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Review article

Benign epilepsy with centrotemporal spikes – Current concepts of diagnosis and treatment

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ABSTRACT

Benign epilepsy with centrotemporal spikes (BECTS) is the most common focal epilepsy of the childhood and also one of the best known. It has a proclivity to start at a particular age and remit spontaneously before adolescence. Majority of patients may avoid long-term treatment, because of the mild course and very good outcome. Only few patients may present cognitive deficits if the proper treatment is not implied. BECTS is a part of heterogeneous group of syndromes that consists of Landau-Kleffner Syndrome (LKS), Continuous Spike-and-Wave during Sleep (CSWS) and Atypical benign partial epilepsy (ABPE). These syndromes may be also a result of various trajectories that BECTS may evolve to. Disease is suggested to have genetic origins, as some patients have relatives with different types of epilepsy. The discovery of the pathogenic mechanism of the disease and implementation of targeted therapy belong to the main challenges in the treatment of these patients.

1. Introduction

1.1. Terminology

Rolandic Epilepsy (RE) or benign epilepsy with centrotemporal Spikes (BECTS) is known to be the most common and one of the best known focal epilepsy of the childhood. Most affected children outgrow the seizures by their teen years, thus it is classified as benign syndrome. Nevertheless there is growing evidence that BECTS may functionally and structurally affect a larger portion of the brain, causing additional abnormalities significantly interfering in lives of affected children [1]. It is characterized as an idiopathic, inherited, self-limiting syndrome with focal onset seizures and subtle structural cerebral abnormalities. Other terms for RE/BECTS used in medical terminology are:

- Benign childhood epilepsy with centrotemporal spikes.
- Benign epilepsy of children with rolandic (centrotemporal) paroxysmal foci.
- Benign rolandic epilepsy (BRE).
- Benign rolandic epilepsy of childhood.
- Centrotemporal epilepsy.
- Sylvian epilepsy.

1.2. History and brief

BECTS has been known to pediatricians for over 60 years, and was first described by Gastaut in 1952 [2]. Rolandic Epilepsy is named after Luigi Rolando, an Italian anatomist known for his pioneer research into localization of function within the

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brain. Seizures are sometimes referred to as sylvian seizures. Appearing at an average age of 5–7 years, when emotional and behavioral regulation is acquired; basic communication skills, number concepts and complex reading is developed [3]. Epileptogenic zone responsible for the autonomic sensory-motor symptomatology in BECTS involves neuronal networks within the lower rolandic somatosensory cortex (region of the Sylvian and Rolandic fissure), especially lower parts of the precentral and postcentral gyrus, that represents the face and the oropharynx bilaterally [1]. Anatomical structures responsible for generating seizures are displayed in Fig. 1.

1.3. *Clinical symptoms*

Maturational age-related instability of that region generates typical clinical manifestations including fundamental features for this syndrome:

- *Unilateral facial sensorimotor symptoms* (30% of patients) – motor seizures are focal, brief (1–3 min), preceded by an aura that consists of somatosensory unilateral symptoms (paraesthesias) of inner cheek, tongue, lips, hand or leg ipsilateral to the affected side of the face [1,4].
  - Sensory symptoms are described as jaw numbness (sometimes only within the corner of the mouth), jerking and pulling to one side, with accompanying speaking difficulties.
  - Motor manifestations may be sudden, lasting from few seconds to a minute, sometimes concurrent with ipsilateral tonic deviation of the mouth. Bursts are low amplitude, manifested by continuous or clonic contractions often limited to lower lip that may spread to ipsiliateral hand. Episodes are more acute in older children [5].
- *Oropharyngolaryngeal symptoms (OPLS)* (present in 50% of patients) – it is the most common clinically observed sensorimotor manifestation.
  - Among sensory symptoms patients complain about numbness, paraesthesias (tingling, tickling, freezing) of the cheek, teeth, gums, tongue, pharynx, larynx. These can be diffuse or strictly limited – even to one tooth.
  - Motor component comprises of strange sounds such as gurgling, grunting, guttural sound, death rattle, especially these let parents know when their child has an episode during sleep.
- *Speech arrest* (40% of patients) – anarthric speaking inability due to loss of the power of coordination of the muscles responsible for the articulation.
- *Hypersalivation* (30% of patients) – a prominent autonomic manifestation, which might be associated with OPLS, hemifacial seizures, and speech arrest [2].

Daytime seizures are almost exclusively simple, partially involving face and tongue. Atypical absence seizures, negative myoclonus and loss of tension are rarely seen [6]. Nocturnal seizures are more frequent, though still present in a small amount. They usually start from lower lip, then spread to an ipsilateral arm, leg or become secondarily generalized. Majority of the generalized tonic–clonic seizures (GTCS) follow rolandic activation, and therefore are secondary, mainly during sleep [7]. Role of sleep in facilitating seizures and their secondary generalization is still yet to be explained. Progression to GTCS occurs in approximately half of children and may be followed by postictal Todd's hemiparesis. Children who experience postictal Todd paralysis are more likely to have

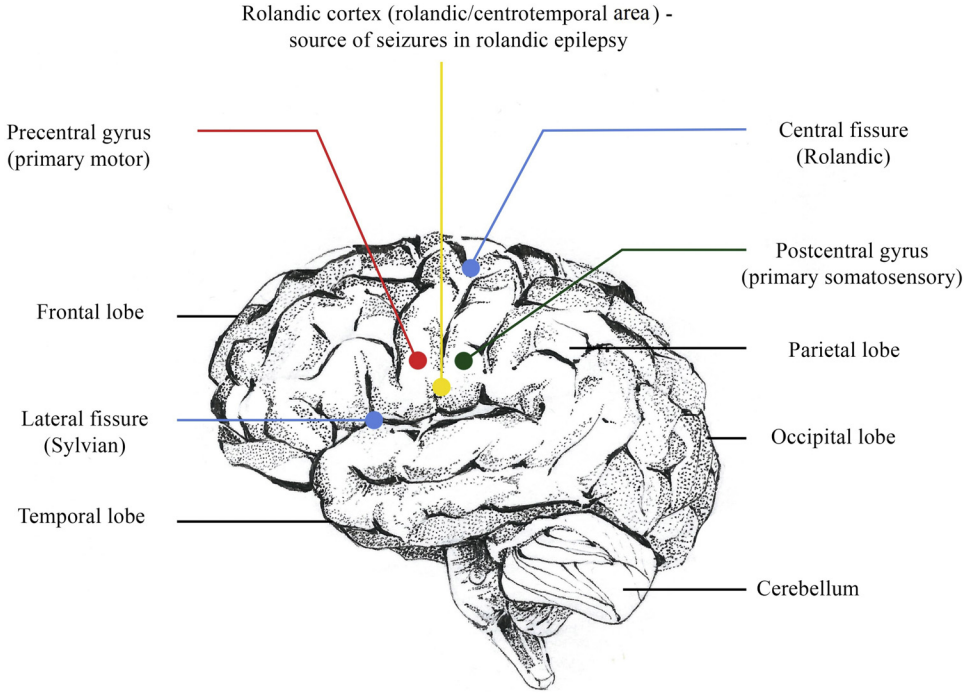

Fig. 1 – Anatomy of the BECTS' epileptogenic zone of the brain.
Figure author: Agnieszka Barańska.

migraine. Migraine is strongly comorbid with BECTS. The prevalence of migraine in BECTS is 15% vs 7% in nonepilepsy probands, and in siblings of probands prevalence was 14% vs 4% in nonepilepsy siblings [8]. Consciousness and memory is fully retained in more than half of the patients, but become impaired during the ictal progress and in one-third there is no recollection of ictal events. Voluntary protrusion of tongue may stop seizures [9].

1.4. *Epidemiology*

Prevalence estimates for 8–25% of childhood epilepsies with overall incidence 10–20:100,000 in children aged 3–15 [1,4]. The disorder occurs more often in boys, with male to female ratio 3:2. The reason for male sex preponderance is unknown [5,10]. Onset of the disease ranges from 3 (always after 2nd year of life) to 14 years (75% within the range of 7–10) with spontaneous remission before 16th year of life in 100% cases [6,11], approximately within 2–4 years from onset [2,12].

2. Genetics

Recent studies have shown a strong correlation between genetics and BECTS development. The first study reporting association with familial incidence of seizures in BECTS was a case report published in 1964, showing that 10% of relatives may have positive family history of epilepsy [13]. Studies published from 1960s to 1990s afterwards confirmed that up to 60% of patients with BECTS have a positive family history of seizures [7]. It is believed that inheritance is autosomal dominant, age-dependent, with slight male preponderance. Genome scans imply more complex mode of inheritance, displaying abnormalities at 15q14, 16p12-11.2, 11p13. It seems that there is a strict evidence for linkage with chromosome 15q14 [5,14,15], though autosomal dominant inheritance with age dependent penetrance rather refers to centrotemporal spikes (CTS) than to BECTS in general [16]. CTS can also be found in healthy children or children with autistic spectrum disorder (ASD) without clinical seizures. The last locus (11p13) is found to be pleiotropic for speech dyspraxia and CTS in BECTS. The latest research adds newly identified risk factor to the pot - four individuals were found carrying mutation (3 duplication and 1 deletion) at Xp22.31 [17]. Typical and atypical BECTS are presumed to have a shared genetic etiology. Latest studies overview present coherent data about genes and mutated loci (Table 1). Exploring multifactorial genetic inheritance we observe genomic heterogenity, and phenotypic variability. Except for GRIN2A and ELP4, most genes were identified in other diseases first and then explored in BECTS.

3. Diagnosis

CTS and typical seizures are said to be sufficient for diagnosis, however only 10% of children fulfilling EEG criteria of CTS actually have seizures. NICE (National Institute of Health and Care Excellence) and SIGN (Scottish Intercollegiate Guidelines Network) stress significance of EEG, with ambulatory follow-up sleep video EEG [18,19]. The spike-waves discharges are activated as the patient enters the NREM sleep. Brain MRI is not recommended as first-line investigation because of the nonlesional nature of these epilepsies. The very low use of neuropsychological assessments (less than 10%) is striking, given the well-documented occurrence of language, literacy and attentional comorbidities in BECTS and their impact on educational achievement and quality of life [20].

3.1. *EEG findings*

Centrotemporal spikes arising independently in the right and/or left hemispheres from a normal background activity without any additional neurological conditions are the hallmark of BECTS [21]. Another common feature is presence of abundant focal Interictal Epileptiform Discharges (IEDs). CTS are broad, diphasic, focal, high-voltage (100–300 microvolts) sharps, with a transverse diapole, and they are often followed by a slow waves over the centrotemporal region (Rolandic area). Ictal manifestations indicative of temporal lobe involvement do not occur in rolandic epilepsy, and the term 'centrotemporal' refers only to the spike topography.

CTS are activated by drowsiness and non-REM sleep, and are mainly high amplitude, sharp and slow wave complexes localized in the C3/C4 (high central) in 30% of patients, and C5/C6 (low central region, midway between central and temporal) electrodes in 70% [1,2]. Number of spikes increases during stages I–IV of sleep. Ictal manifestations are more frequently observed (75%) during NREM (Non-Rapid Eye Movement) sleep, mainly at sleep or just before awakening, they can be ipsi- or contralateral to the symptomatogenic side and they are often multifocal [4]. Approximately 75% of EEG discharges are localized, affecting well-delineated brain regions [22,23]. Spike focus is unilateral in 60% and may shift from side to side over time or may be bilateral in 40%, with bilateral discharges occurring synchronously or asynchronously. Discharges occur in clusters, with a frequency of 1.5–3 Hz. Exemplary EEG records are shown in Figs. 2–7.

CTS are not specific for BECTS and may be present in 2% of healthy children, of whom less than 10% develop BECTS [24,9]. Age-dependent CTS may occur in cerebral tumors, Rett syndrome, fraX syndrome, focal cortical dysplasia, Continuous Spike Waves during Sleep (CSWS), Landau–Kleffner syndrome (LKS), atypical benign partial epilepsy, headaches, speech, behavioral and learning difficulties, ASD, and Attention Deficit Hyperactivity Disorder (ADHD) [25].

4. Evolution and the outcomes

BECTS is well known for having various paths of development. Majority of patients run a typical, mild course with very good outcomes. Nevertheless, during the active phase of the disease development of reversible, linguistic cognitive and behavioral problems may be observed. Symptoms tend to be more noticeable when the disease starts before age of 8 years, and when EEG displays high rate of multifocal EEG spikes occurrence (focal EEG spikes may impair long-term learning and memory consolidation in sleep) [20]. The prognosis remains excellent, and with less than 2% of cases developing absence seizures or generalized tonic–clonic seizures (GTCS) in

Table 1 – Summary on the genetics data in BECTS.

Mutated molecule/ proteins	Gene location	Molecular mechanism	Disorders with this mutation	Targeted therapy
ELP4	**11p13** – one area showed strong and compelling evidence for linkage to CTS [35].	The Elongator Complex (also called PAXNEB) – especially Elp 4,5,6 maintain translational fidelity via regulation of tRNA modifications. Noncoding mutation in ELP4 gene impairs brain development, resulting in susceptibility to seizures and neurodevelopmental disorders. ELP4 is associated with the pathogenesis of BECTS and has a strong effect on risk for CTS in BECTS families [35–40].	Familial dysautonomia (FD), intellectual disability (ID), amyotrophic lateral sclerosis (ALS), BECTS [39] and other disorders followed by CTS presence, i.e. speech disorder, developmental coordination disorder, attention deficit-hyperactivity disorder [37], general developmental delay, speech and language disorders, autism spectrum disorders [40].	Currently not available.
GRIN2A	**16p13.2** [41].	Glutamate ionotropic N-methyl-D-aspartate (NMDA) receptor type subunit 2A is a known ion-channel having a strong impact on brain development and function [41]. GRIN2A encodes the GluN2A subunit of the NMDAR, that plays critical role in normal neuronal development, synaptic plasticity and memory [42]. GRIN2A mutation is higher in the severe end of the BECTS/Atypical BECTS, though it is still the most relevant gene for BECTS [43]. Mutation of receptor-coding genes or antibodies directed against receptor peptides may lead to epilepsy, developmental delay and autoimmune encephalitis [44].	Epilepsy-aphasia syndrome (EAS) [42]: BECTS and subtypes which are believed to be more severe BECTS variants i.e. LKS, ESES/ CSWS, ABPE [44,45], Atypical BECTS [40], mental retardation, speech dyspraxia, autism, families with a history of centrotemporal spikes (CTS). GRIN2A mutations among epilepsies of the EAS, are observed in frequency from 2.1% in BECTS to 20% in CSWS [38] or 4.9 to 17.6% [46].	**Memantine** – NMDA receptor blocker – the potential for personalized genomics and therapeutics [45]. **GluN2A**-selective positive allosteric modulator to rescue the phenotype of mutations with reduced glutamate potency [42]. Patients with epilepsy and GRIN2A mutation may be candidates for immunotherapy [41].
BDNF	**11p13** (its locus lays in close proximity to ELP4 gene, which enhances the possibility that BDNF and ELP4 act together in BECTS [36].	Brain-derived neurotrophic factor – involved in development, degeneration and differentiation of central nervous system. It appears to play an important role in epileptogenesis in the hippocampus specifically as an effector of recurrent epileptic seizures in the dentate gyrus [35,36]. The concentration of BDNF in serum is associated with disease severity in people with epilepsy, as decreases in serum BDNF are correlated with seizure frequency [35].	Hyperexcitability (epilepsy).	Currently not available.

Table 1 (*Continued*)

Mutated molecule/ proteins	Gene location	Molecular mechanism	Disorders with this mutation	Targeted therapy
KCNQ2, KNCQ3	**20q.30.13** – KNCQ2 [47]. **8q24** – KNCQ3 [48].	Potassium voltage-gated channel subfamily Q members 2 and 3. They represent the molecular basis of the M-current (I_{KM}), with a critical role in spike frequency adaptation and control of neuronal excitability, which defects are responsible for BFNC (benign familial neonatal convulsions) BFNC type 1 is said to later develop to BECTS in some cases [47,49]. Among epileptic conditions linked to channelopathies, potassium channel subunits mutations represent the largest category, most of which were found in KCNQ2 [50].	Pathologic reduction in KCNQ2/3 channel activity is involved in different classes of seizures, including BECTS, neuropathic pain, migraine, anxiety, attention deficient-hyperactivity disorder, schizophrenia, mania, and bipolar disease [51,52]. Both loss-of-function and gain-of-function KCNQ2 variants can lead to various forms of neonatal epilepsy, majority are loss-of-function [53].	**Protein arginine methyltransferase 1 (Prmt1)** opens KCNQ by methylation, preventing neuronal hyperexcitability and seizures [50]. **Retigabine (RTG)/Ezogabine (EZO)** – a KCNQ agonist and **Flupirtine**, its closely-related analog (nonopioid analgesic), the only KCNQ openers approved for human use by the U.S. Food and Drug Administration (FDA), but has recently been limited due to rising concerns regarding its adverse effects [54,55]. **RL648_81** new specific KCNQ2/3 activator, mutated from RTG, 15 times more potent and also more selective than retigabine [52]. Over-expressing calmodulin protein opens KCNQ, tending to hyperpolarize neurons and decrease excitability [56].
DEPDC5	**22q12.2-q12.3** – mutation in 22q12 causes familial focal epilepsy with variable foci-1 (FFEVF1) [57–59].	DEP Domain-Containing 5 gene also known as KIAA0645. Responsible for neuronal signal transduction [58]. Forms a part of the GATOR1 (GAP activity toward rags) complex, a negative regulator of the mammalian target of rapamycin (mTOR) pathway. Loss-of-function mutations in DEPDC5, an inhibitor of the mTOR pathway could conceivably contribute to hyperexcitability. DEPDC5 mutations are the most frequent cause in familial focal epilepsies, and differ from any other mutations in ion channel encoding genes by the presence of cortical malformations [60]. To date it is the most common cause of familial focal epilepsies.	Various mutations ranging from apparently nonlesional focal epilepsies to malformation-associated focal epileptic syndromes, i.e. focal cortical dysplasia (FCD) and hemimegalencephaly. Families may show patterns that are effectively subsets of FFEVF, individuals with BECTS have also been described [59,60].	**Targeted mTOR therapies** – DEPDC5 agonists would likely be anti-epileptogenic and more selective than currently available mTOR inhibitors [5,61].
RBFOX1/3	**16p13** – RBFOX1 [62]. **17q25.3** – RBFOX3 [63].	The RNA-binding Fox (Rbfox) family of splicing factors is comprised of three members, Rbfox1 (Fox-1 or A2BP1), Rbfox2 (Fox-2 or RBM9), and Rbfox3 (Fox-3, HRNBP3 or NeuN). Deletion of the RBFOX1 gene results in heightened susceptibility to spontaneous and kainic acid-induced seizures, displayed electrophysiologically in the dentate gyrus [63–66].	BECTS (RBFOX 1 and 3), ASD, mental retardation, epilepsy, CTS without seizures, mental retardation, seizures, hypotonia, uneven gait, mild facial dysmorphism, fluctuating liver enzymes, and features of autism [62,66,67].	Currently not available.

Table 1 (Continued)

Mutated molecule/ proteins	Gene location	Molecular mechanism	Disorders with this mutation	Targeted therapy
GABAA-R	**5q34** – GABRG2, GABRA1 [68].	Gamma-aminobutyric acid type A receptor $GABA_A$-R-ligand-gated Cl^- channels mediating most of the fast inhibitory synaptic transmissions in the brain. $GABA_A$-Rs mutations are commonplace for different epileptic syndromes. GABA-A receptors are pentameric, consisting of proteins from several subunit classes: alpha, beta, gamma, delta and rho. Mutations in Gamma-aminobutyric acid type A receptor gamma2 subunit (GABRG2) gene have been associated with epilepsy and febrile seizures [37].	BECTS/Atypical BECTS (mutation in GABRG2), childhood absence epilepsy (ECA2) and febrile seizures [37,69,70].	**Benzodiazepine** – binding site residues in the GABRG2 protein [71]. **Medial ganglionic eminence interneuron progenitors (MGE-IPs)** attenuates cortical seizure propagation [72]. Grafting inhibitory interneurons into seizure foci might relieve refractory seizures.

adult life. Adults who had recovered from BECTS did not have general negative outcomes in the field of development, education, employment, and social adaptation [26].

Atypical BECTS is less common, the seizures occur only in the daytime, Todd's paralysis may be prolonged or even transform into status epilepticus. It is more prone to develop unfavorable syndromes with neuropsychological impairments, such as LKS or CSWS containing EEG pattern known as Epileptic encephalopathy with status epilepticus in sleep (ESES) [5,11]. On the other hand CSWS and LKS can evolve from typical too BECTS in 1.3–4.6% cases [1,27]. Slowing or regression of cognitive development in children with epilepsy is primarily due to neural network malfunction caused by seizures and abnormal interictal activity (cortical or subcortical or both) [2,22]. In BECTS learning difficulties can persist even after a long-lasting seizure free period. Progressive cognitive dysfunction predominates the clinical symptoms among the group called epileptic encephalopathies (BECTS, LKS, CSWS) [28]. The most crucial features were summarized in Table 2.

Rolandic area is thought to be associated with ADHD, particularly impulsivity [11,29]. Children with rolandic spikes present lower result of neuropsychological assessment and exhibit more symptoms of hyperactivity impulsivity than those without EEG discharges [30]. Seizures in ADHD are more often focal than generalized and appear in 6 to 53% cases [31].

Highly prevalent cognitive limitations in RE, present in 40% of patients during the active phase of disease, are reading disability (RD), speech sound disorder (SSD) and language impairment [3]. These symptoms may be common in families of BECTS patients and may be preceding seizures [20,32]. SSD resolves around 5–6 years of age. RD is commonly associated with BECTS and might have a pervasive impact on school outcome and merits early recognition and intervention.

Among other problems which may be seen in these patients are neurobehavioral problems, visuomotor impairments, spatial perception impairments, orientation problems, psychiatric disorders, dyscalculia and dyslexia [1]. BECTS patients perform significantly worse than controls at tasks of expressive language, verbal learning efficiency, motor and psychomotor speed and dexterity [6,21], prompting a re-evaluation of the ''benign'' nature of this epilepsy. Implementation of the treatment should be considered in an early phase of the disease to suppress IEDs and prevent further progression of deficits.

5. Therapy management and drug selection

Seeing as the course of the disease is oftentimes benign, the need for treatment implementation has been debated for decades. Children do not need AED when seizures are infrequent, mild or nocturnal only. Treatment also seems to be unnecessary when disease onset is close to the natural range of remission, which is said to be after 2–4 years from onset and before the age of 16 years [4,19]. Most patients will not require anticonvulsant therapy except for the patients who develop daytime seizures, very frequent nocturnal seizures, as well as patients who evolve to ESES or develop

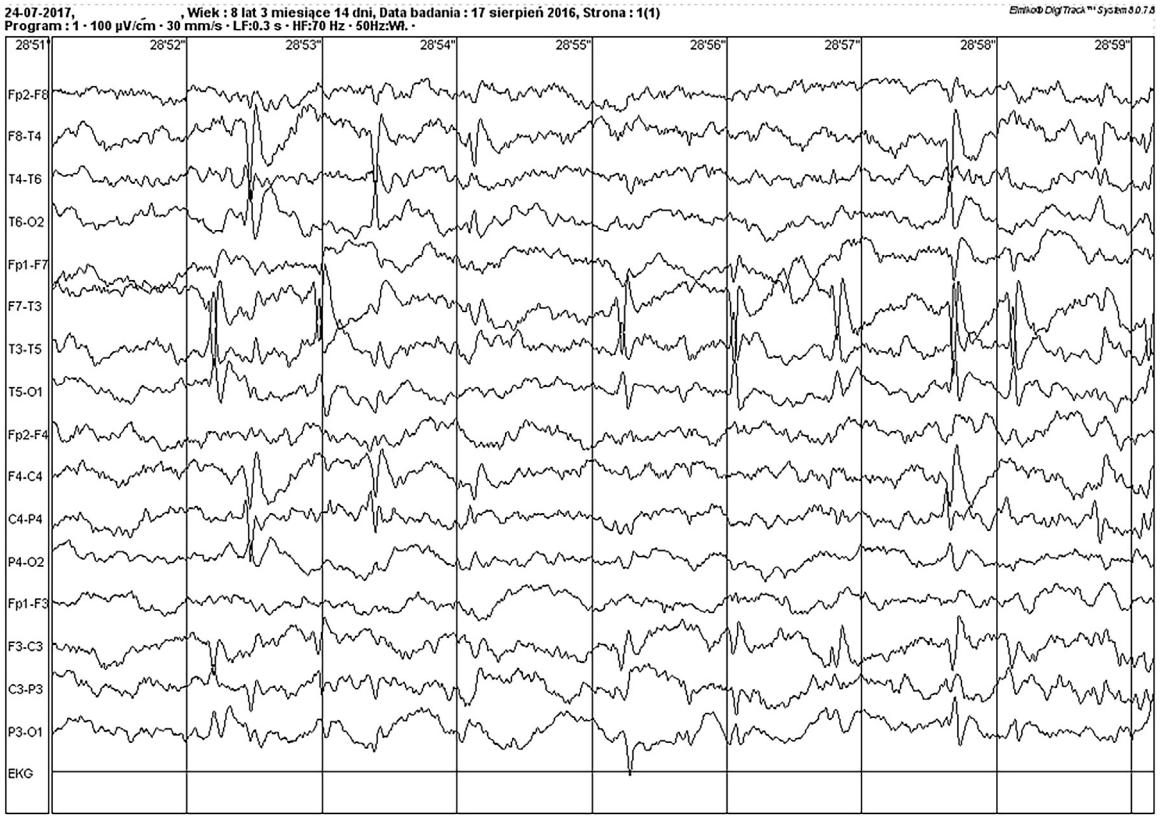

Fig. 2 – Centrotemporal spikes occurring bilaterally shifting to the left side.

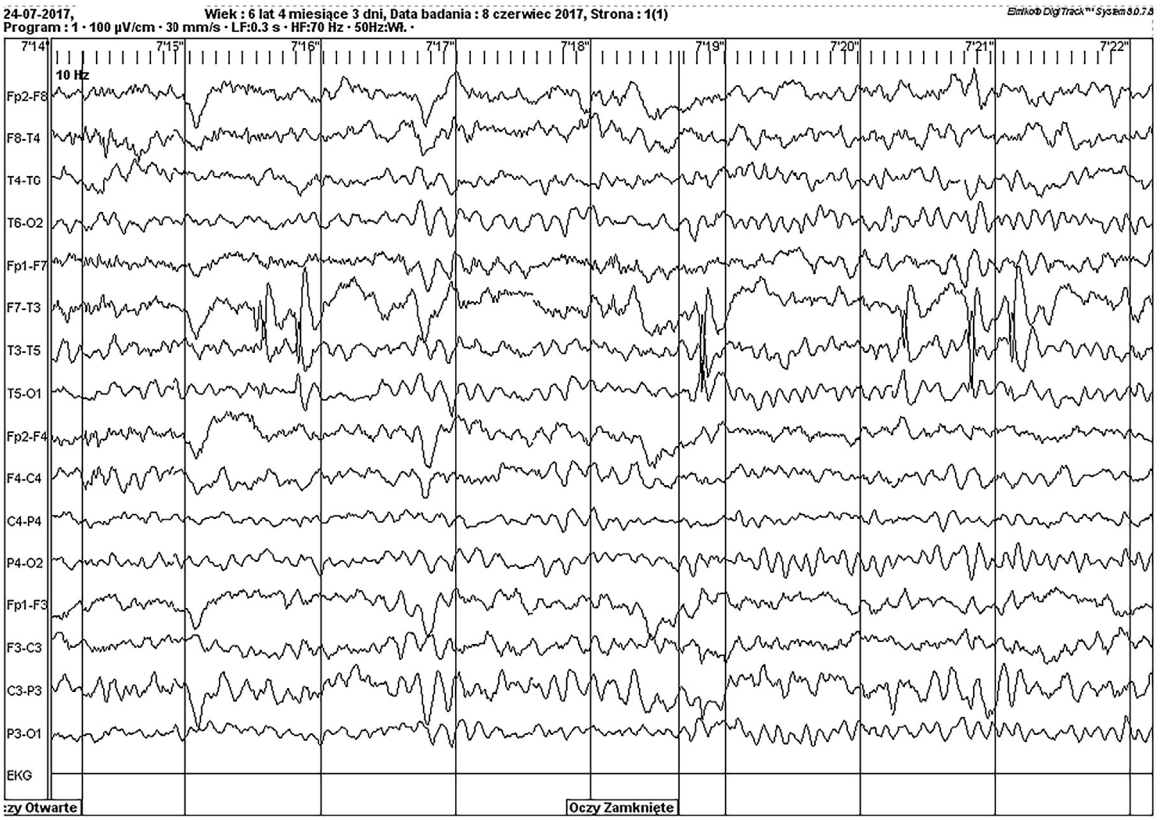

Fig. 3 – discharges occurring on the left side with the phase return over the central temporal area, single SW (spike-and-wave) complexes.

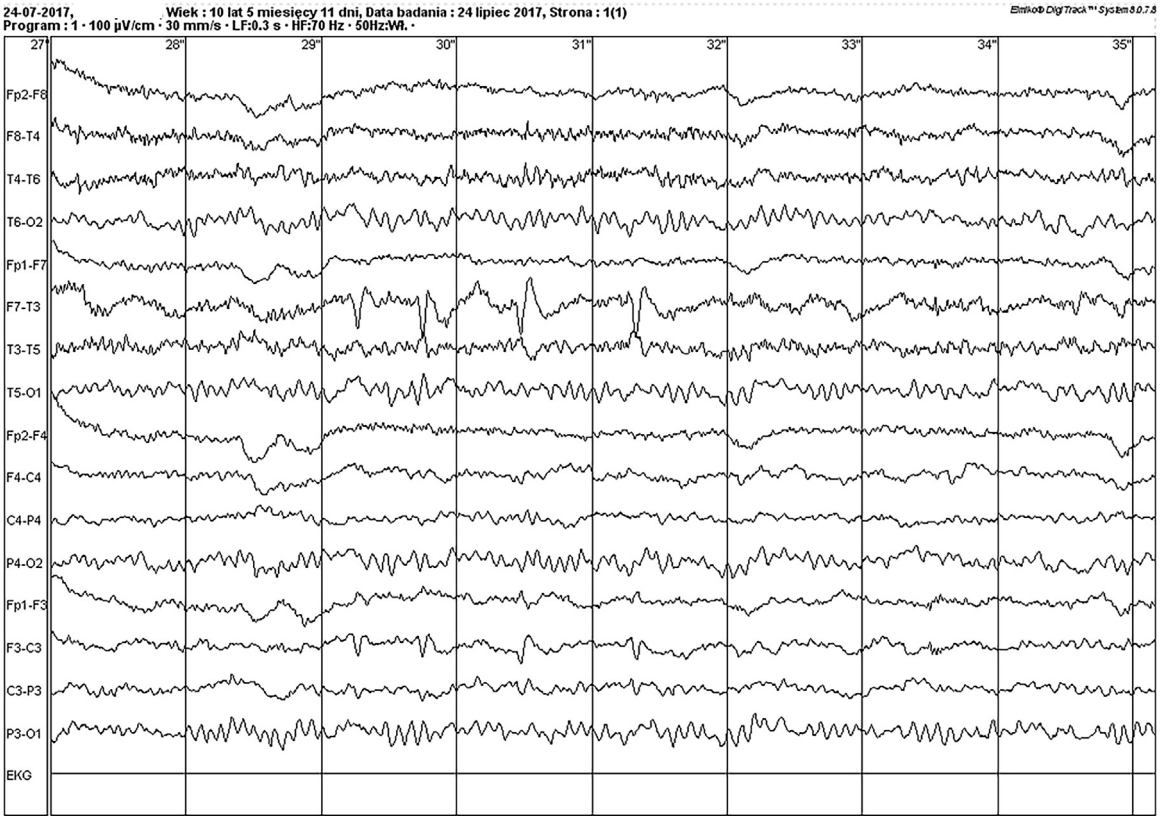

Fig. 4 – discharges in left central temporal and central area, single SW (spike-and-wave) complexes.

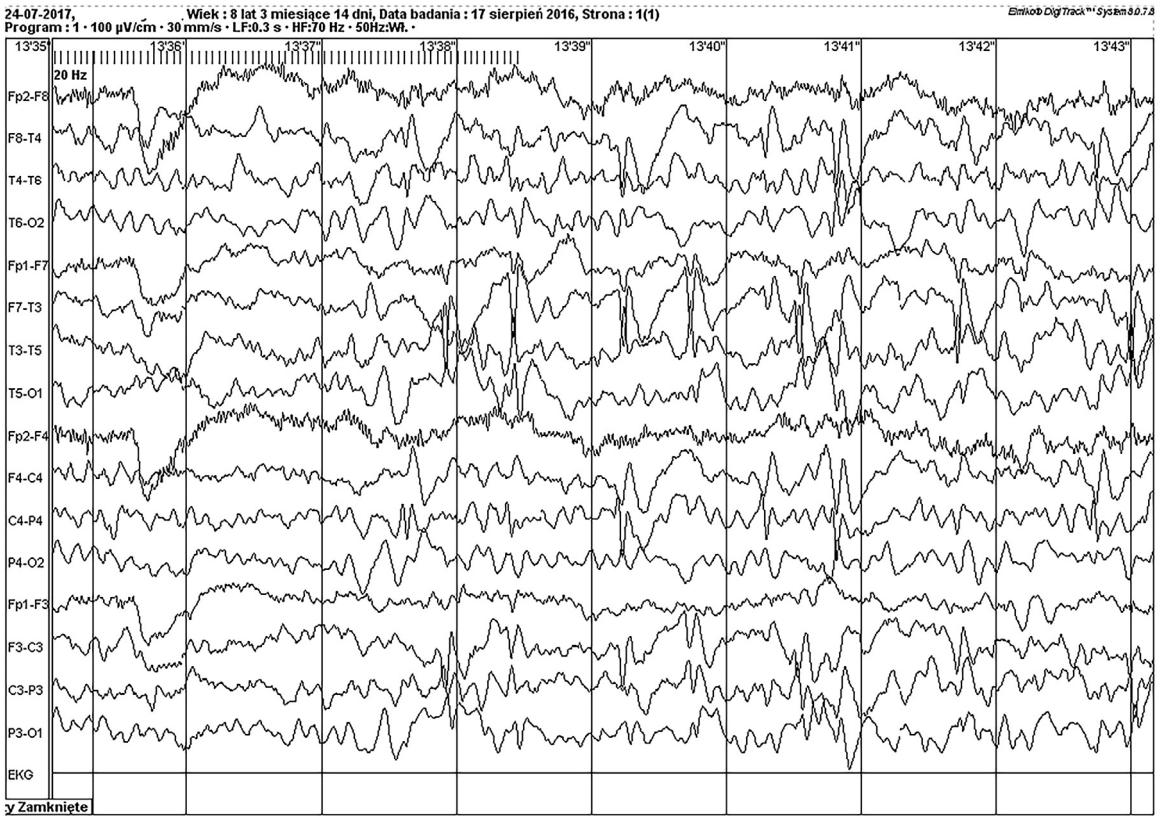

Fig. 5 – Bilaterally and independently on the left and right side, synchronically, with the phase return over the central temporal and central region, SW complexes with left side dominancy.

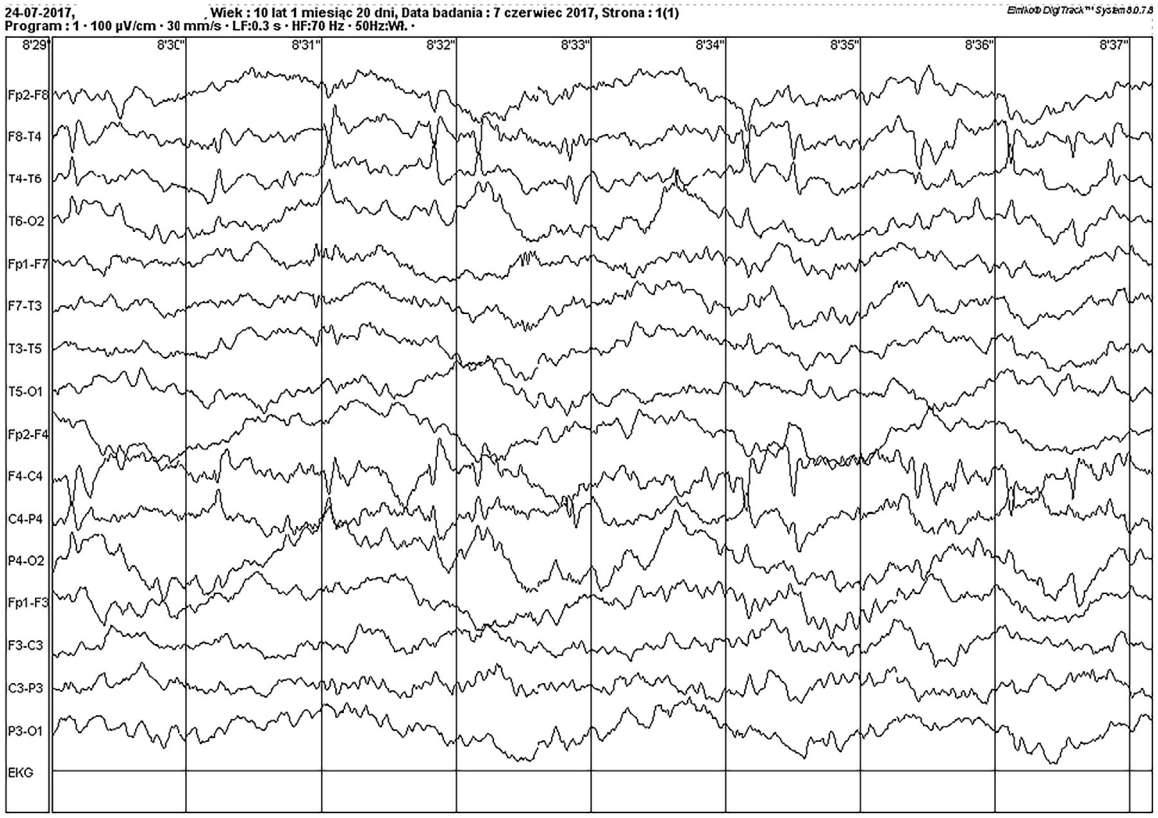

Fig. 6 – Right sided discharges with the phase return over the cantral temporal and central area, single SW complexes.

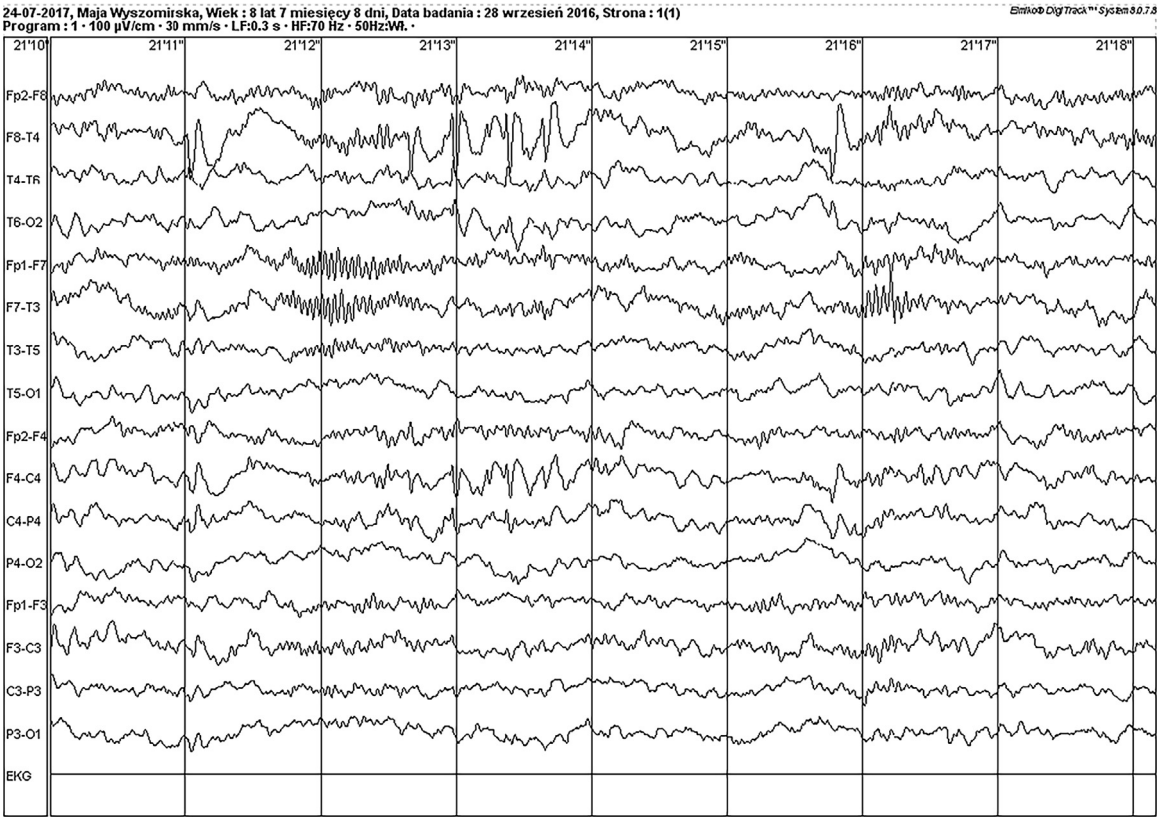

Fig. 7 – Right sided discharges with the phase return over the cantral temporal and central area.

Table 2 – Summary on epileptic encephalopathies.

	BECTS	CSWS	LKS
Incidence	• 8–25% of childhood epilepsies • Male to female ratio 3:2	• 0.2–0.5% of childhood epilepsies • Male to female ratio 3:2	• Rare (>300 described cases) • Male to female ratio 2:1
Age of onset (peak)	• 3–15 years (peak 7–10 years)	• 2 months–12 years (peak 4–5 years)	• 2–10 years (peak 5–7 years)
Clinical symptoms	• Majority have mild infrequent seizures, 10–20% have only one seizure ever, 20% have frequent seizures, mostly nocturnal (parents and children often do not realize that the child is having seizures) • Neuropsychological deficits are visible during the active phase of the disease (i.e. speech sound disorder, reading disorder, linguistic problems) which may affect development and bring educational problems • Rarely anxiety, depression • No neuroradiological abnormalities, or subtle cortical volume losses in particular areas	• Seizures are initial symptoms in 80% of patients, they occur in vast majority of the patients • Neuropsychological disturbances are initial symptoms in 20% • Decline in intellectual performance happens during the ESES period • Rarely psychotic episodes can be present • Common neuroradiological abnormalities (33–50% of the patients), mostly thalamic prenatal/perinatal injuries (hemorrhagic/ischemic), furthermore unilateral or diffuse atrophy, porencephaly, pachygyria, cortical development disorders, perisylvian polymicrogyria, hydrocephalus	• Seizures are initial symptoms in 60%, they occur in 70–80% of patients, 20–30% do not have seizures at all • Aphasia is initial symptom in 40%, acquired childhood aphasia (loss of receptive and later expressive language) in previously normal children who developed age-appropriate speech. The most often is verbal agnosia. Behavioral disturbances are common (50–70%), usually are connected to the language, intellect is unimpaired • Rarely acute anxiety can be present • No brain lesions or very subtle, volumetric changes seen in MRI - volume reduction in the temporal cortex
Seizure characteristics	• Sensorimotor symptoms including face unilaterally oropharyngolaryngeal symptoms, speech arrest and hypersalivation. Generalized tonic–clonic seizures sometimes with consequent Todd's hemiparesis. • Infrequent nocturnal seizures, and rare daytime seizures, benign and self-limited	• Generalized tonic–clonic, simple partial motor, absence or atypical absences, unilateral status, atonic seizures leading to falls • Numerous seizures a day, often nocturnal, benign and self-limited	• Generalized clonic, simple partial motor, atypical absences, unilateral status, no atonic seizures, subtle seizures (motor or sensory) • Infrequent seizures, often nocturnal, benign and self-limited
EEG features	• Usually normal background activity, rare generalized SWs, central in 30%, low central 70%, centrotemporal focal or multifocal discharges, unilateral or/and bilateral, activated by non-REM sleep	• Usually normal background activity, frequent generalized SWs (SW index >85%) – more or less unilateral or focal, ESES pattern (SW index of 85–100%), frontotemporal and frontocentral focus of discharges, persisting on three or more recordings over a period of at least 1 month, EEG patterns occurs during night as soon as the patient falls asleep (non-REM)	• Usually normal background activity, rare generalized SWs, mainly temporal, posterotemporal and parietooccipital focus of discharges, paroxysmal EEG abnormalities that increase during sleep (REM) - increase in discharge rate and a wider spread of the paroxysmal activities, pattern may also present features of ESES
Drug response	• Seizures are easily controlled, some patients may not need the treatment at all • Rarely BECTS is resistant for medication • Rarely reversible, linguistic, cognitive and behavioral problems during active phase, symptoms are more noticeable when disease starts earlier • Prognosis is very good	• Seizures are easily controlled • Carbamazepine, phenytoin and phenobarbital can precipitate CSWS in some children • Recovery is possible spontaneously and after treatment (drugs, steroids, IgG, subpial transection) • Prognosis is poor after long duration of ESES (>3 years)	• Seizures are easily controlled • Outcome is worse if the deficits emerge earlier than seizures • Carbamazepine and phenytoin may aggravate seizures, even lead to ESES • Recovery is possible spontaneously and after treatment (drugs, steroids, IgG, subpial transection) • After months to years aphasia stabilizes and usually improves before adulthood

status epilepticus. These groups of patients need special attention instead of ''wait-and-see'' strategy [1].

Which drug should be chosen as initial treatment is not easy to determine. According to Pediatric expert consensus survey drugs of first choice are oxcarbazepine and carbamazepine. International League Against Epilepsy (ILAE) recommend carbamazepine and valproic acid [33]. NICE recommends carbamazepine (CBZ), lamotrigine (LTG), levetiracetam (LEV), oxcarbazepine (OXC) and valproic acid (VPA) as a first-line monotherapy [18,19]. In light of the relatively few adverse effects during drug therapy with LEV, many clinicians use it as the first-line medication. International practice diverges widely: Sulthiame (which is said to be deteriorating cognitive functions) is considered as a first-line in Germany, Austria, Japan and Israel. VPA respectively in France, and LEV in USA. Polish recommendations include carbamazepine and lamotrigine as the first-line treatment, and levetiracetam and oxcarbazepine as a second line [34]. Children with bilateral findings on EEG a similar, good response to treatment with either sodium valproate or carbamazepine or oxcarbazepine. However children with unilateral findings on EEG were found to respond better to Carbamazepine or Oxcarbazepine [4].

Whether regular AED treatment overall mitigates or exacerbates the frequent cognitive and attentional comorbidities is still a matter of debates [19]. Seizure-free patients (seizures cessation for at least 12 months) have greater cortical thinning in MR imaging, exhibit higher baseline IQ scores and socioeconomic status (reflected in parental education) when compared to the nonremitted subgroup [21].

6. General conclusion

Knowledge about BECTS is growing in thanks to the efforts of clinicians to assess comorbities of the syndrome. Until recent years management was mostly wait-and-see strategy. Aside from seizures, cognitive and behavioral comorbidities cause substantial impact affecting about 2/3 children with this syndrome. BECTS children can avoid AED, because most of the abnormalities undergo long-lasting remission during adolescence with accompanying EEG improvement. Recent genetic discoveries of BECTS origins bring hope for targeted antiepileptic therapy and improvement of life quality of the patients.

Conflict of interest

None declared.

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None declared.

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