

Absence Epilepsy: Older vs Newer AEDs

Jeffrey R. Tenney, MD, PhD
Sejal V. Jain, MD*

Address

*Comprehensive Epilepsy Center, Division of Neurology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
Email: Sejal.jain@cchmc.org

Published online: 27 March 2014

© Springer Science+Business Media New York 2014

This article is part of the Topical Collection on *Epilepsy*

Keywords Epilepsy · Antiepileptic drugs · Treatment · AED · Childhood absence epilepsy · Juvenile absence epilepsy · Jeavons syndrome

Opinion statement

Over the last one to two decades, several new antiepileptic drugs (AEDs) have become available. These medications have different mechanisms of action, metabolism, efficacy, and side effect profiles. Hence, it has become possible to customize medications for a particular patient. It has also become possible to use various combinations of treatments for refractory epilepsies. As medication options have increased, our goal has shifted to not only to maximize seizure control but also to minimize side effects. However, the older AEDs are still widely used. So the question arises—are newer medications better than older AEDs for the treatment of absence epilepsy? Based on a large multicenter class I study, older AEDs—ethosuximide and valproic acid—are more efficacious than newer AEDs. Due to reduced side effects, ethosuximide remains the first line treatment for childhood absence epilepsy.

Introduction

Absence epilepsy is the most common pediatric epilepsy syndrome and absence seizures are part of many forms of pediatric and adult epilepsies. Typical absence seizures are characterized as generalized seizures that consist of multiple, brief (up to 20 seconds) impairments of consciousness that have an abrupt onset and offset [1]. Absences are unique among seizure types because of their pharmacologic treatments and characteristic bilaterally synchronous 3 Hz spike wave discharges on electroencephalography (EEG). A typical

absence seizure is manifested behaviorally as a “staring spell” and can be accompanied by atonic postures such as drooping of the head and/or automatisms such as lip smacking. The majority of children affected by absence seizures will become seizure-free as they enter adulthood [2–7]. Even though studies have concluded that these seizures cause no long-term cellular damage, absence seizures have increasingly been shown to interfere with social and intellectual development during childhood [8••, 9••, 10–14].

This review will describe the various clinical syndromes associated with absence seizures. We will also discuss the evidence supporting various anti-epileptic drug treatments available for these disorders.

Clinical syndromes

Childhood absence epilepsy

Childhood Absence Epilepsy (CAE) is a pediatric epilepsy syndrome occurring in 10–17% of all childhood onset epilepsy, making it the most common pediatric epilepsy syndrome [15, 16]. The incidence of childhood absence epilepsy in the United States is 1.9 to 8 per 100,000 usually occurring in children between the ages of 4 years and adolescence, with girls affected more than boys [17]. The International League Against Epilepsy defines CAE as having very frequent (multiple per day) absences in children of school age (peak manifestation of 6–7 years) and an EEG with bilateral, synchronous, and symmetrical spike wave discharges at 3 Hz [18]. In 2005, this was modified to include age criteria with onset of seizures between 4 and 10 years, with a peak between 5 and 7 years [19]. It has since become clear that there is a rare subset of patients with onset of absence seizures under the age of 4 years, a proportion of whom have glucose transporter type 1 deficiency [20].

Reported remission rates for CAE have ranged from 21–74% [2, 21, 3–5, 22–24, 6, 25, 26, 7, 27–30]. Prospective cohort studies have reported seizure free rates of 57–74% [2–6, 25]. In addition, patients with CAE have been reported to have increased rates of adverse behavioral, psychiatric, language, and cognitive comorbidities (including attention problems, anxiety, depression, social isolation and low self-esteem) [14, 31, 13]. The 2010 Childhood Absence Epilepsy study reported that 35% of subjects had pretreatment attention deficits that did not abate even after seizure freedom was attained [9, 32].

Although labeled a “benign” syndrome, the clinical course of CAE is variable, it is associated with significant comorbidities, and remission rates are lower than in other classic “benign” idiopathic epilepsies such as Benign Rolandic Epilepsy [33].

Juvenile absence epilepsy

Juvenile absence epilepsy (JAE) is a distinct clinical syndrome from CAE, although there is some considerable overlap. Patients with JAE experience absences as the main seizure type and as the name implies, onset begins between 10 and 17 years of age [34]. Absences in JAE tend to be associated with a less severe impairment of consciousness and they lack a pyknoleptic pattern (ie, only one or a few absences daily) [35]. In addition, generalized tonic clonic seizures are much more common in JAE and have been reported to eventually occur in almost 80% of patients [36].

The prognosis of JAE has not been well studied. There is some evidence that rates of seizure freedom are greater for those patients with only absences than those with absences plus generalized tonic clonic seizures [37]. JAE is also thought to persist into adulthood at higher rates than CAE.

Jeavons syndrome

Eyelid myoclonia with absences (EMA) is classified as the International League Against Epilepsy as absence seizures with special features [38]. EMA can occur with idiopathic, cryptogenic, or symptomatic epilepsies. These are characterized by prominent eyelid jerking with upward eye deviation that is often triggered by eye closure. The ictal EEG findings consist of 3–6 Hz generalized polyspike and wave complexes with occasional occipital paroxysmal bursts preceding the generalized discharges [39]. The idiopathic form of EMA is referred to as Jeavons syndrome with seizures triggered by eye closure and all patients are photosensitive [40].

The long term prognosis for Jeavons syndrome has not been studied. There is some evidence that it is a life-long disorder which is resistant to medical treatment [41].

Treatment

Childhood absence epilepsy

A total of eight randomized control trials (RCTs) for the treatment of CAE have been reported (Table 1). One of these was a class I RCT and the remaining seven are classified as class III RCTs because of multiple methodological limitations and provide insufficient evidence to inform clinical practice [42]. Valproic acid was the most commonly studied antiepileptic drug (AED) (n=5) followed by ethosuximide (n=4), lamotrigine (n=3), levetiracetam (n=1), and gabapentin (n=1).

The one class I RCT was a 446 patient, 32 center double-blind, randomized, superiority trial that compared the efficacy and tolerability of ethosuximide, valproic acid, and lamotrigine [9••]. At the week 16–20 visit, subjects on ethosuximide (53 %) and valproic acid (58 %) had significantly higher freedom from failure rates than lamotrigine (29 %, $P<0.001$). Subjects taking ethosuximide had significantly less attention dysfunction compared with subjects on valproic acid (33 % vs 49 %, $P=0.03$) so these findings imply that ethosuximide is the optimal initial monotherapy for CAE [9••]. However, this optimal monotherapy still failed in 55 % of the subjects at 12 months (16 % because of continued seizures, 25 % because of intolerable side effects, 19 % withdrew from study) [9••]. At 12-month follow-up, only 37 % of the subjects achieved freedom from treatment failure on the first AED. Subjects on ethosuximide (45 %) and valproic acid (44 %) had significantly higher freedom from failure rates than lamotrigine (21 %). Intolerable adverse events were higher in the valproic acid group (0.037) [8••].

The usefulness of levetiracetam could not be determined based on the class III placebo-controlled trial because the study did not show statistically significant difference between the placebo and levetiracetam. [43•]. In addition, gabapentin has been established as ineffective for absence seizures and there are class IV reports demonstrating that car-

Table 1. RCT evaluating the treatment efficacy in absence epilepsy

Study	Study population	Tx	Results	Study type [42]
Sato et al 1982[59]	Absence sz	Monotherapy with ETH vs VPA	NS difference between Tx for sz freedom	RCT III
Callaghan et al 1982[60]	New onset typical absence sz	Monotherapy with ETH vs VPA	NS difference between Tx for sz freedom	RCT III
Martinovic et al 1983[61]	Typical absence sz	monotherapy with ETH vs VPA	NS difference between Tx for sz freedom	RCT III
Trudeau et al 1996[47]	New onset absence epilepsy	Monotherapy with gabapentin	NS difference in sz frequency between gabapentin vs placebo	RCT III
Frank et al 1999[52]	Typical absence sz	LTG monotherapy	62 % remained sz free compared with 21 % on placebo	RCT I (open label escalation followed by taper and placebo or LTG)
Coppola et al 2004[50]	CAE or JAE	Monotherapy with LTG Vs VPA	68 % sz free on VPA, 53 % on LTG	RCT III
Fattore et al 2011[43•]	CAE or JAE	LEV monotherapy	24 % sz free compared with 5 % on placebo (NS)	RCT III
Glauser et al 2013[8••]	New onset CAE	Monotherapy with ETH Vs VPA Vs LTG	Freedom from failure 45 % ETH, 44 % VPA, 21 % LTG (S)	RCT I

CAE childhood absence epilepsy, ETH ethosuximide, JAE juvenile absence epilepsy, LEV levetiracetam, LTG lamotrigine, RCT randomized controlled trial, sz seizure, Tx treatment, VPA valproic acid.

bamazepine, oxcarbazepine, phenobarbital, phenytoin, tiagabine, and vigabatrin may worsen or precipitate absence seizures [44–47].

Nonpharmacologic treatments for refractory absence seizures have also been investigated. Vagus nerve stimulation in nine patients was reported to have a mean reduction in daily seizure frequency of 53 % and a 50 % responder rate of 55 % [48•]. The ketogenic and modified Atkins diets have also been reported to have a >50 % seizure reduction in 82 % of patients which was not correlated with age, number of previous anti-convulsants, or gender [49].

Table 2 lists case series that evaluated the efficacy of various AEDs. Because these studies were not randomized, the level of evidence supported by these studies is limited. Several case series reporting outcomes with lamotrigine treatment suggested wide variability in degree of seizure control [50–52]. Another case study evaluating the effects of levetiracetam showed efficacy for seizure freedom [53]. A study evaluating the effects of topiramate was terminated due to the lack of efficacy [54].

Juvenile absence epilepsy

No RCTs have been conducted for treatment of JAE. Expert opinion surveys in the US and Europe found valproic acid and lamotrigine to be

Table 2. Other studies evaluating the treatment efficacy in absence epilepsy

Study	Study population	Tx	Results	Study type
Buoni et al 1999[62]	Typical absence and absence sz refractory to VPA and ETH	LTG monotherapy and LTG add-on	All subjects became sz free	Observational
Coppola et al 2004[51]	Newly diagnosed absence sz	LTG monotherapy	55 % sz free	Observational
Holmes et al 2008[63]	Newly diagnosed Typical absence sz	LTG monotherapy	81 % sz free on EEG with HV	Observational
Verrotti et al 2008[53]	Newly diagnosed Typical absence sz	LEV monotherapy	57 % clinically sz free	Observational
Pina-Garza et al 2011[54]	CAE	TPM monotherapy	Study terminated because of lack of efficacy	Observational

CAE childhood absence epilepsy, LEV levetiracetam, LTG lamotrigine, sz seizure, TPM topiramate

the most common initial treatments [55, 56]. Second line treatments with limited evidence of modest efficacy have included ethosuximide, amantadine, and the ketogenic diet [43•, 49].

Jeavons syndrome

Reports have indicated that Jeavons syndrome is resistant to pharmacologic treatment [41]. Avoidance of seizure precipitants can be important and non-pharmacologic treatments for photosensitive patients, such as wearing special glasses, can be of benefit [57]. A study evaluating the effect of add-on levetiracetam reported 80 % responder rate for number of days with seizure and number of generalized tonic clonic seizures, at 12 weeks evaluation [58]. Medications most commonly referenced for treatment of Jeavons' syndrome have been valproic acid, ethosuximide, benzodiazepines, levetiracetam, and phenobarbital.

Conclusions

Based on the available evidence, older AEDs—ethosuximide and valproic acid—are more efficacious than newer AEDs. Because of reduced side effects, ethosuximide remains the first line treatment for childhood absence epilepsy. There is a lack of class I randomized studies as well as comparison studies for the treatment of other absence epilepsies. In addition, despite advances in the understanding of the pathophysiology and treatment of absence seizures during the past decade, there is still much to learn. The criteria for syndrome classification of CAE, JAE, and Jeavons' syndrome remain unclear and may be best based on a yet unknown biomarker. The ongoing Childhood Absence Epilepsy study aims to address many of these issues for CAE [8••], but questions related to JAE and Jeavons' syndrome remain unanswered.

Compliance with Ethics Guidelines

Conflict of Interest

Jeffrey R. Tenney has received grant support from Citizens United for Research in Epilepsy (CURE). Sejal Jain declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Penry JK, Dreifuss FE. Automatism associated with the absence of petit mal epilepsy. *Arch Neurol*. 1969;21(2):142–9.
2. Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S, Beckerman B, et al. Two-year remission and subsequent relapse in children with newly diagnosed epilepsy. *Epilepsia*. 2001;42(12):1553–62.
3. Fois A, Malandrini F, Mostardini R. Clinical experiences of petit mal. *Brain Dev*. 1987;9(1):54–9.
4. Loiseau P, Pestre M, Dartigues JF, Commenges D, Barberger-Gateau C, Cohadon S. Long-term prognosis in two forms of childhood epilepsy: typical absence seizures and epilepsy with rolandic (centrotemporal) EEG foci. *Ann Neurol*. 1983;13(6):642–8.
5. Sato S, Dreifuss FE, Penry JK, Kirby DD, Palesch Y. Long-term follow-up of absence seizures. *Neurology*. 1983;33(12):1590–5.
6. Sillanpaa M, Jalava M, Kaleva O, Shinnar S. Long-term prognosis of seizures with onset in childhood. *N Engl J Med*. 1998;338(24):1715–22.
7. Trinka E, Baumgartner S, Unterberger I, Unterrainer J, Luef G, Haberlandt E, et al. Long-term prognosis for childhood and juvenile absence epilepsy. *J Neurol*. 2004;251(10):1235–41.
8. •• Glauser TA, Cnaan A, Shinnar S, Hirtz DG, Dlugos D, Masur D, et al. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy: initial monotherapy outcomes at 12 months. *Epilepsia*. 2013;54(1):141–55.
9. •• Glauser TA, Cnaan A, Shinnar S, Hirtz DG, Dlugos D, Masur D, et al. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy. *N Engl J Med*. 2010;362(9):790–9.
10. This article reports initial results from a large multi-center, randomized controlled study in children with CAE.
10. Henkin Y, Sadeh M, Kivity S, Shabtai E, Kishon-Rabin L, Gadoth N. Cognitive function in idiopathic generalized epilepsy of childhood. *Dev Med Child Neurol*. 2005;47(2):126–32.
11. Levav M, Mirsky AF, Herault J, Xiong L, Amir N, Andermann E. Familial association of neuropsychological traits in patients with generalized and partial seizure disorders. *J Clin Exp Neuropsychol*. 2002;24(3):311–26.
12. Pavone P, Bianchini R, Trifiletti RR, Incorpora G, Pavone A, Parano E. Neuropsychological assessment in children with absence epilepsy. *Neurology*. 2001;56(8):1047–51.
13. Vega C, Guo J, Killory B, Danielson N, Vestal M, Berman R, et al. Symptoms of anxiety and depression in childhood absence epilepsy. *Epilepsia*. 2011;52(8):e70–4.
14. Wirrell EC, Camfield CS, Camfield PR, Dooley JM, Gordon KE, Smith B. Long-term psychosocial outcome in typical absence epilepsy. Sometimes a wolf in sheeps' clothing. *Arch Pediatr Adolesc Med*. 1997;151(2):152–8.
15. Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S, Beckerman B. How well can epilepsy syndromes be identified at diagnosis? A reassessment 2 years after initial diagnosis. *Epilepsia*. 2000;41(10):1269–75.
16. Jallon P, Loiseau P, Loiseau J. Newly diagnosed unprovoked epileptic seizures: presentation at diagnosis in CAROLE study. *Coordination Active du Réseau Observatoire Longitudinal de l'Épilepsie*. *Epilepsia*. 2001;42(4):464–75.

17. Panayiotopoulos CP. Typical absence seizures and their treatment. *Arch Dis Child*. 1999;81(4):351–5.
 18. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia*. 1989;30(4):389–99.
 19. Fisher RS, van Emde BW, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia*. 2005;46(4):470–2.
 20. Mullen SA, Suls A, De Jonghe P, Berkovic SF, Scheffer IE. Absence epilepsies with widely variable onset are a key feature of familial GLUT1 deficiency. *Neurology*. 2010;75(5):432–40.
 21. Bouma PA, Westendorp RG, van Dijk JG, Peters AC, Brouwer OF. The outcome of absence epilepsy: a meta-analysis. *Neurology*. 1996;47(3):802–8.
 22. Bartolomei F, Roger J, Bureau M, Genton P, Dravet C, Viallat D, et al. Prognostic factors for childhood and juvenile absence epilepsies. *Eur Neurol*. 1997;37(3):169–75.
 23. 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(7):944–9.
 24. Grosso S, Galimberti D, Vezzosi P, Farnetani M, Di Bartolo RM, Bazzotti S, et al. Childhood absence epilepsy: evolution and prognostic factors. *Epilepsia*. 2005;46(11):1796–801.
 25. Sillanpaa M, Jalava M, Shinnar S. Epilepsy syndromes in patients with childhood-onset seizures in Finland. *Pediatr Neurol*. 1999;21(2):533–7.
 26. Sinclair DB, Unwala H. Absence epilepsy in childhood: electroencephalography (EEG) does not predict outcome. *J Child Neurol*. 2007;22(7):799–802.
 27. Wirrell E, Camfield C, Camfield P, Dooley J. Prognostic significance of failure of the initial antiepileptic drug in children with absence epilepsy. *Epilepsia*. 2001;42(6):760–3.
 28. Wirrell EC, Camfield CS, Camfield PR, Gordon KE, Dooley JM. Long-term prognosis of typical childhood absence epilepsy: remission or progression to juvenile myoclonic epilepsy [see comments]. *Neurology*. 1996;47(4):912–8.
 29. Wirrell EC, Camfield PR, Camfield CS, Dooley JM, Gordon KE. Accidental injury is a serious risk in children with typical absence epilepsy [see comments]. *Arch Neurol*. 1996;53(9):929–32.
 30. Yoshinaga H, Ohtsuka Y, Tamai K, Tamura I, Ito M, Ohmori I, et al. EEG in childhood absence epilepsy. *Seizure*. 2004;13(5):296–302.
 31. Caplan R, Siddarth P, Stahl L, Lanphier E, Vona P, Gurbani S, et al. Childhood absence epilepsy: behavioral, cognitive, and linguistic comorbidities. *Epilepsia*. 2008;49(11):1838–46.
 32. Masur D, Shinnar S, Cnaan A, Shinnar RC, Clark P, Wang J, et al. Pretreatment cognitive deficits and treatment effects on attention in childhood absence epilepsy. *Neurology*. 2013;81(18):1572–80.
 33. Shinnar S, Berg AT, Moshe SL, Kang H, O'Dell C, Alemany M, et al. Discontinuing antiepileptic drugs in children with epilepsy: a prospective study. *Ann Neurol*. 1994;35(5):534–45.
 34. Loiseau P, Duche B, Pedespan JM. Absence epilepsies. *Epilepsia*. 1995;36(12):1182–6.
 35. Dreifuss FEND. Classification of epilepsies in childhood. In: Pellock JMDW, Bourgeois BF, editors. *Pediatric epilepsy: diagnosis and therapy*. 2nd ed. New York: Demos Medical Publishing; 2001. p. 74–5.
 36. Wolf P, Inoue Y. Therapeutic response of absence seizures in patients of an epilepsy clinic for adolescents and adults. *J Neurol*. 1984;231(4):225–9.
 37. Tovia E, Goldberg-Stern H, Shahar E, Kramer U. Outcome of children with juvenile absence epilepsy. *J Child Neurol*. 2006;21(9):766–8.
 38. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde BW, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia*. 2010;51(4):676–85.
 39. Senbil N, Soyer O, Turanlı G, Gurer YK. Fixation-off sensitivity and generalized epileptic EEG induced by eyes closed. *Pediatr Neurol*. 2006;35(5):363–6.
 40. Striano S, Capovilla G, Sofia V, Romeo A, Rubboli G, Striano P, et al. Eyelid myoclonia with absences (Jeavons syndrome): a well-defined idiopathic generalized epilepsy syndrome or a spectrum of photosensitive conditions? *Epilepsia*. 2009;50 Suppl 5:15–9.
 41. Panayiotopoulos CP. Typical absence seizures and related epileptic syndromes: assessment of current state and directions for future research. *Epilepsia*. 2008;49(12):2131–9.
 42. Glauser T, Ben-Menachem E, Bourgeois B, Cnaan A, Chadwick D, Guerreiro C, et al. ILAE treatment guidelines: evidence-based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia*. 2006;47(7):1094–120.
 43. Fattore C, Boniver C, Capovilla G, Cerminara C, Citterio A, Coppola G, et al. A multicenter, randomized, placebo-controlled trial of levetiracetam in children and adolescents with newly diagnosed absence epilepsy. *Epilepsia*. 2011;52(4):802–9.
- This article reports results from a recent Class III study evaluating the efficacy of levetiracetam in patients with absence epilepsy.

44. Genton P. When antiepileptic drugs aggravate epilepsy. *Brain Dev.* 2000;22(2):75–80.
45. Guerrini R, Belmonte A, Genton P. Antiepileptic drug-induced worsening of seizures in children. *Epilepsia.* 1998;39 Suppl 3:S2–S10.
46. Somerville ER. Some treatments cause seizure aggravation in idiopathic epilepsies (especially absence epilepsy). *Epilepsia.* 2009;50 Suppl 8:31–6.
47. Trudeau V, Myers S, LaMoreaux L, Anhut H, Garofalo E, Ebersole J. Gabapentin in naive childhood absence epilepsy: results from two double-blind, placebo-controlled, multicenter studies. *J Child Neurol.* 1996;11(6):470–5.
48. • Arya R, Greiner HM, Lewis A, Mangano FT, Gonsalves C, Holland KD, et al. Vagus nerve stimulation for medically refractory absence epilepsy. *Seizure.* 2013;22(4):267–70.
- This article reports results from a small retrospective study, evaluating seizure outcomes in patients with absence epilepsy being treated with VNS.
49. Groomes LB, Pyzik PL, Turner Z, Dorward JL, Goode VH, Kossoff EH. Do patients with absence epilepsy respond to ketogenic diets? *J Child Neurol.* 2011;26(2):160–5.
50. Coppola G, Auricchio G, Federico R, Carotenuto M, Pascotto A. Lamotrigine versus valproic acid as first-line monotherapy in newly diagnosed typical absence seizures: an open-label, randomized, parallel-group study. *Epilepsia.* 2004;45(9):1049–53.
51. Coppola G, Licciardi F, Sciscio N, Russo F, Carotenuto M, Pascotto A. Lamotrigine as first-line drug in childhood absence epilepsy: a clinical and neurophysiological study. *Brain Dev.* 2004;26(1):26–9.
52. Frank LM, Enlow T, Holmes GL, Manasco P, Concannon S, Chen C, et al. Lamictal (lamotrigine) monotherapy for typical absence seizures in children. *Epilepsia.* 1999;40(7):973–9.
53. Verrotti A, Cerminara C, Domizio S, Mohn A, Franzoni E, Coppola G, et al. Levetiracetam in absence epilepsy. *Dev Med Child Neurol.* 2008;50(11):850–3.
54. Pina-Garza JE, Schwarzman L, Wiegand F, Hulihan J. A pilot study of topiramate in childhood absence epilepsy. *Acta Neurol Scand.* 2011;123(1):54–9.
55. Wheless JW, Clarke DF, Carpenter D. Treatment of pediatric epilepsy: expert opinion. *J Child Neurol.* 2005;20 Suppl 1:S1–S56. quiz S9 60.
56. Wheless JW, Clarke DF, Arzimanoglou A, Carpenter D. Treatment of pediatric epilepsy: European expert opinion, 2007. *Epileptic Disord.* 2007;9(4):353–412.
57. Appleton RE, Panayiotopoulos CP, Acomb BA, Beirne M. Eyelid myoclonia with typical absences: an epilepsy syndrome. *J Neurol Neurosurg Psychiatry.* 1993;56(12):1312–6.
58. Striano P, Sofia V, Capovilla G, Rubboli G, Di Bonaventura C, Coppola A, et al. A pilot trial of levetiracetam in eyelid myoclonia with absences (Jeavons syndrome). *Epilepsia.* 2008;49(3):425–30.
59. Sato S, White BG, Penry JK, Dreifuss FE, Sackellares JC, Kupferberg HJ. Valproic acid versus ethosuximide in the treatment of absence seizures. *Neurology.* 1982;32(2):157–63.
60. Callaghan N, O'Hare J, O'Driscoll D, O'Neill B, Daly M. Comparative study of ethosuximide and sodium valproate in the treatment of typical absence seizures (petit mal). *Dev Med Child Neurol.* 1982;24(6):830–6.
61. Martinovic Z. Comparison of ethosuximide with sodium valproate as monotherapies of absence seizures. *Advances in Epileptology: XIVth Epilepsy International Symposium*, New York: Raven Press; 1983.
62. Buoni S, Grosso S, Fois A. Lamotrigine in typical absence epilepsy. *Brain Dev.* 1999;21(5):303–6.
63. Holmes GL, Frank LM, Sheth RD, Philbrook B, Wooten JD, Vuong A, et al. Lamotrigine monotherapy for newly diagnosed typical absence seizures in children. *Epilepsy Res.* 2008;82(2–3):124–32.