Eyelid myoclonia with and without absences

By **C P Panayiotopoulos MD PhD** (Dr. Panayiotopoulos of St. Thomas' Hospital has no relevant financial relationships to disclose.)
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Introduction

This article includes discussion of eyelid myoclonia with and without absences, eyelid myoclonia, eyelid myoclonus, and Jeavons syndrome. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

Overview

Eyelid myoclonia with or without absences is a form of epileptic seizure manifesting with myoclonic jerks of the eyelids, often with brief absences. These seizures are mainly precipitated by closing of the eyes and lights. They occur in symptomatic, possibly symptomatic, and idiopathic generalized epilepsies. Most authors support the view that eyelid myoclonia with absences is the defining seizure type of an idiopathic syndrome (Jeavons syndrome) of reflex epilepsy, which is genetically determined, has age-related onset, and affects otherwise normal children, with a female preponderance. Jeavons syndrome is probably lifelong with continuing seizures in adult life. Eyelid myoclonia is often confused with facial tics or self-induction of seizures. In this article, the author details developments in the clinical manifestations, pathophysiology, genetics, and pharmacological treatment of eyelid myoclonia with absences.

Key points

- Eyelid myoclonia with absences is a distinct type of epileptic seizure that is often misdiagnosed as facial tics or another nonepileptic paroxysmal event of eyelid jerking.
- The characteristic eyelid myoclonia, if seen once, will never be forgotten or confused with other conditions.
- A main misconception is that eyelid myoclonia with or without absences is an attempt to self-induce seizures.
- Jeavons syndrome is a type of reflex photosensitive epilepsy that is clinically marked with eyelid myoclonia.
- Jeavons syndrome is myoclonic, rather than absence, epilepsy.

Historical note and terminology

The first documentation of eyelid myoclonia was by Radovici and colleagues. They reported and filmed the seizures of a 20-year-old man who, from the age of 10 years, had photically induced "frequent and spasmodic blinking of the eyelids with rhythmical movements [of] both rotating and elevating of the head towards the sun" (Radovici et al 1932).

In 1977 Jeavons described “eyelid myoclonia and absences” as follows (Jeavons 1977):

> Eyelid myoclonia and absences show a marked jerking of the eyelids immediately after eye-closure and there is an associated brief bilateral spike and wave activity. The eyelid movement is like rapid blinking and the eyes deviate upwards, in contrast to the very slight flicker of eyelids which may be seen in a typical absence in which the eyes look straight ahead. Brief absences may occur spontaneously and are accompanied by 3 Hz spike and wave discharges.... All patients are photosensitive. The mean age of onset is 6 years.

Eyelid myoclonia with absences has been studied extensively (Dalla Bernandina et al 1989; Gobbi et al 1989; Appleton et al 1993; Bianchi and Italian League Against Epilepsy 1995; Ferrie et al 1996; Giannakodimos and Panayiotopoulos 1996; Panayiotopoulos et al 1996a; Panayiotopoulos et al 1996b; Striano et al 2002; Striano et al 2009; Ferrie 2004; Covanis 2007; Covanis 2010; Panayiotopoulos 2005; Panayiotopoulos 2010; Joshi and Patrick 2007; Capovilla et al

2009; Caraballo et al 2009; Perez-Errazquin et al 2010; Vaudano et al 2014; Nar Senol et al 2015). In recognition of Jeavons' contribution, Duncan and Panayiotopoulos proposed the name “Jeavons syndrome” for eyelid myoclonia with absences in a book devoted to this condition (Duncan and Panayiotopoulos 1996); see also (Panayiotopoulos 2005; Panayiotopoulos 2010; Covanis 2007; Covanis 2010; Striano et al 2009). However, the ILAE formal reports do not recognize Jeavons syndrome (eyelid myoclonia with absences) as a separate syndrome (Engel 2001; Engel 2006; Berg 2010). Instead, eyelid myoclonia, the seizure, is classified as a myoclonic seizure type by the ILAE Task Force as follows:

> Eyelid myoclonia: The degree to which these recurrent events (5 to 6 Hz) are associated with impairment of consciousness has not been adequately documented, and should be. In some patients, they can be provoked by eye closure. The seizure type, however, does exist as a unique entity (Engel 2006).

Furthermore, the 2010 ILAE proposals classify eyelid myoclonia as a type of absence seizure with special features: (1) typical, (2) atypical, and (3) absence with special features (myoclonic absence and eyelid myoclonia) (Berg et al 2010). In the ILAE “Epilepsy Diagnosis” manual, absences with eyelid myoclonia are considered as 1 of the 4 types of generalized absence seizures (typical, atypical, myoclonic, with eyelid myoclonia) and are described as follows (Commission on Classification and Terminology of the International League Against Epilepsy 2017):

> Absence with eyelid myoclonia. Absence with eyelid myoclonia is absence seizures accompanied by brief, repetitive, often rhythmic, fast (4 to 6 Hz) myoclonic jerks of the eyelids with simultaneous upward deviation of the eyeballs and extension of the head. Seizures are typically very brief (less than 6 seconds in duration), and multiple seizures occur on a daily basis. Mostly awareness is retained.
>
> Caution. If myoclonic seizure with abduction of the upper limbs, then consider myoclonic absence seizures.
>
> *EEG background*. Please refer to specific syndrome in which this seizure type occurs.
>
> *Ictal EEG*. High amplitude generalized spike-and-wave and polyspike-and-wave at a frequency of 3 to 6Hz, triggered by eye closure and intermittent photic stimulation.
>
> Caution. Slow spike-and-wave (less than 2.5 Hz) is not seen.
>
> *Differential diagnosis.*
>
> - Myoclonic absence: 3 Hz myoclonic jerks of upper limbs with tonic abduction.
> - Typical absence (with eyelid flutter)
>
> *Related syndromes.*
>
> - Epilepsy with eyelid myoclonias
> - Occasionally seen in other genetic generalized epilepsies and Dravet syndrome

A genetic generalized epilepsy is an epilepsy with generalized seizures associated with generalized epileptiform EEG patterns, such as generalized spike wave activity (Commission on Classification and Terminology of the International League Against Epilepsy 2017).

The latest ILAE position paper of the operational classification of seizure types considers “absence with eyelid myoclonia” as a new seizure type categorized as a nonmotor seizure (Fisher et al 2017a; Fisher et al 2017b):

> Generalized seizures are divided into motor and nonmotor (absence) seizures. Nonmotor (absence) seizures are typical or atypical, or seizures that present prominent myoclonic activity or eyelid myoclonia. Further subdivisions are similar to those of the 1981 classification, with the addition of myoclonic-atonic seizures, common in epilepsy with myoclonic-atonic seizures (Doose syndrome), myoclonic-tonic-clonic seizures common in juvenile myoclonic epilepsy, myoclonic absence, and absence seizures with eyelid myoclonia seen in the syndrome described by Jeavons and elsewhere. Generalized manifestations of seizures can be asymmetrical, rendering difficult the distinction from focal-onset seizures. The word “absence” has a common meaning, but an “absent stare” is not synonymous with an absence seizure, since arrest of activity also occurs in other seizure types.

Further, this report clarifies the following (Fisher et al 2017a; Fisher et al 2017b):

> "Seizures with eyelid myoclonia could logically have been placed under the motor category, but since eyelid myoclonia are most significant as features of absence seizures, seizures with eyelid myoclonia were placed in the nonmotor/absence category. Seizures with eyelid myoclonia may even rarely display focal features. Similarly, myoclonic absence seizures potentially have features of both absence and motor seizures, and could have been placed in either group. However, it is recognized that awareness and responsiveness can be at least partially retained during some generalized seizures, for example, with brief absence seizures, including absence seizures with eyelid myoclonias or myoclonic seizures.

In this article and other publications, a significant number of video-EEG recordings are included to document that eyelid myoclonia is the more obvious clinical manifestation and can also occur alone without impairment of consciousness (Burneo et al 2004; Panayiotopoulos 2005; Covanis 2007; Hannawi et al 2014; Brinciotti and Matricardi 2015). In eyelid myoclonia with absences, impairment of consciousness is usually mildly impaired (absence). "The eyelid movements are very obvious and can be seen at a distance--parents often regard them as ticks" (Jeavons 1996).

Clinical manifestations

Presentation and course

Eyelid myoclonia with absences has 2 components. The initial and more prominent of these components is eyelid myoclonia. This may or may not progress to the second component, which is mild impairment of consciousness (absence). The seizure starts and ends abruptly with a duration of 3 to 5 seconds. Giannakodimos and Panayiotopoulos documented the clinical manifestations of eyelid myoclonia with absences with video-EEG studies as follows (Giannakodimos and Panayiotopoulos 1996).

Eyelid myoclonia. Eyelid myoclonia occurs mainly during the first second of the EEG discharge and consists of repetitive, often rhythmic, fast (4 to 6 Hz), small- or large-range myoclonic jerks of the eyelids. The eyelid jerks vary in force, amplitude, and numbers, even for the same patient. In each seizure, there are more than 3 repetitive eyelid jerks.{embed="pagecomponents/media_embed" entry_id="10577"}{embed="pagecomponents/media_embed" entry_id="10578"} Occasionally, there may only be a single jerk, but often there is a series of rapid eyelid tremor-like jerks.{embed="pagecomponents/media_embed" entry_id="10579"}{embed="pagecomponents/media_embed" entry_id="10580"} There typically is a concomitant tonic contraction of the eyelids, where the eyes often assume a semi-open position, irrespective of the position of the eyes at the start of seizure. Vertical jerking and upwards deviation of the eyeballs as well as simultaneous jerks of the eyebrows and the head frequently occur, as does lateral deviation of the eyes and the head. Eyelid myoclonia may also be associated with jerks of the hands.{embed="pagecomponents/media_embed" entry_id="10581"} Rarely, the tonic component of the eyelid semi-opening and the deviation of the eyes and head may be more predominant than the clonic components.

Once seen, eyelid myoclonia will not be forgotten. It is distinctly different from the random or rhythmic eyelid closing or fluttering during the course of typical absences in other epileptic syndromes (Panayiotopoulos et al 1996a; Hannawi et al 2014).

Impairment of consciousness (absence). Absence follows the eyelid myoclonia while the eyelid jerking continues less violently than in the onset. Impairment of consciousness is usually mild, manifested with cessation, repetition, errors, and delays of breath counting on video-EEG. Automatisms are not observed.{embed="pagecomponents/media_embed" entry_id="17677"}

An interesting symptom is the rare occurrence of a "pleasurable" feeling during the absence, which may be related to "self-induction" in some patients.

Headache and eyelid myoclonia. Ictal headache has been associated with eyelid myoclonia in only one report (Fanella et al 2015). This was a case of a 40-year-old woman affected by eyelid myoclonia with absences with a history of prolonged headache attacks. A video-EEG recording performed during one of these episodes showed subcontinuous epileptic activity consisting of generalized spike-and-wave discharges clinically associated with intense headache.

Precipitating factors of eyelid myoclonia with absences. The most potent precipitating factor is eye closure: voluntary, involuntary, or reflex. The majority of the seizures are induced immediately after closure of the eyes in the presence of uninterrupted light. Eye closure in total darkness is ineffective. Intermittent photic stimulation potentates the effect of eye closure and is capable of inducing seizures when eyes are open or closed. Photosensitivity declines with age, whereas eye closure is likely to remain a lifelong precipitating factor (Giannakodimos and Panayiotopoulos 1996). However, there are patients in whom eyelid myoclonia occurs only during photic stimulation.{embed="pagecomponents/media_embed" entry_id="10582"}

Eyelid myoclonia with or without absences is usually the prominent seizure type of an idiopathic photosensitive epilepsy (Jeavons syndrome), which is defined as an idiopathic epileptic syndrome manifested with frequent (pyknoleptic) seizures, consisting of eyelid myoclonia often associated with absences (Panayiotopoulos 2005; Panayiotopoulos 2010). Onset is usually in early childhood. The seizures are brief (3 to 6 seconds) and occur mainly after eye closure. They consist of eyelid myoclonia, which persists throughout the attack with or without absences. Absences without eyelid myoclonia do not occur. The eyelid myoclonia consists of marked, rhythmic, and fast jerks of the eyelids and is often associated with jerky upward deviation of the eyeballs and retropulsion of the head. There is probably an associated tonic component of the involved muscles. If the seizure is prolonged, impairment of consciousness occurs. The latter is mild or moderately severe without associated automatisms. Milder seizures of eyelid myoclonia without absences are common, particularly in adults and treated patients, and they may occur without EEG accompaniments. All patients are highly photosensitive in childhood, but this declines with age. Infrequent generalized tonic-clonic seizures, either induced by light or spontaneous, are probably inevitable in the long-term and are likely to occur after sleep deprivation, fatigue, and alcohol indulgence. Myoclonic jerks of the limbs may occur but are infrequent and random. The eyelid myoclonia of Jeavons syndrome is resistant to treatment and may be life-long. However, clinical absences may become less frequent with age.{embed="pagecomponents/media_embed" entry_id="18867"}

Prognosis and complications

Eyelid myoclonia is highly resistant to treatment, occurring many times per day, often without apparent absences, and even without demonstrable photosensitivity. Generalized tonic-clonic seizures and absence status may be unavoidable in adult life, either as the result of accumulating precipitating factors, or more often, due to inappropriate medication (Panayiotopoulos 2005; Panayiotopoulos 2010). In Jeavons syndrome, neuropsychological evaluations of patients showed that performance was below average on measures of global IQ, processing speed and rote, verbal learning coupled with average nonverbal reasoning, and sustained attention (Fournier-Goodnight et al 2015). There was also evidence of impaired higher-level verbal reasoning. Although global IQ ranged from low average to borderline impaired, no participant could be accurately described as impaired or having intellectual disability given the consistently average performance noted on some higher-order tasks, including nonverbal reasoning.

Clinical vignette

Clinical vignette 1. Typical case of Jeavons syndrome. From the age of 5, a woman experienced the onset of frequent seizures manifested with brief, but marked, eyelid myoclonia and absences with mild or moderate impairment of consciousness, and these continued into her adult life. Absences improved, but eyelid myoclonia continued daily with ethosuximide treatment. At the age of 26, an attempt by a neurologist to substitute ethosuximide with carbamazepine resulted in nonconvulsive status epilepticus. With continuous eyelid myoclonia and absences, she became confused: “My eyes were continuously jerking. I was unable to look after myself, and was drowsy and off work for a few days.”{embed="pagecomponents/media_embed" entry_id="10577"}

She suffered a total of 6 generalized tonic-clonic seizures throughout her life, starting at the age of 13 years. Two generalized tonic-clonic seizures were induced by lights, and the others occurred after sleep deprivation, alcohol indulgence, or inappropriate change of medication. Eyelid myoclonia and generalized tonic-clonic seizures occurred mainly in the morning after awakening. Seizures improved dramatically when valproate was added to ethosuximide at the age of 31 years, but she continued to have brief seizures of eyelid myoclonia without absences or generalized tonic-clonic seizures. Ethosuximide was later replaced by clonazepam 0.5 mg nocte, which controlled the eyelid myoclonia. At 39 years of age, she had been seizure free for 4 years on clonazepam 0.5 mg and valproate 2000 mg daily.

Over the years, she was frequently questioned regarding self-induction, which she thoroughly denied. “Why?” she

said. “It gives me no pleasure, and it is socially embarrassing.” Similar clinical and EEG seizures also occurred while the eyes were closed. Furthermore, it is unlikely that self-induction would be attempted in social situations, such as at her wedding.

Clinical vignette 2. Difficulty differentiating genuine seizures of eyelid myoclonia from self-induced eyelid myoclonia. A 10-year-old girl had onset of frequent daily seizures from 4 years of age. The seizure duration averaged 3 to 5 seconds. Seizures consisted of marked eyelid myoclonia and tonic upward deviation of the eyes accompanied by, at most, a mild impairment of consciousness. In more severe attacks, there was a retropulsive jerk of the head, shoulders, and sometimes limbs. These would occasionally lead to falls. The vast majority of the seizures were light-induced, with sudden increases in background illumination, especially when going into bright sunlight. Watching television and playing video games were less powerful stimuli. Occasional independent myoclonic jerks of her limbs were described. Typical absences unaccompanied by eyelid phenomena did not occur. She did not have generalized tonic-clonic seizures. The girl was suspected of self-induced seizures.

At follow-up at the age of 20 years, she was on valproate 800 mg bd, lamotrigine 50 mg bd, and clonazepam 0.5 mg bd. Her EEG showed only mild photoparoxysmal responses. There was no evidence of self-induction.

Clinical vignette 3. Jeavons syndrome (eyelid myoclonia with absences). A 17-year-old woman started having eyelid myoclonia and myoclonic jerks at around the age of 9 to 11 years. Myoclonic jerks affected her hands or head, together or independently, and occurred at any time of the day, but particularly when she was tired or under stress. Eyelid myoclonia with brief mild absence was more frequent. This often occurred alone without other jerks of the hands. Her first generalized tonic-clonic seizure occurred at the age of 17 years. Although highly photosensitive on video-EEG, she did not give a clinical history of photosensitivity. She had also suffered from a few episodes of eyelid myoclonia status epilepticus. Furthermore, on a few occasions, she had visual symptoms prior to or during eyelid myoclonia and jerks (vision became blurred, visual fields restricted, and visual hallucinations of various colors in front of her eyes). She was resistant to appropriate medication.{embed="pagecomponents/media_embed" entry_id="10581"}

Clinical vignette 4. Self-induced photosensitive epilepsy imitating eyelid myoclonia. A normal 22-year-old woman had onset of eyelid myoclonia with absences–like eyelid blinking from the age of 10 to 11 years. She was strongly and compulsively attracted to the sun and fluorescent lights, in front of which she performed fast repetitive eye opening and closing. This was followed by axial and limb jerks, and on 3 occasions, generalized tonic-clonic seizures. She liked it and explained that it relieved tension: “I do not do it on purpose, but I do not exactly avoid it...I do not actually deliberately go out to find some bright light, but if I find it I am happy...I would like to stop doing it, but it is a funny nice feeling. I cannot say it is nice, it is a relief...In a way, it is a play between me and the sun...It is a mixture of feelings. On the one hand, I do not want to do it, but on the other hand it is releasing something...No, it is not sexual. I know it is strange...”{embed="pagecomponents/media_embed" entry_id="10582"}

Biological basis

Localization

Eyelid myoclonia with absences is a generalized epileptic seizure with generalized multiple spike-and-slow wave discharges that may be of higher amplitude in the anterior or posterior regions.

Pathophysiology

The underlying pathogenesis is not known. Eyelid myoclonia with absences mainly manifests with regional eyelid myoclonia. As opposed to other photosensitive epilepsies, eye closure is more potent than photic stimulation as a triggering factor. However, eye closure requires the presence of light, and is entirely ineffective in darkness (Giannakodimos and Panayiotopoulos 1996; Panayiotopoulos 1998; Panayiotopoulos 2010), which may explain why continuous light also triggers seizures in these patients. Another intriguing feature is that some patients may manifest with features of photosensitivity and fixation-off sensitivity, which have opposing characteristics (Panayiotopoulos 1998; Panayiotopoulos 2010; Koutroumanidis et al 2009). It is possible that in patients with eyelid myoclonia with absences, there is a malfunctioning of alpha rhythm generators (Panayiotopoulos et al 1996b) and that both the magnocellular and parvocellular systems are functionally disturbed (Wilkins 1999).

Liu and colleagues studied the ictal and interictal epileptic activity in 4 patients with eyelid myoclonia with absences

using EEG-fMRI (Liu et al 2008). The main regions of activation included thalamus, mesial frontal cortex, middle parietal lobe, temporal lobe, insula, midline structures, and cerebellum. Deactivations were mainly in the anterior frontal lobe, posterior parietal lobe, and posterior cingulate gyrus. Thalamic blood oxygenation level-dependent (BOLD) change was predominantly activation in most of the cases. The distribution of activation associated with ictal epileptic discharges was wider, and the distribution of deactivation was closer to pericortex compared with the BOLD change linked with interictal epileptic discharges.

Vaudano and associates investigated the functional and structural brain correlates of eyelid myoclonus and absence seizures triggered by eye closure (Vaudano et al 2014). Fifteen patients with eyelid myoclonia with absences, 14 patients with idiopathic generalized epilepsies without eyelid myoclonus, and 16 healthy controls underwent an EEG-correlated fMRI and voxel brain morphometry (VBM) protocol. The functional study consisted of 30-second epochs of eyes-open and eyes-closed conditions. The following EEG events were marked, and the relative fMRI maps obtained: (1) eye closure times, (2) spontaneous blinking, and (3) spontaneous and eye closure-triggered spike and wave discharges. Within-group and between-groups comparisons were performed for fMRI and VBM data as appropriate. It was found that eyelid myoclonia with absences compared to the other 2 groups had: (1) higher blood oxygenation level-dependent (BOLD) signal related to the eye closure over the visual cortex, the posterior thalamus, and the network implicated in the motor control of eye closure, saccades, and eye pursuit movements; and (2) increments in the gray matter concentration at the visual cortex and thalamic pulvinar, whereas decrements were observed at the bilateral frontal eye field area. No BOLD differences were detected when comparing the spike-wave discharges in eyelid myoclonia with absences and idiopathic generalized epilepsy. Thus, these results demonstrated altered anatomo-functional properties of the visual system in eyelid myoclonia with absences. These abnormalities involve a circuit encompassing the occipital cortex and the cortical/subcortical systems physiologically involved in the motor control of eye closure and eye movements (Vaudano et al 2014). These findings are consistent with a study of the possible contribution of the brainstem structures in the pathophysiology of eyelid myoclonus (Altiokka-Uzun et al 2017). Brainstem excitabilities were examined by blink reflex studies. There were no statistical differences between patients with eyelid myoclonia, healthy subjects, and patients with juvenile myoclonic epilepsy.

In a report, Rudolf and colleagues performed whole-exome sequencing in a family with eyelid myoclonia with absences (Rudolf et al 2016). They found a nonsense variant (c.196C>T/p.(Arg66*)) in the retinoid-related nuclear receptor (RORB), which encodes the beta retinoid-related orphan nuclear receptor (RORbeta), in 4 affected family members. In addition, 2 de novo variants (c.218T>C/p.(Leu73Pro)); c.1249_1251delACG/p.(Thr417del)) were identified in sporadic patients by trio-based exome sequencing. They also found 2 de novo deletions in patients with behavioral and cognitive impairment and epilepsy: a 52-kb microdeletion involving exons 5 to 10 of RORB and a larger 9q21 microdeletion. Furthermore, they identified a patient with intellectual disability and a balanced translocation where one breakpoint truncates RORB and refined the phenotype of a reported patient with RORB deletion. The data support the role of RORB gene variants/copy number variations in neurodevelopmental disorders, including epilepsy, and especially in generalized epilepsies with predominant absence seizures.

Eyelid myoclonia (the seizure) may occur in various conditions. Those supporting eyelid myoclonia with absences as a syndrome (Jeavons syndrome) argue that this is a genetically determined homogeneous condition that may be different from most other idiopathic generalized epilepsy syndromes (Bianchi and Italian League Against Epilepsy 1995; Duncan and Panayiotopoulos 1996; Parker et al 1996; Panayiotopoulos 2005; Panayiotopoulos 2010; Caraballo et al 2009; Striano et al 2009; Sadleir et al 2012; Nar Senol et al 2015). In a large-scale genetic study of idiopathic generalized epilepsies, Bianchi and colleagues reported concordance of the syndrome in families of probands with eyelid myoclonia with absences (Bianchi and Italian League Against Epilepsy 1995). Parker and colleagues reported that of 18 patients with eyelid myoclonia with absences, 14 had a family history of epilepsies (Parker et al 1996). Four patients had other family members affected by a similar type of epileptic condition. Eyelid myoclonia with absences in monozygotic twins has been reported (Adachi et al 2005), and, rarely, benign myoclonic epilepsy of infancy (Moutaouakil et al 2010) or cryptogenic myoclonic epilepsy of early childhood (Ohya et al 2012) may evolve to eyelid myoclonia with absences.

In a study by Sadleir and colleagues, individuals with eyelid myoclonia with absences were ascertained by referral and through the investigators' clinical practices (Sadleir et al 2012). All available family members were assessed for seizures using a validated seizure questionnaire. Electroclinical data were obtained on each proband and all affected family members' pedigrees were constructed. Families were analyzed for phenotypic patterns. Eighteen individuals with eyelid myoclonia with absences were recruited. A history of seizures was found in 34 relatives in 15 (83%) of 18

families. In terms of epilepsy syndromes, 9 relatives from 7 of 15 families had febrile seizures. Two relatives had eyelid myoclonia with absences. Classical genetic generalized epilepsy (idiopathic generalized epilepsy) syndromes were seen in 5 relatives: 2 generalized tonic-clonic seizures alone, 2 childhood absence epilepsy, and 1 juvenile myoclonic epilepsy. Genetic epilepsy with febrile seizures plus (GEFS+) phenotypes occurred in 16 relatives. On review of the epilepsy syndromes within each family, 7 families had a pattern consistent with GEFS+, whereas 3 families had classical idiopathic generalized epilepsy. The authors concluded that the clinical genetics of eyelid myoclonia is suggestive of complex inheritance with shared genetic determinants overlapping with both classical idiopathic generalized epilepsy and GEFS+. The epilepsy syndromes in relatives of probands with eyelid myoclonia with absences differ from those found in families of probands with childhood absence epilepsy, supporting the concept that patients with eyelid myoclonia with absences have a syndrome that is distinct from childhood absence epilepsy. This presumably reflects different genetic components contributing to their genetic architecture (Sadleir et al 2012). Jeavons syndrome also appears to be homogeneous in people of different race and ethnicity (Yang et al 2012).

The EEG ictal accompaniments of eyelid myoclonia with absences are generalized discharges of mainly polyspikes and polyspike-slow waves at a frequency of 3 to 6 Hz (usually more than 4 Hz) and a duration of 3 to 6 seconds (typically around 3 seconds and seldom more than 5 seconds).{embed="pagecomponents/media_embed" entry_id="10577"}{embed="pagecomponents/media_embed" entry_id="10578"}{embed="pagecomponents/media_embed" entry_id="10579"}{embed="pagecomponents/media_embed" entry_id="10580"} Polyspikes are more abundant and are often continuous (uninterrupted by slow waves) in the first 1 to 2 seconds from onset. Polyspike-and-slow waves usually follow this multiple-spike opening phase of the discharge. The onset of the EEG discharge either precedes the eyelid jerks or is simultaneous to them (Giannakodimos and Panayiotopoulos 1996). However, on some occasions, fast eyelid movements (with eyes closed) following eye closure may precede the discharge.{embed="pagecomponents/media_embed" entry_id="10583"}{embed="pagecomponents/media_embed" entry_id="10584"}

Epidemiology"

The prevalence of Jeavons syndrome is around 3% among adult patients with epileptic disorders and 13% among those with idiopathic generalized epilepsies with absences (Giannakodimos and Panayiotopoulos 1996). There is a 2-fold preponderance of girls.

Differential diagnosis

Seizure phenomenology

Eyelid myoclonia is often misdiagnosed as facial tics, sometimes for many years even though the characteristic eyelid myoclonia, if seen once, will never be forgotten or confused with other conditions (Panayiotopoulos 2005; Panayiotopoulos 2010; Burneo et al 2004; Hannawi et al 2014). The seizures can be easily captured in mobile phones as demonstrated in parental videos seen on YouTube|WebSite:YouTube}{WebURL:https://www.youtube.com/watch?v=5ljj2P2MgiA}|YouTube.

The EEG ictal manifestations consist mainly of generalized polyspike-waves at 3 to 6 Hz, which are more likely to occur after eye closure in an illuminated room. Total darkness abolishes the abnormalities related to eye closure. PPR are recorded from all untreated young patients.

However, eyelid myoclonia may also occur in idiopathic generalized epilepsies with absences other than Jeavons syndromes as well as structural/metabolic epilepsies with absences, including Dravet syndrome, ring chromosome 20 syndrome, l-2 hydroxyglutaric aciduria, and SYNGAP1-associated intellectual disability and epilepsy (Duncan and Panayiotopoulos 1996; Mete et al 2012; Tsuda et al 2013; Nar Senol et al 2015; Mignot et al 2016; Vignoli et al 2016). Overlapping cases with juvenile myoclonic epilepsy have been reported (Yalcin et al 2006). Nonepileptic paroxysmal eyelid movements consisting of eyelid closure, upturning of the eyes, and rapid eyelid flutter have been described in patients with generalized photosensitive epilepsy and eyelid myoclonia (Camfield et al 2004; Brinciotti and Matricardi 2015).

In a retrospective study, Capovilla and colleagues described 18 patients with eyelid myoclonia who also had impairment of intellectual functions and EEG of fast generalized polyspikes/polyspikes and waves (Capovilla et al

2009). All patients were photosensitive, highly pharmacoresistent, and had generalized tonic-clonic seizures that were mostly nocturnal.

Symptomatic or cryptogenic epilepsies. In symptomatic or cryptogenic epilepsies, eyelid myoclonia with absences may be a predominant seizure type with or without photosensitivity. Diagnostic confusion between patients with symptomatic or cryptogenic epilepsies who exhibit ictal eyelid myoclonia, and those suffering from eyelid myoclonia with absences, will rarely be a problem if the clinical background is considered in detail. Mental retardation, neurologic signs, and severely abnormal background EEG as found in patients with symptomatic or cryptogenic epilepsies are incompatible with an idiopathic syndrome such as eyelid myoclonia with absences. Focal EEG abnormalities are common in eyelid myoclonia with absences, but when severe or persistent, they are likely to indicate an underlying structural abnormality. Seizures in this syndrome are brief and stereotyped; occasional independent myoclonic jerks of the limbs or body and GTCS are the only other seizure types that occur (Giannakodimos and Panayiotopoulos 1996). In cryptogenic or symptomatic cases, eyelid myoclonia may be an inconstant ictal feature and may be associated with seizures both of variable duration and of different types, such as atypical absences and tonic, atonic, or partial seizures. Activation of seizures by eye closure in symptomatic or cryptogenic cases may be rarer than eyelid myoclonia with absences (Ferrie et al 1994; Ferrie et al 1996).

Idiopathic generalized epilepsies with absences. In idiopathic generalized epilepsies with absences, eyelid myoclonia should be differentiated from other eyelid manifestations that may occur during the absence. In particular, Panayiotopoulos and colleagues studied 90 patients with idiopathic generalized epilepsy, along with 536 video-EEG recordings of typical absences (greater than 2.5 to 3 Hz spike- or polyspike-and-slow waves with clinical manifestations) (Panayiotopoulos et al 1996a). All patients had typical absences either alone, with myoclonic jerks, GTCS, or both. Syndromes included: childhood absence epilepsy, juvenile absence epilepsy, myoclonic absence epilepsy, perioral myoclonia with absences, phantom absences with GTCS, absences with single myoclonic jerks, and other unclassified syndromes of idiopathic generalized epilepsy with typical absences (Panayiotopoulos 2005). Thirty-nine (43.3%) of the 90 patients had eyelid or eye-related ictal clinical manifestations.

Only the most prominent eyelid manifestations were considered. They were classified as consistent if they occurred in every absence of the same patient. An inconsistent classification was given if they were present in some but not all of the absences. Symptoms often overlapped in the same patient and even for the same seizure. It was found that:

(1) Eyelid myoclonia consistently occurred in 5 patients.

(2) Eyelid fluttering consistently occurred in 4 patients and was inconsistent in another 4 patients.

(3) Random or repetitive eyelid blinks, similar to spontaneous normal eyelid blinking, consistently occurred in 6 patients. Another 14 had inconsistent eyelid blinking during the absence ictus.

(4) Predominantly rhythmic and vertical eyebrow oscillations were observed in 5 patients.

(5) One patient had vertical nystagmus.

Thus, 39 out of the 90 patients had ictal manifestations from the eyelids and eyes, but in only 5 of them (5.6%) were the ictal manifestations similar to those occurring in the syndrome of eyelid myoclonia with absences.{embed="pagecomponents/media_embed" entry_id="10585"} Only 1 of those 5 patients was photosensitive, and only 1 experienced absences provoked by eye closure.

Conversely, 20 patients (22.2%) had clinical or video-EEG-documented photosensitivity, but only 5 of them had eyelid and eye-related ictal clinical manifestations during the absences. Two patients had random eyelid blinking, which is strikingly different from the eyelid myoclonia. Two patients had fast rhythmic eyelid fluttering. One patient had eyelid myoclonia with absences–like manifestations.

Eye closures and eyelid myoclonia–like attempts for self-induction in photosensitive epilepsy. Eyelid myoclonia with absences, often occurring after eye closure in the presence of light and often exaggerated by intermittent photic stimulation, should not be considered as a self-induced maneuver (Panayiotopoulos et al 1996b). The EEG ictal discharge precedes or coincides with the eyelid myoclonia. These patients do not need to produce conditions of intermittent photic stimulation for self-induction. Simply closing the eyes would be more potent.

However, self-induced photosensitive epilepsy is well known and well documented. These patients need to produce

intermittent photic stimulation in order to deliberately self-induce seizures (Binnie 1996; Panayiotopoulos et al 1996b; Panayiotopoulos 2010). They do this by using various maneuvers such as waving their hands in front of their eyes or with repetitive eye closures while looking at the sun or a bright light source. The latter may sometimes imitate eyelid myoclonia.

Clinical vignette 2 describes the difficulty in differentiating genuine seizures of eyelid myoclonia from self-induced eyelid myoclonia (Parker et al 1996). One of the patient's habitual daily seizures was captured on video-EEG. On slow motion study, closing of the eyes was followed within half a second by 3 fast eyelid movements while the eyes remained closed. Opening of the eyes coincided with the first spike of the generalized discharge. During some of the seizures, there was also myoclonic jerking of limbs.

The opening and closing of the eyes is an ictal event as it starts together with the spike and wave. It is important to note the manifestations of the first half second without EEG abnormalities. Similar clinical events also occurred during intermittent photic stimulation immediately preceding the generalized discharges when closing the eyes on command.{embed="pagecomponents/media_embed" entry_id="10584"} It seems that these are also ictal events induced by eye closure and light. However, one cannot completely deny the possibility of a light-dependent tick that may generate a seizure (Kent et al 1998). Certainly, these are not deliberate attempts for self-induction.

In view of reports implicating slow eye closure in self-induction (Darby et al 1980; Binnie 1996), Panayiotopoulos and colleagues extensively interviewed and studied video-EEG of 17 adult patients with eyelid myoclonia with absences (Panayiotopoulos et al 1996b). None of 15 patients admitted were suspected of self-induced seizures. On the contrary, they considered eyelid myoclonia as a socially embarrassing condition. They were relieved when the seizures improved with medication, and they showed excellent compliance. Although other types of seizures were controlled in most patients, the eyelid myoclonia continued, but was less severe and frequent than before appropriate treatment began. This is contrary to self-induction, in which eyelid myoclonia should be more forceful after treatment if its purpose was to induce seizures. Furthermore, the authors considered it unlikely that self-induction would be attempted in social situations, such as the patients' weddings. “The eyes flicker is a reflex to the light,” explained one of their patients. "I will be looking over there, and the sunshine will be coming through on that side. And my head, without me even knowing, it automatically turns. You cannot stop it. And it goes like this, and your head has an automatic reaction to go back to the sunlight and start flickering the eyes, and you try to pull yourself away..." This description may be arbitrarily taken as indirect evidence of self-induction despite strong denial as such by the patients. However, this is similar to the well-known phenomenon of the “attraction movement” when light is presented and other manifestations of the optic fixation reflexes when volitional movements of the eyes are unattainable or weak (Walsh 1957).

Two patients were suspected of self-induction. One of them had frequent slow eye-closure EEG abnormalities, but she never admitted self-induction. She insisted “I do not know when I am doing it…It gives me no pleasure, and it is a social embarrassment.” The other patient admitted in a video recorded interview that she occasionally does it voluntarily: "Yes, I can do it on purpose like that (she imitates rapid eyelid blinking with upwards deviation of the eyes). But that is because there are times that my eyes start to want to go and do it, and I know they want to do it because they are strained and sore and they will sting, and so if I just do it, it relaxes them...that is a rare occasion. But other than that, I do not know. It just goes on. There have been incidences I have walked into a pole, or into a car. I did not do that on purpose."{embed="pagecomponents/media_embed" entry_id="10582"}

Kent and colleagues reported that 5 of the 6 patients with eyelid myoclonia with absences demonstrated various compulsive or tic-like symptoms, including premonitory sensations, compulsive urges, and a sense of relief associated with the absence attacks. Separate facial tics not associated with absences were also evident in at least 2 children. They stressed that "the argument that self-induction does not occur in eyelid myoclonia with absences assumes its deliberate nature, which may not necessarily be the case for a proportion of these children. Compulsive “self-induction” may be similar to the phenomenology described in Tourette syndrome, where individuals experience motor and vocal tics and obsessive compulsive symptoms. The relationship between this argument and EEG findings in eyelid myoclonia with absences would presume that the initial eyeball roll or eye closure and eye blinking (seen in Tourette syndrome) are tic-like symptoms, which cause the absences and discharges of eyelid myoclonia with absences in those who are photosensitive. In this model, the self-induction of discharges in an individual may or may not be deliberate, or might even go unnoticed by the patient. The beneficial response of some so-called “self-inducers” to the proconvulsive dopamine antagonists (commonly prescribed for Tourette syndrome) lends further support to this argument" (Kent et al 1998).

Forced eyelid closures and eyelid fluttering in occipital seizures. Forced eyelid closure and eyelid blinking is also an ictal clinical symptom in partial seizures described both in symptomatic and idiopathic occipital epilepsy. It may be an early ictal sign and has a forced quality that may be distinguished from the more casual blinking associated with many other partial seizures. It usually occurs after the phase of visual hallucinations, at a stage in which consciousness is impaired, and heralds the impending secondarily generalized convulsions. However, it may also occur alone, inconspicuous in appearance and not suspected as a seizure event, documented only with video-EEG recordings in occipital photosensitive patients (Panayiotopoulos 2010).

Paroxysmal eyelid movements are a confusing feature of generalized photosensitive epilepsy. Camfield and colleagues reported persistent, frequent, nonepileptic paroxysmal eyelid movements in 19 children and adults with well controlled generalized photosensitive epilepsy (Camfield et al 2004). Seventeen patients were female and 2 male. In 2 children, paroxysmal eyelid movements began 2 to 4 years before their epilepsy was noted. In the remainder, it was noted when epilepsy was first diagnosed. Age at last follow-up was 8 to 38 years (average 21 years) with an average follow-up of 9 years. All patients showed photosensitive generalized spike-wave discharges on EEG. Paroxysmal eyelid movements were a source of diagnostic confusion, but direct examination and video during EEG recording distinguished the attacks from absence seizures. In all cases, epileptic seizures were completely or nearly completely controlled with AEDs, but the paroxysmal eyelid movements did not resolve with age. In 12 cases, there was a family history of the eyelid disorder without epilepsy. Similarly, Brinciotti and Matricardi studied 26 patients with epilepsy who presented with paroxysmal eyelid movements (Brinciotti and Matricardi 2015). The epilepsy was idiopathic generalized (8 cases), idiopathic focal (6 cases), symptomatic focal (5 cases), and reflex epilepsy (7 cases). Paroxysmal eyelid movements and blinking were analyzed by video-EEG recordings at rest and during intermittent photic stimulation, pattern stimulation, and TV watching. Blink rate was evaluated during 3 different conditions: at rest, during a TV-viewing period, and at the occurrence of paroxysmal eyelid movements. The paroxysmal eyelid movements ranged from 8 to 12.5 Hz and were accompanied by a significant increase in blinking compared to the rest condition and TV watching. Photoparoxysmal EEG responses were found in 25 cases and were associated with pattern sensitivity in 22; only one patient was sensitive to pattern, but not photic, stimulation. Visually induced seizures were recorded in 20 cases, triggered by both stimuli (photic and pattern stimulation) in 11 patients; seizures were triggered by pattern stimulation (but not photic stimulation) in 5 patients, photic stimulation (but not pattern stimulation) in 3 patients, and TV watching (but not photic or pattern stimulation) in one patient. Epileptic eyelid myoclonia was noted in 17 patients. The authors concluded that the coexistence of paroxysmal eyelid movements, photoparoxysmal EEG responses, increased blinking, and epileptic eyelid myoclonia suggests an underlying dysfunction involving cortical-subcortical neural networks according to the recent concept of system epilepsies.

Eyelid manifestations in normal people. With the possible exception of the violent myoclonic jerks of eyelid myoclonia, all other eyelid symptoms during absence seizures are manifested by normal people in their everyday life. The eyes and the eyelids are the most sensitive and expressive parts of our body. There is considerable literature on the subject and its neuropathy (Hall 1945; Bour et al 2000).

From a small sample of people appearing in televised interviews, round table discussions, and debates, Panayiotopoulos and colleagues reached the following conclusions (Panayiotopoulos et al 1996a):

> (1) When under tension, the rate of the spontaneous blinks increases significantly. In some people this may become repetitive in clusters of 3 to 5 per second, showing close similarities to that described in self-induced photosensitive epilepsy. This type of repetitive blinking was apparent either at the beginning of the utterance (like a breath before starting a sentence) or at the end (like a relief). It was particularly apparent when talking on sensitive matters and was not observed when the same people were not participating in the discussion. These eyelid manifestations are like tics. Other normal subjects may close their eyelids partially, with brief transient fluttering.
>
> (2) Slow and sustained eye closure was rarely manifested. It was observed mainly in women who were discussing their distress, anger, or frustrations.
>
> (3) Less frequently, eyes were widely opened with a cessation of spontaneous blinks.

What the eyelids do could not be simpler: they open and close. However, this limited repertoire belies the complexity of the behavioral requirements of the eyelids. They must protect the eyes and especially the cornea…or an efficient compromise between and unobstructed vision the eyelids must change position in synchrony with vertical eye

movements...Eyelid position is modulated by autonomic functions regulating, for example, arousal...They are intimately concerned with facial expression...Thus, we have a simple movement that is under voluntary, automatic, reflex, emotional, and autonomic control (Plant 1996).

da Conceicao and colleagues analyzed the characteristics of blinking and eye closure in 20 patients with eyelid myoclonia by video-EEG (da Conceicao et al 2015). In 18 patients, eyelid myoclonia occurred spontaneously while awake, 10 on eye closure, and only 1 during intermittent photic stimulation. Eyelid myoclonia assumed the form of flicker, flutter, or jerk and is accompanied by generalized discharges, spiky posterior alpha, theta rhythm, or absence of any EEG abnormality. Analysis of the characteristics of blinking had no statistical differences between patients and healthy subjects. The rate of blinks and eyelid myoclonia increased during speech and decreased during reading. Eyelid myoclonia never occurred during blinking or in the dark (da Conceicao et al 2015).

Underlying disorders

Eyelid myoclonia with absences is usually the prominent seizure type of an idiopathic generalized epilepsy condition that has not been accepted in the ILAE's current designation of a syndrome (Engel 2001; Berg et al 2010; Commission on Classification and Terminology of the International League Against Epilepsy 2017). However, it may also occur in symptomatic or cryptogenic epilepsies as a predominant seizure type, with or without photosensitivity. Eyelid myoclonia may also occur in other idiopathic generalized epilepsies with absences.

Eyelid and other ictal manifestations may cluster together in idiopathic photosensitive epilepsy (Jeavons syndrome). The following conclusions are based on long video-EEG studies and extensive reviews of 17 adults and 3 children with eyelid myoclonia with absences (Ferrie et al 1996; Giannakodimos and Panayiotopoulos 1996; Panayiotopoulos et al 1996a, 1996b; Parker et al 1996; Panayiotopoulos 2005; Panayiotopoulos 2010):

(1) Eyelid myoclonia with absences is the most typical type of seizures with this syndrome.

(2) Eyelid myoclonia is often associated with jerks of the eyeballs, head, or other muscles, and may terminate without discernible absence. This is the most common type of seizure in this syndrome. This may be the only seizure type for treated patients. These seizures are brief, usually lasting for 1 to 2 seconds. The ictal EEG manifestations are mainly polyspike discharges of brief duration (1 to 2 seconds, or rarely 3 to 5 seconds).

(3) Milder ictal eyelid manifestations consist of either abortive eyelid myoclonia with eyelid tremor-like jerks or fast eyelid fluttering. The eyes remain closed while the upper eyelids exhibit small range, fast fluttering that would be difficult to appreciate without close-up video-EEG recordings. They are brief seizures, usually lasting for less than 1 second or, sometimes, 1 to 3 seconds. These may be seen together with the more severe types of eyelid myoclonia with or without absences. However, they can also be the only type of seizures, particularly in patients on the appropriate medication. They are associated with polyspikes in the ictal EEG.

Slow eye closure may occur, but the EEG discharges of mainly polyspikes are usually apparent before the termination of the eye-closure artifact, indicating that the tonic component of the eye closure was an ictal phenomenon. We have never observed the repetitive eye blink-like movements of self-induced photosensitive epilepsy in ictal absences of eyelid myoclonia with absences. Absences never occurred without some form of eyelid myoclonia preceding their onset.

(4) Absence status epilepticus with eyelid myoclonia. Continuous clusters of prolonged seizures of eyelid myoclonia with absences may occur as the result of accumulating precipitating factors, discontinuation, or inappropriate treatment. It is more likely to occur on awakening. (Smith 1996; Agathonikou et al 1998; Wakamoto et al 1999; Baykan et al 2002; Panayiotopoulos 2005; Panayiotopoulos 2010; Koutroumanidis et al 2010).

Eyelid ictal manifestations in typical absence seizures of other idiopathic generalized epilepsies. Eyelid myoclonia can only rarely be seen in typical absence seizures of idiopathic generalized epilepsies other than Jeavons syndrome. In a study of 60 such patients with video-EEG recorded absence seizures, only 5 had eyelid myoclonia. Of these 5 patients, only 1 was also photosensitive, and only 1 experienced seizures precipitated by eye closure (Panayiotopoulos et al 1996a).

Some patients may have eyelid myoclonia with absences without photosensitivity.{embed="pagecomponents/media_embed" entry_id="10585"} Also rarely, eyelid myoclonia with or without absences may occur in the same child, along with typical absence seizures without eyelid myoclonia (Ferrie et al 1996).{embed="pagecomponents/media_embed" entry_id="10586"}

Eyelid myoclonia with absences in cryptogenic or symptomatic generalized epilepsies. Eyelid phenomena are commonly seen during nonconvulsive seizures in children with cryptogenic and symptomatic generalized epilepsies. These include eyelid blinking and flutter. True eyelid myoclonia is less common (Ferrie et al 1996; Panayiotopoulos 1998).

Diagnostic workup

The video-EEG is the single most important procedure for diagnosis of eyelid myoclonia with absences. The EEG is dominated with high amplitude discharges of spike-and-slow waves at 3 to 6 Hz. These are brief (1 to 5 seconds) and are commonly associated with clinical manifestations of eyelid myoclonia of varying severity. They occasionally appear simultaneous with any impairment of cognition. They often occur immediately (within 0.5 to 2 seconds) after closing the eyes in an illuminated recording room. They are eliminated in total darkness. Photoparoxysmal responses are recorded from all untreated young patients and may be absent in older patients on medication. Photosensitivity and fixation-off sensitivity may occur together (Panayiotopoulos 1998). A normal EEG is rare, even in well-controlled patients. EEG discharges are also enhanced by hyperventilation.

A study emphasized a high incidence of (1) focal interictal epileptiform discharges from the posterior head region, and (2) predominant focal posterior ictal epileptiform discharges preceding generalized epileptiform discharges (Viravan et al 2011). Focal frontal spikes may sometimes precede the generalized discharges (Takahashi et al 2015). According to a report from China, there is a predominantly male group with frontal predominant epileptiform discharges, eyelid myoclonia, and eyes rolling up and a predominantly female group with occipital predominant epileptiform discharges with eyelid myoclonia alone (Wang et al 2014).

Sleep EEG patterns are normal. Generalized discharges of polyspikes-and-slow waves are more likely to increase during sleep, but a reduction is occasionally observed. The discharges are shorter and devoid of discernible clinical manifestations of any type, even in those patients who have numerous seizures during the alert state.

EEG and clinical manifestations deteriorate consistently after awakening.

Management

Lifelong treatment with medication may be necessary for patients with eyelid myoclonia with absences. In the absence of controlled therapeutic trials, it is not possible to draw scientifically valued conclusions about the most effective approach to the drug treatment of eyelid myoclonia with absences.

Based on anecdotal evidence, the drugs of choice are those also used for other idiopathic generalized epilepsies with absences and myoclonias (Panayiotopoulos 2005; Panayiotopoulos 2010). Historically, a combination of sodium valproate and ethosuximide has been considered to be the most effective regimen. However, clonazepam, which is highly effective in myoclonic jerks, may be a valid option. Small doses of lamotrigine added to sodium valproate may result in dramatic improvement because of their possible pharmacodynamic interaction (Ferrie et al 1995). Lamotrigine alone may exaggerate myoclonic jerks.

Levetiracetam may be effective because of its anti-myoclonic and anti-photosensitive properties (Panayiotopoulos 2010; Striano et al 2008). In a multicenter open-label trial of levetiracetam in Italy, 35 patients with a mean age of 19 ± 6 years were recruited (Striano et al 2008; Parissis et al 2014). Twenty-seven had previously undergone 1 to 5 adequate trials of antiepileptic drugs. Levetiracetam was administrated at a starting dose of 10 mg/kg/day up to 50 to 60 mg/kg/day in 2 doses. The treatment period included a 5- to 6-week up-titration phase and a 12-week evaluation phase. The number of days with eyelid myoclonia (ie, days with seizures) and number of generalized tonic-clonic seizures were evaluated. Prior to levetiracetam, the median number of days with seizures per month was 12 ± 8.2. Twenty-one patients experienced generalized tonic-clonic seizures (median number per month: 1 ± 0.2). Thirty-four subjects completed the trial. Levetiracetam was well tolerated (mean dose: 1985 mg/day). Responders were 28 of 35 patients (80%), 9 taking levetiracetam as monotherapy. Six patients were seizure free, 15 had 75% or greater seizure reduction, and 7 had over 50% seizure reduction. Generalized tonic-clonic seizures remitted in 14 of 21 patients

(66.6%). The number per month of days with seizures (median: 12 vs. 5; p = 0.0001) and generalized tonic-clonic seizures (median: 1 vs. 0; p = 0.0001) decreased compared to baseline period. Disappearance or clear reduction in paroxysmal abnormalities at eye closure occurred in 20 of the responders and photoparoxysmal response in 19. Mean follow-up was 23.9 ± 18.5 months.

Carbamazepine, oxcarbazepine (Menon et al 2011), gabapentin, phenytoin, pregabalin, tiagabine, and vigabatrin are contraindicated (Panayiotopoulos 2005; Panayiotopoulos 2010).

Nonpharmacological treatments used for photosensitive patients should be employed in Jeavons syndrome when photosensitivity persists (Wilkins et al 1999; Covanis et al 2004). Wearing special tinted glasses (Wilkins et al 1999; Covanis et al 2004) or the commercially available blue Z1 lenses may be beneficial (Capovilla et al 2006). Self-induced seizures might be modifiable by psychiatric intervention or behavioral modification.

Outcomes

Appropriate treatment usually results in significant reduction of seizures and prevention of eyelid myoclonia status epilepticus, as well as generalized tonic clonic seizures.

Special considerations

Pregnancy

For women at childbearing age, see pregnancy and epilepsy.

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**References especially recommended by the author or editor for general reading.

ICD and OMIM codes

ICD codes

ICD-9:
Generalized nonconvulsive epilepsy: 345.0
Petit mal status: 345.2

ICD-10:
Generalized idiopathic epilepsy and epileptic syndromes: G40.3
Petit mal status epilepticus: G41.1

Profile

Age range of presentation

02-05 years
06-12 years
13-18 years

Sex preponderance

female>male

Family history

Family history may be obtained

Heredity

Heredity may be a factor

Differential diagnosis list

facial tics
symptomatic generalized epilepsy
idiopathic generalized epilepsy with absences
Dravet syndrome
l-2 hydroxyglutaric aciduria

juvenile myoclonic epilepsy
generalized photosensitive epilepsy
cryptogenic generalized epilepsy
atypical absences
tonic seizures
atonic seizures
partial seizures
random eyelid blinking
self-induced photosensitive epilepsy
self-induced eyelid myoclonia
attraction movement
tics
obsessive-compulsive symptoms
forced eyelid closures
eyelid fluttering
symptomatic occipital epilepsy
idiopathic occipital epilepsy

Other topics to consider

Absence status epilepticus
Childhood absence epilepsy
Epilepsy
Levetiracetam
Myoclonic absences
Typical absences
Visual-sensitive epilepsies