Original article

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Non-epileptic myoclonic attacks in infancy: three cases

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ABSTRACT – Since the first cases of abnormal paroxystic movements in normal infants were described, the importance of accurate characterization of this medical condition has been increasingly confirmed in the literature. Non-epileptic attacks mimic epileptic paroxysms in clinical presentation, but they have a typically benign course and are unresponsive to pharmacological treatment. An evident feature of the syndrome is its extreme variability in clinical manifestation. Here, we describe three normal infants with two similar forms of non-epileptic paroxysms. Electroclinical manifestations and profile of evolution were investigated. Ictal video-EEG polygraphic recordings were obtained for each patient. The increasing number of such reported clinical cases in the literature may contribute to high quality systematic reviews and the development of useful guidelines in the future. The clinical heterogeneity of non-epileptic attacks, together with the relative rarity of the condition, may make differential diagnosis with epileptic attacks very challenging. [*Published with video sequences*]

Key words: non-epileptic attacks, infancy, head drop, video-EEG recording

In the seventies, the first cases of abnormal paroxystic movements in normal infants were described (Fejerman, 1977; Lombroso and Fejerman, 1977). In 1976, Fejerman had noticed for the first time that, despite the fact these children appeared to be affected by West syndrome (WS), they did not evolve negatively and had an ictal and interictal EEG which was "always normal". Thus, the new syndrome was considered as an imitator rather than a benign variant of WS; the syndrome was definitively distinguished from WS, irrespective of aetiology and pathogenesis (Maydell *et al*., 2001).

The importance of accurate characterization of this phenomenon, of mimicking epileptic attacks yet with a typical benign course and unresponsiveness to pharmacological treatment, was further confirmed in the literature.

Over time, many different names were given to the new syndrome; benign myoclonus of early infancy (BMEI) (Lombroso and Fejerman, 1977), benign

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non-epileptic infantile spasms (Dravet *et al*., 1986), non-epileptic attacks (NEAs), non-epileptic paroxysms, paroxysmal non-epileptic disorders (PNEDs), and Fejerman syndrome (FS) (Dalla Bernardina, 2009) were the most common in the literature.

One of the most critical features of the syndrome is its extreme variability with regards to clinical manifestation (Fejerman, 1984; Dravet *et al*., 1986; Galletti *et al*., 1989; Maydell *et al*., 2001), and for this reason it was proposed to represent a spectrum of different conditions (Caraballo *et al*., 2009).

Based on an analysis of clinical and electromyographic (EMG) features of a large series of infants, Caraballo *et al*. proposed a classification of all manifestations of the syndrome into five subgroups. Of these, four included specific paroxysms (positive and negative myoclonia, and shuddering and spasms) affecting various parts of the body, while the fifth subgroup included cases in which more than one type of motor phenomenon was present (Caraballo *et al*., 2009).

Recently, Capovilla *et al*. described a new variant of NEAs, named "head atonic attacks" (HAAs), in three children (Capovilla *et al*., 2013). The clinical presentation of infants was characterized by stereotypic abrupt movements of head dropping caused by loss of muscle tone of the neck, occurring several times per day, irrespective of circadian cycles and of any known triggering factors. The EEG recordings were characterized by artefacts resembling high-voltage slow waves, and this appearance led to the initial misdiagnosis of WS. Spontaneous resolution of the episodes, together with drug resistance and the absence of neuropsychological deterioration, confirmed that a diagnosis of WS was inappropriate, in favour of a diagnosis of HAA.

Here, we describe three normal infants presenting with similar forms of NEAs. We believe that this report may contribute to a better knowledge of the condition and problem in order for all clinicians to reach an early recognition strategy for these children.

Case studies

We present three infants referred to the Epilepsy Center of San Paolo Hospital, Milan and to the Neuropsychiatry Department of Spedali Civili, Brescia, Italy. Electroclinical features and profile of evolution were studied for each, with particular attention to: family and personal history of epilepsy, psychomotor development, age at onset and at disappearance of attacks, frequency and timing of occurrence of attacks during the day, and pattern of occurrence and triggering factors. Ictal video-EEG polygraphic recordings were obtained for all the patients.

Case 1

A female patient was born after an uneventful pregnancy and normal perinatal period. She had normal growth and psychomotor development. No neurological diseases were reported in the family. At 11 months and 3 weeks of age, the infant started to have daily episodes of paroxystic head drop-like movements, isolated or in clusters of three to five, arrhythmic, and more or less intense. They were sometimes associated with blepharospasm and/or myoclonic activity of the shoulders, with proximal flexion and abduction of upper limbs, at times followed by brief (2-3-second) apparent stunning, and rarely crying. They were observed only in wakefulness and only in an upright position, without apparent triggering factors or circadian correlations.

Episodes were recorded by video-EEG; an interictal atypical slow and sharp activity in the posterior regions on the right hemisphere, present both in wakefulness and in non-REM sleep, was detected (*figure 1*). This activity was recorded in several EEGs and maintained the same slow and sometimes sharp characteristic over time, thus it was not considered to be artefactual. Ictal recording of the episodes showed, on the EMG trace of the neck muscles, a negative myoclonic activity, synchronous with clinical episodes and with artefacts on the EEG (*video sequence 1, figure 2*).

Considering atonic attacks to be highly suggestive of epilepsy and atypical interictal EEG activity, treatment with vigabatrin (GVG), up to 100 mg/kg/die, was started (Pesaturo *et al*., 2011).

In the meantime, one month from the start, the episodes stopped and the EEG abnormalities disappeared. Concomitantly, brain MRI, first level metabolic and genetic screening (karyotyping), together with development evaluation (Bayley Development Scale) resulted normal.

Psychomotor development at follow-up, after 10 months, was completely normal.

Case 2

A male patient was born after a pregnancy complicated by maternal cytomegalovirus (CMV) infection. At birth, the urine and blood of the newborn were negative for CMV. Brain ultrasound was also normal. Growth and psychomotor profile were normal.

At the age of 6 months, the child started to have head drop attacks, which, in a few days, became very frequent, only in wakefulness. The attacks were reported to be generally isolated, without triggering factors. Episodes were recorded during video-EEG; the EMN trace of neck and deltoids showed a brief contraction, while the EEG trace did not show any ictal modification in cerebral activity (*video sequence 2*, *figure 3*).

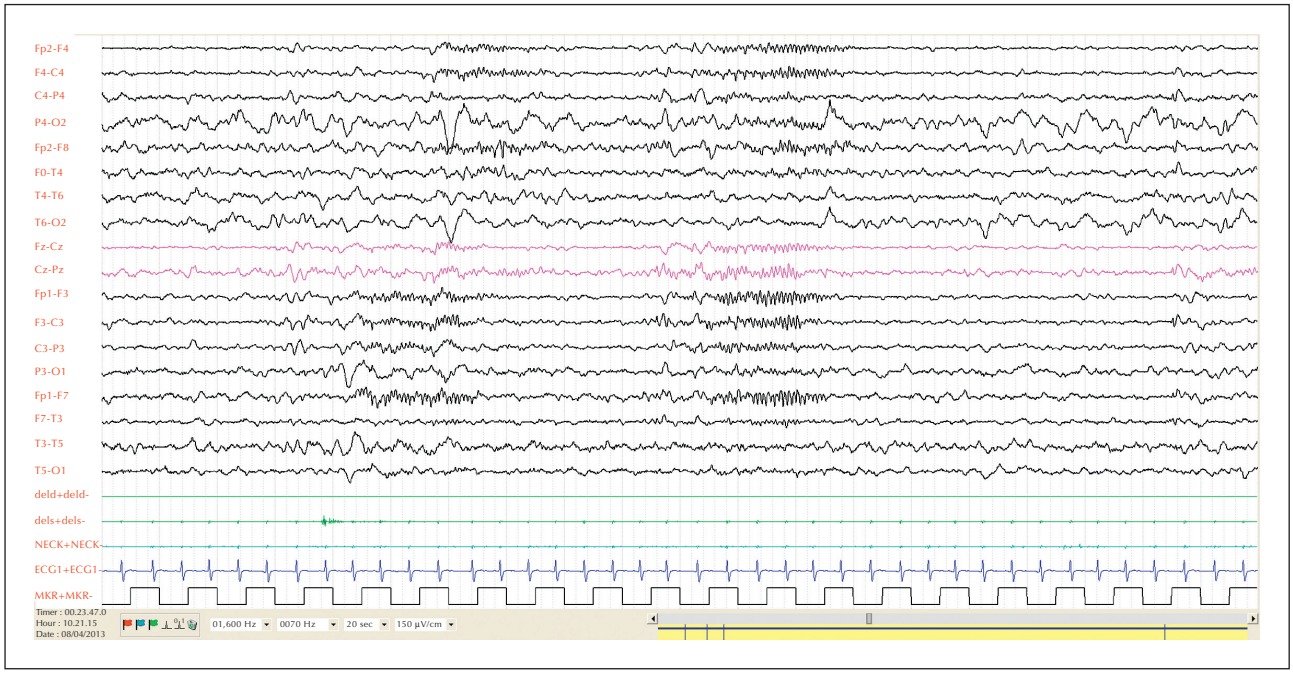

Figure 1. Video-EEG polygraphic recording in Case 1 showing interictal atypical slow and sharp activity in the posterior regions on the right hemisphere in non-REM sleep. The EMG traces include deltoid muscles (Dx: right; SX: left), and neck muscle is the obliquus capitis superior muscle, a small muscle in the upper back part of the neck.

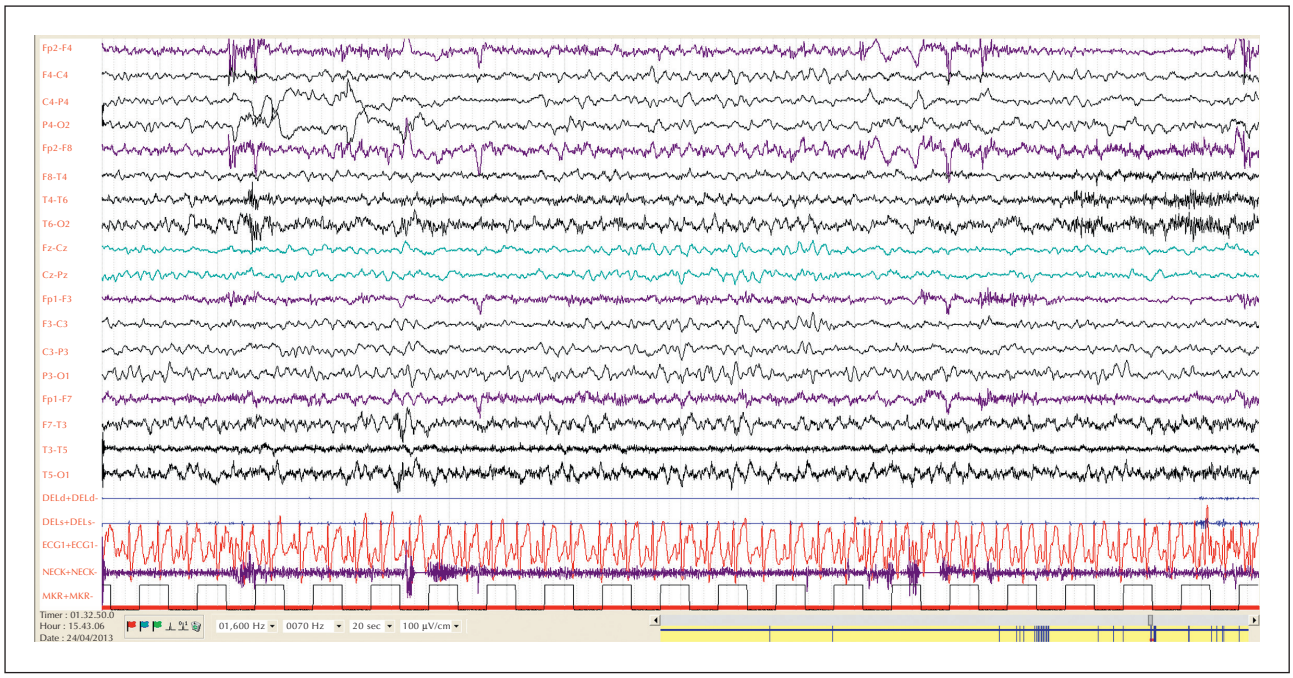

Figure 2. Ictal recording of the episodes in Case 1 showing a negative myoclonic activity on the EMG trace of the neck muscles, synchronous with clinical episodes and with artefacts on EEG (see also *video sequence 1*). The EMG traces include deltoid muscles (Dx: right; SX: left), and the neck muscle is the obliquus capitis superior muscle.

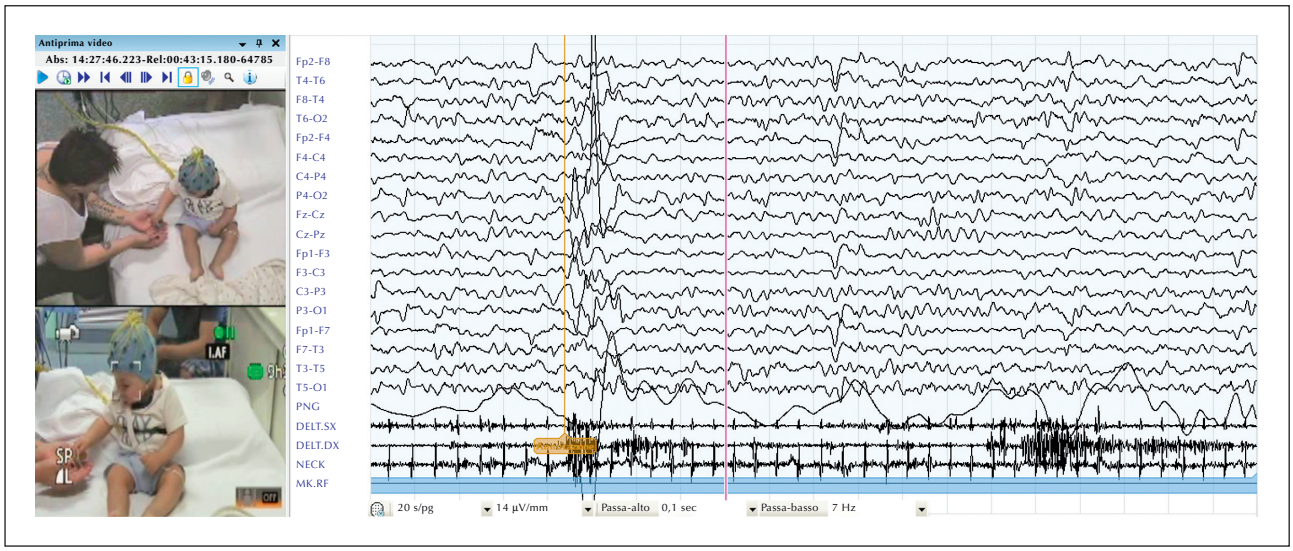

Figure 3. Video-EEG recording in Case 2; the EMN trace of neck and deltoids shows a brief contraction, while the EEG trace does not show any ictal modification in cerebral activity (see also *video sequence 2*). The EMG traces include deltoid muscles (Dx: right; SX: left) and the neck muscle is the obliquus capitis superior muscle.

Head drop attacks were considered to be non-epileptic and no treatment was prescribed.
The infant was followed with clinical and EEG monitoring; episodes disappeared spontaneously after three months.
Psychomotor development was completely normal at follow-up, after 10 months.

Case 3

A female patient was born after an uneventful pregnancy, at term, by natural delivery. She had normal growth and psychomotor development.
A first degree cousin with infantile-onset seizures, symptomatic of a cerebral tumour, was reported.
At 8 months of age, she began to have episodes of sudden head dropping with blepharospasm, occurring initially twice per day. Within a month, the episodes were very frequent, up to 20 per day, without any relationship to meals, sleep or emotional state.
She was evaluated at the age of 9 months; neurological examination was unremarkable and psychomotor development, assessed by the Griffith Scale, was within the normal range. Several video-EEG recordings during wakefulness and sleep did not show any paroxysmal activity.
Episodes were recorded and characterized by brief head dropping, evident over the neck according to the EMG, without any EEG correlate (*video sequence 3*). The episodes were diagnosed as non-epileptic and no treatment was given. The child was followed with periodic clinical consultations.
The phenomena ended within two months.
After four years of follow-up, the child did not present any seizures, nor neurological problems, and her psychomotor development was normal.

Limitations

Even though the follow-up of the first two cases described here was limited to 10 months, the complete remission of symptoms and healthy appearance in infants of 1 to 2 years of age, with a suspicion of infantile spasms (IS), can actually be considered relatively significant. Moreover, non-epileptic paroxystic events do not appear to be a relapsing condition (Brunquell *et al.*, 1990; Caraballo *et al.*, 2003).

Discussion

Differential diagnosis between epileptic and non-epileptic paroxysms can be very challenging, especially in infants. In order to perform a correct differential diagnosis between WS and NEAs, it has been suggested to focus on essentially three points: psychomotor delay, EEG, and seizures (Caraballo *et al.*, 2009).

Psychomotor delay

Psychomotor delay is frequently associated with WS and never determined by NEAs (Caraballo *et al.*, 2009). Cognitive outcome in children with IS is highly dependent on aetiology (Pellock *et al.*, 2010). Patients with cryptogenic IS and early effective treatment (within

one month from the onset) can reach normal cognitive development, even at long-term follow-up (Kivity *et al*., 2004; Rener-Primec *et al*., 2006).
Besides cryptogenic aetiology, recognized favourable factors are the following: age at onset of ≥4 months, absence of atypical spasms and partial seizures, absence of asymmetric EEG abnormalities, short treatment lag, and an early and sustained response to treatment (Riikonen, 2010).
All the patients described here had normal psychomotor development preceding and following the onset of the paroxystic episodes.

EEG

EEG is always normal during NEAs (Caraballo *et al*., 2009), and when this continues into the mid and long term, it can be helpful in the differential diagnosis between epileptic and non-epileptic conditions. However, the onset of abnormalities on the EEG do not always occur early (Hancock *et al*., 2009). EEG abnormalities are almost always present in WS (Caraballo *et al*., 2009), but the presence of interictal EEG abnormalities does not exclude the diagnosis of a non-epileptic condition (Brunquell *et al*., 1990); thus an abnormal EEG should not necessarily be considered in the diagnosis of an epileptic condition.
Moreover, an EEG can be abnormal but not typically hypsarrhythmic in WS (Hrachovy *et al*., 1984). Some years ago, a case report clearly faced the problem of the nosological definition of those patients who present with a clinical appearance of epileptic spasms but without the hypsarrhythmia typical of WS, and with or without focal paroxysmal discharges on interictal EEG (Caraballo *et al*., 2003).
The appearance of transient focal EEG abnormalities in Case 1 led to further diagnostic investigations and initial drug prescription; strict management of the patient and punctual diagnostic re-evaluation allowed a correct interpretation of the episodes.
The EEG of the other infants described here did not show any abnormalities in repeated recordings during wakefulness and sleep, making an easier and earlier recognition of the non-epileptic condition.

Seizures

Seizures are present during either wakefulness or sleep in WS, but especially in wakefulness and less frequently in sleep in NEAs (Caraballo *et al*., 2009).
The paroxysmal events presented by the children descibed here were evident only in wakefulness. Regarding the phenotypes of paroxysms, a complete description of some of these (benign myoclonus of early infancy) was reported by Caraballo *et al*. in 2009. Among the types of motor phenomena, atonia or negative myoclonus in the muscles of the neck and trunk have been rarely described (four patients in a series of 102) (Caraballo *et al*., 2009). Recently, Capovilla *et al*. (2013) clarified the characteristics of this variant, referred to as HAAs, providing video-EEG documentation in three infants.
Based on the differential analysis of video recordings between epileptic and non-epileptic head drop attacks, it was observed that rapid head drops followed by a slower recovery to the upright position were significantly more frequent in epileptic patients, while head bobs consisting of repetitive nods were observed only in the non-epileptic group (Brunquell *et al*., 1990).
The three children reported here showed episodes which were clinically similar and characterized by rapid head drops, with the exception of Case 1 who occasionally had repetitive head bobs.
Ictal video-EEG recordings demonstrated the polygraphic features of the episodes, which were not related to any ictal EEG paroxysms, however, the EMG trace of neck muscles demonstrated a clear negative myoclonic activity, synchronous with clinical events (Case 1) or a brief contraction (Case 2 and 3). Thus, we were able to classify episodes in Case 1 as HAAs and in Case 2 and 3 as NEAs.
Regarding familiarity, little is known about the possibility of a significant recurrence of paroxysms in the same pedigree. More information regarding this aspect of non-epileptic attacks may make it possible to better orient clinical practice, as opposed to hypothesizing, or excluding, a genetic basis for the condition (Galletti *et al*., 1989).

Conclusions

Although some useful information regarding the differential diagnosis between epileptic and non-epileptic events in children is available in the literature, this is not sufficient to prepare a consensus on guidelines.
Firstly, there are very few reports with significantly large sample sizes (Fejerman, 1980; Brunquell *et al*., 1990; Caraballo *et al*., 2009). This is understandable based on the relative rarity of this condition. Moreover, there are very few clinical cases reported with video-EEG recordings and complete description of clinical presentation and management (Caraballo *et al*., 2003; Capovilla, 2011; Capovilla *et al*., 2013). Few reports have focused on the problem of differential diagnosis between epileptic and non-epileptic paroxysms in children (Brunquell *et al*., 1990; Chitre, 2012) and no guidelines are provided to specifically help clinicians choose between measures of intervention and observation in the early management and early differential diagnosis

of these two clinical conditions. Therefore, in such cases, only video-EEG polygraphic recording of the ictal event can lead to a correct differential diagnosis. □

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Legends for video sequences

Video sequence 1

Repetitive episodes of head drop attacks, in standing position, associated with negative myoclonic activity on EMG (neck muscle).

Video sequence 2

Isolated and sudden head drop attack (brief contraction of deltoids and neck muscle).

Video sequence 3

Brief head drop without any EEG correlate.

Key words for video research on www.epilepticdisorders.com
Syndrome: non epileptic paroxysmal disorder
Etiology: unknown
Phenomenology: non epileptic paroxysmal event; myoclonus (non-epileptic); drop attacks
Localization: not applicable

References

Brunquell P, Mc Keever M, Russman BS. Differentiation of epileptic from nonepileptic head drops in children. *Epilepsia* 1990; 31: 401-5.

Capovilla G. Shaking body attacks: A new type of benign non-epileptic attack in infancy. *Epileptic Disord* 2011; 13: 140-4.

Capovilla G, Montagnini A, Peruzzi C, Beccaria F. Head atonic attacks: A new type of benign non-epileptic attack in infancy strongly mimicring epilepsy. *Epileptic Disord* 2013; 15: 44-8.

Caraballo RH, Fejerman N, Dalla Bernardina B, *et al*. Epileptic spasms in clusters without hypsarrhytmia in infancy. *Epileptic Disord* 2003; 5: 109-13.

Caraballo RH, Capovilla G, Vigevano F, Beccaria F, Specchio N, Fejerman N. The spectrum of benign myoclonus of early infancy: Clinical and neuropsychologic features in 102 patients. *Epilepsia* 2009; 50: 1176-83.

Chitre M. Pitfalls in the diagnosis and misdiagnosis of epilepsy. *Paediatr child health* 2012; 23: 237-42.

Dalla Bernardina B. Benign myoclonus of early infancy or Fejerman syndrome. *Epilepsia* 2009; 50: 1289-300.

Dravet C, Giraud N, Bureau M, Roger J. Benign myoclonus of early infancy or benign non-epileptic infantile spasms. *Neuropediatrics* 1986; 17: 33-8.

Fejerman N. Mioclonias benignas de la infancia temprana. Comunicacion peliminar. Actas IV jornadas rioplatenses de neurologia infantil 1976. *Neuropediatria Latinoamericana* 1977: 131-4.

Fejerman N. Myoclonies benignes du nourisson. Communication at the 6th meeting of Societé de neurologie infantile. Luxemburg, 1980.

Fejerman N. Benign myoclonus of early childhood. *An Esp Pediatr* 1984; 21: 725-31.

Galletti F, Brinciotti M, Emanuelli O. Familial occurrence of benign myoclonus of early infancy. *Epilepsia* 1989; 30: 579-81.

Hancock EC, Osborne JP, Edwards SW. *Treatment of infantile spasms*. The Cochrane Collaboration, John Wiley & Sons Ltd, 2009: 1-56.

Hrachovy RA, Frost Jr. JD, Glaze DG. Hypsarrhytmia: Variations on the theme. *Epilepsia* 1984; 25: 317-25.

Kivity S, Lerman P, Ariel R, Danziger Y, Mimouni M, Shinnar S. Long-term cognitive outcomes of a cohort of children with cryptogenic infantile spasms treated with high-dose adrenocorticotropic hormone. *Epilepsia* 2004; 45: 255-62.

Lombroso CT, Fejerman N. Benign myoclonus of early infancy. *Ann Neurol* 1977; 1: 138-43.

Maydell BV, Berenson F, Rothner AD, Wyllie E, Kotagal P. Benign myoclonus of early infancy: An imitator of West's syndrome. *J Child Neurol* 2001; 16: 109-12.

Pellock JM, Hrachovy R, Shinnar S, *et al*. Infantile spasms: A U.S. consensus report. *Epilepsia* 2010; 51: 2175-89.

Pesaturo KA, Spooner LM, Belliveau P. Vigabatrin for infantile spasms. *Pharmacotherapy* 2011; 31: 298-311.

Rener-Primec Z, Stare J, Neubauer D. The risk of lower mental outcome in infantile spasms increases after three weeks of hypsarrhythmia duration. *Epilepsia* 2006; 47: 2202-5.

Riikonen RS. Favourable prognostic factors with infantile spasms. *Eur J Paediatr Neurol* 2010; 14: 13-8.