2012; Masur *et al.*, 2013).

Several studies have attempted to classify EOAE and determine whether it represents an entity distinct from syndromes already described. Among these previous studies, the clinical characteristics and outcome of patients were highly variable. This may be explained by differences among the inclusion criteria, including diverging definitions of "typical" absences. Some authors excluded any motor symptoms, in particular rhythmic myoclonic jerks, while others used broader inclusion criteria (Chaix *et al.*, 2003; Caraballo *et al.*, 2011). To avoid this bias, we selected patients before the age of 4, referred due to loss of consciousness with normal development and neurological examination, whose first video-EEG showed absence seizures that fulfilled EEG criteria for TAbs.

Polygraphy showed that eight out of the nine patients in our series had rhythmic myoclonic jerks, synchronous with SW complexes, lasting from the onset to the end of the EEG discharge. Myoclonic jerks, along with absences, could also be evocative of epilepsy with myoclonic absences (EMA) or eyelid myoclonia with absence (ELMA; also called Jeavons syndrome). EMA was excluded in our patients because the myoclonic jerks involved the facial area and neck muscles without any involvement of the limbs. Moreover, the myoclonic jerks were never accompanied by a tonic component, as seen in EMA (Bureau and Tassinari, 2005). The absences in our patients were the only seizure type and were rather shorter (2-14 seconds) than those usually observed in EMA (Bureau and Tassinari, 2005). ELMA was also excluded in our patients because eye closure did not trigger any absence seizures or any changes on EEG. Our patients did not exhibit any photoparoxysmal response (Giannakodimos and Panayiotopoulos, 1996). Finally, both EMA and ELMA are frequently associated with pharmacoresistance and the occurrence of generalized tonic-clonic seizures (Bureau and Tassinari, 2005). A previous video-polygraphic study focusing on myoclonic manifestations, associated with typical absences in CAE (*n*=12), reported findings similar to our observation, *i.e.* the occurrence of rhythmic myoclonic jerks restricted to a limited area of the face or neck, synchronous with the SW complexes on EEG (Capovilla *et al.*, 2001). In several studies in which the characteristics of TAbs in CAE were precisely described, the occurrence of rhythmic myoclonic jerks in TAbs was reported (Holmes *et al.*, 1987; Capovilla *et al.*, 2001; Sadleir *et al.*, 2006). However, this is a relatively rare observation. Myoclonic jerks have been reported to occur during 12.9% TAbs, based on the analysis of 426 TAbs from 27 children in one study (Holmes *et al.*, 1987) and four from 47 children from another study (Sadleir *et al.*, 2006). The high frequency of myoclonic jerks in our patients (88%) might be an age-related feature.

We also found a correlation between the mean duration of absences and the age of the patients. The low number of patients in our study is clearly a limitation. Interestingly, a correlation between the duration of absence and brain development has previously been demonstrated in GAERS rats (Marescaux *et al.*, 1992; Carçak *et al.*, 2008). The progressive emergence of absence seizures in GAERS is correlated with SW discharges from postnatal day 20 (P20) to P60, and is

also associated with a resistance to developing motor seizures (Stage 5) in an amygdala-kindling model (Carçak *et al*., 2008). However, it is difficult at present to further extrapolate these experimental findings since they have not been investigated with regards to developmental changes in GAERS. We might hypothesize that brain maturation processes could allow a progressive emergence of seizure overtime.

Although all of our patients except for the one with GLUT-1 DS achieved seizure freedom, half of them required a combination of two antiepileptic drugs, whereas in CAE, 75% of patients were reported to be seizure-free with monotherapy (Glauser *et al*., 2010). Moreover, for five of the six patients whose follow-up lasted for more than two years, treatment could be stopped with no relapse. These results differ from some series in which antiepileptic drugs were difficult to withdraw due to ongoing seizures, relapses or a high frequency of additional seizure occurrence (Chaix *et al*., 2003; Shahar *et al*., 2007).

In conclusion, our patients appeared to exhibit EOAE, a homogenous epileptic syndrome that can be considered as an early-onset variant of CAE. The presence of myoclonic features was not correlated with a poor outcome, as seen in EMA. However, in contrast to patients with CAE, the response to treatment and requirement for support at school was an issue for some of our patients. The high frequency of motor symptoms may be a distinctive age-related feature. The small number of patients in our study was a limitation. The incidence of motor symptoms, as well as the relationship between the duration of absences and the motor component during brain development, should be further assessed in infants and children. □

Disclosures.
None of the authors have any conflict of interest to disclose.

Legend for video sequence

Video of clinical features during a video-EEG recording showing rhythmic myoclonic jerks of frontal muscles.

Key words for video research on www.epilepticdisorders.com

Phenomenology: absence, myoclonic
Localisation: generalized
Epilepsy syndrome: childhood epilepsy
Aetiology: idiopathic

References

Agostinelli S, Traverso M, Accorsi P, *et al*. Early-onset absence epilepsy: *SLC2A1* gene analysis and treatment evolution. *Eur J Neurol* 2013; 20: 856-9.

Arsov T, Mullen SA, Damiano JA, *et al*. Early onset absence epilepsy: 1 in 10 cases is caused by GLUT1 deficiency. *Epilepsia* 2012; 53: e204-7.

Belcastro V, Caraballo RH, Romeo A, Striano P. Early-onset absence epilepsy aggravated by valproic acid: a video-EEG report. *Epileptic Disord* 2013; 15: 440-3.

Bureau M, Tassinari CA. Epilepsy with myoclonic absences. *Brain Dev* 2005; 27: 178-84.

Capovilla G, Rubboli G, Beccaria F, *et al*. A clinical spectrum of the myoclonic manifestations associated with typical absences in childhood absence epilepsy. A video-polygraphic study. *Epileptic Disord* 2001; 3: 57-62.

Caraballo RH, Darra F, Fontana E, Garcia R, Monese E, Dalla Bernardina B. Absence seizures in the first 3 years of life: an electroclinical study of 46 cases. *Epilepsia* 2011; 52: 393-400.

Carçak N, Aker RG, Ozdemir O, Demiralp T, Onat FY. The relationship between age-related development of spike-and-wave discharges and the resistance to amygdaloid kindling in rats with genetic absence epilepsy. *Neurobiol Dis* 2008; 32: 355-63.

Cavazzuti GB, Ferrari F, Galli V, Benatti A. Epilepsy with typical absence seizures with onset during the first year of life. *Epilepsia* 1989; 30: 802-6.

Chaix Y, Daquin G, Monteiro F, Villeneuve N, Laguitton V, Genton P. Absence epilepsy with onset before age three years: a heterogeneous and often severe condition. *Epilepsia* 2003; 44: 944-9.

D'Agati E, Cerminara C, Casarelli L, Pitzianti M, Curatolo P. Attention and executive functions profile in childhood absence epilepsy. *Brain Dev* 2012; 34: 812-7.

De Marco P. Petit mal epilepsy during early infancy. *Clin EEG Electroencephalogr* 1980; 11: 38-40.

Giannakodimos S, Panayiotopoulos CP. Eyelid myoclonia with absences in adults: a clinical and video-EEG study. *Epilepsia* 1996; 37: 36-44.

Giordano L, Vignoli A, Cusmai R, *et al*. Early onset absence epilepsy with onset in the first year of life: a multicenter cohort study. *Epilepsia* 2013; 54(7): 66-9.

Glauser TA, Cnaan A, Shinnar S, *et al*. Ethosuximide, valproic acid and lamotrigine in childhood absence epilepsy. *N Engl J Med* 2010; 362: 790-9.

Holmes GL, McKeever M, Adamson M. Absence seizures in children: clinical and electroencephalographic features. *Ann Neurol* 1987; 21: 268-73.

Leary LD, Wang D, Nordli DR, Engelstad K, De Vivo DC. Seizure characterization and electroencephalographic features in Glut-1 deficiency syndrome. *Epilepsia* 2003; 44: 701-7.

Marescaux C, Vergnes M, Depaulis A. Genetic absence epilepsy in rats from Strasbourg-a review. *J Neural Transm* 1992; 35: 37-69.

Masur D, Shinnar S, Cnaan A, *et al*. Pretreatment cognitive deficits and treatment effects on attention in childhood absence epilepsy. *Neurology* 2013; 81: 1572-80.

Muhle H, Helbig I, Frøslev TG, *et al*. The role of SLC2A1 in early onset and childhood absence epilepsies. *Epilepsy Res* 2013; 105: 229-33.

Panayiotopoulos CP. Typical absence seizures and related epileptic syndromes: assessment of current state and directions for future research. *Epilepsia* 2008; 49: 2131-9.

Sadleir LG, Farrell K, Smith S, Connolly MB, Scheffer IE. Electroclinical features of absence seizures in childhood absence epilepsy. *Neurology* 2006; 67: 413-8.

Shahar E, Genizi J, Nevo Y, Kaufman R, Cabot S, Zelnik N. Typical absence epilepsy presenting prior to age of 3 years: an uncommon form of idiopathic generalized epilepsy. *Eur J Paediatr Neurol* 2007; 11: 346-52.

Suls A, Mullen SA, Weber YG, *et al*. Early-onset absence epilepsy caused by mutations in the glucose transporter GLUT1. *Ann Neurol* 2009; 66: 415-9.

Verrotti A, Agostinelli S, Olivieri C, Chiarelli F, Curatolo P. Early-onset pure absence epilepsy: a distinct epileptic syndrome. *Acta Paediatr* 2011a; 100: 647-50.

Verrotti A, Olivieri C, Agostinelli S, *et al*. Long term outcome in children affected by absence epilepsy with onset before the age of three years. *Epilepsy Behav* 2011b; 20: 366-9.

TEST YOURSELF

(1) Typical absences as the only seizure type observed in a child before the age of 4 is consistent with which of the following diagnoses:
A. Epilepsy with focal seizures
B. GLUT1 deficiency syndrome
C. The first symptoms of Lennox-Gastaut syndrome
D. Early-onset childhood absence epilepsy
E. The first symptoms of epilepsy with myoclonic atonic seizures

(2) What is the metabolic aetiology of 1/10 cases of early-onset absence epilepsy?
A. Mitochondrial disorders
B. Pyruvate deficiency
C. GLUT1 deficiency syndrome
D. Menkes disease
E. Biotinidase deficiency

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".