

# Myoclonic epilepsy in infancy: one or two diseases?

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In a critical review published this year in the June issue of *Epileptic Disorders*, Verrotti and collaborators (Verrotti *et al.*, 2013) summarised the available data on reflex myoclonic epilepsy in infancy (RMEI). Myoclonic epilepsy in infancy (MEI) has been defined as an electroclinical syndrome in the recent report by the ILAE Commission on Classification and Terminology (Berg *et al.*, 2010). In a previous report (Engel, 2001), this syndrome was referred to as “benign myoclonic epilepsy in infancy” (BMEI), as it was reported at the time it was first described by Charlotte Dravet and Michelle Bureau (Dravet and Bureau, 1981).

Myoclonic epilepsy in infancy is an idiopathic epilepsy characterised by the occurrence of myoclonic seizures as the only seizure type (except for rare simple febrile seizures) in the first three years of life in children with normal development. A distinction between reflex myoclonic epilepsy in infancy and BMEI was first proposed by Ricci *et al.* (1995).

In their review, Verrotti *et al.* propose to maintain a distinction between MEI and RMEI based on the existence of triggering factors, the existence of some untreated

cases with favourable evolution, the absence of seizure relapse in RMEI, and possible genetic factors. However, almost half of the patients with RMEI also suffer from spontaneous seizures (Guerrini *et al.*, 2012). We also previously reported patients with MEI ( $n=2$ ) who had good outcome despite the fact they were untreated (Auvin *et al.*, 2006). One of our patients that had reflex induced myoclonic seizures experienced a seizure relapse and was later classified as myoclonic astatic epilepsy (Auvin *et al.*, 2012).

Moreover, it is important to remind ourselves that there are no distinctive EEG features between the two entities. With regards to the small number of patients reported with MEI and RMEI, we believe that it is currently impossible to draw any firm conclusions. We suggest that reflex-induced myoclonic seizures in infants should be *intensively* investigated by an accurate anamnesis and by performing acoustic and touch stimuli during the video-EEG recording in all patients suspected to have MEI. These symptoms might be considered as an additional indicator for the diagnosis and prognosis. Indeed, in most publications, the prognosis for long-term seizure freedom, cognitive functions, and behaviour appears actually better in patients with RMEI than in those with MEI without reflex seizures (Guerrini *et al.*, 2012; Verrotti *et al.*, 2013). There are several elements that point to the probable role of genetic factors in MEI (age, frequent familial history, and occurrence of other generalised epilepsy during follow-up). Verrotti *et al.* highlighted that some genetic factors might also contribute to the occurrence of reflex myoclonic seizures (Verrotti *et al.*, 2013).

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When MEI is distinguished from other epilepsy syndromes with myoclonic seizures (myoclonic seizures only and normal development with mostly favourable outcome), at the onset of the disease, it is not always easy to exclude neurometabolic disorders. The review by Verrotti *et al.* (2013) addresses this issue. In most patients, metabolic investigations are not indicated as long as the treatment controls the seizures and development remains normal.

It is now clear that the prognosis of MEI is not always favourable. The neuropsychological outcome is generally good, as observed in 60.9% of 23 patients in the literature, including those with RMEI, who were followed until at least the age of 15 years. However, developmental delay and cognitive and behavioural difficulties have been reported in 39.1% of these patients (Guerrini *et al.*, 2012). In addition, other epilepsy syndromes may develop following MEI in rare cases: juvenile myoclonic epilepsy (Auvin *et al.*, 2006), childhood absence epilepsy (Mangano *et al.*, 2011), and eyelid myoclonia with absence (Prats-Vinas *et al.*, 2002; Moutaouakil *et al.*, 2010).

Outside the debate regarding the existence of two rare forms of infantile epilepsies, it is clear that some attitudes remain critical in the case of MEI. The first attitude is a careful assessment of the patient and the second is to provide an accurate prognosis. The development of new genetic techniques may contribute to the debate on the distinction between RMEI and MEI. The use of whole exome sequencing in a large electroclinical study of patients with MEI, with a specific test for reflex-induced myoclonic seizures, would provide robust data on the existence or not of two syndromes and the underlying pathogenic mechanisms.

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