ORIGINAL ARTICLE



# Co-existence of Rolandic and 3 Hz Spike-Wave Discharges on EEG in Children with Epilepsy

*Anita N. Datta, Laura Wallbank, Peter K. H. Wong*

**ABSTRACT:** ***Objective:*** Benign epilepsy of childhood with central temporal spikes (BECTS) and absence epilepsy are common epilepsy syndromes in children with similar age of onset and favorable prognosis. However, the co-existence of the electrocardiogram (EEG) findings of rolandic spike and 3 Hz generalized spike-wave (GSW) discharges is extremely rare, with few cases reported in the literature. Our objective was to characterize the EEG findings of these syndromes in children in our center and review the electro-clinical features. ***Methods:*** All EEGs at BC Children's Hospital are entered in a database, which include EEG findings and clinical data. Patients with both centro-temporal spikes and 3 Hz GSW discharges were identified from the database and clinical data were reviewed. ***Results:*** Among the 43,061 patients in the database from 1992 to 2017, 1426 with isolated rolandic discharges and 528 patients with isolated 3 Hz GSW discharges were identified, and 20 (0.05%) patients had both findings: 3/20 had BECTS, and subsequently developed childhood absence epilepsy and 17/20 had no seizures characteristic for BECTS. At follow-up, 17 (85%) were seizure-free, 1 (5%) had rare, and 2 (10%) had frequent seizures. ***Conclusions:*** This is the largest reported group of patients to our knowledge with the co-existence of rolandic and 3 Hz GSW discharges on EEGs in one institution, not drug-induced. As the presence of both findings is extremely rare, distinct pathophysiological mechanisms are likely. The majority had excellent seizure control at follow-up, similar to what would be expected for each type of epilepsy alone.

**RÉSUMÉ: Coexistence de décharges rolandiques et de décharges à pointes-ondes de 3 Hz observées au moment d'EEG réalisés chez des enfants atteints d'épilepsie**. ***Objectif***: L'épilepsie bénigne de l'enfance à pointes centro-temporales (ou épilepsie rolandique bénigne [ERB]) et l'absence épileptique sont des syndromes épileptiques communs chez des enfants dont le pronostic est favorable et dont l'apparition des premiers symptômes s'est produite à un âge similaire. Cependant, la coexistence, lors d'EEG, de résultats montrant des décharges rolandiques et des décharges à pointes-ondes continues de 3 Hz demeure extrêmement rare, peu de cas ayant été signalés dans la littérature scientifique. Notre objectif a donc consisté à décrire les résultats d'EEG liés à ces syndromes dans le cas d'enfants fréquentant notre établissement et à examiner leurs caractéristiques électro-cliniques. ***Méthodes***: En plus de certaines données cliniques, tous les résultats d'EEG réalisés au *BC Children's Hospital* sont saisis dans une base de données. Tant les jeunes patients donnant à voir des décharges à pointes centro-temporales que ceux atteints de décharges à pointes-ondes continues de 3 Hz ont été identifiés à partir de cette base de données. Leurs données cliniques ont été ensuite passées en revue. ***Résultats***: Sur un total de 43 061 jeunes patients présents dans la base de données de 1992 à 2017, nous en avons identifié 1426 avec des décharges rolandiques isolées et 528 avec des décharges isolées à pointes-ondes de 3 Hz. À noter que seulement vingt d'entre eux, soit 0,05 %, étaient concernés par ces deux types de décharge. À cet égard, 3 sur 20 étaient atteints d'ERB et ont développé ultérieurement un syndrome d'absence épileptique; chez les 17 autres, aucune convulsion caractéristique de l'ERB n'a été observée. Lors d'un suivi, 17 (85 %) d'entre eux n'avaient plus de crises convulsives tandis que 1 (5 %) avait exceptionnellement des crises et 2 (10 %), des crises fréquentes. ***Conclusions***: À notre connaissance, il s'agit là du plus vaste groupe déclaré de patients donnant à voir, lors d'EGG menés au sein d'un seul établissement, une coexistence entre des décharges rolandiques et des décharges à pointes-ondes de 3 Hz, et ce, sans qu'elles n'aient été causées par des médicaments. Considérant que la présence de ces deux phénomènes est particulièrement inhabituelle, le rôle de divers mécanismes pathophysiologiques est fort probable. Fait à souligner, la majorité de ces patients ont pu montrer, au moment de leur suivi, une excellente maîtrise de leurs crises convulsives, maîtrise semblable à celle à laquelle on pourrait s'attendre pour chaque type d'épilepsie pris individuellement.

**Keywords:** Epilepsy—Pediatric, Absence epilepsy, Benign rolandic epilepsy, EEG

doi:10.1017/cjn.2018.364 Can J Neurol Sci. 2019; 46: 64-70

## Introduction

Benign epilepsy of childhood with central temporal spikes (BECTS) is the most common benign partial epilepsy of childhood, accounting for 13%-23% of all childhood epilepsies.[1,2] Typical EEG findings consist of diphasic spikes or sharp waves with prominent after-coming slow waves. Spikes have a characteristic of horizontal dipole configuration, with maximal

From the Department of Pediatrics, Division of Neurology, BC Children's Hospital, Vancouver, British Columbia, Canada (AND, PKHW); Department of Diagnostic Neurophysiology, BC Children's Hospital, Vancouver, British Columbia, Canada (LW, PKHW).

Received July 11, 2018. Final Revisions Submitted August 22, 2018. Date of Acceptance September 16, 2018.

*Correspondence to:* Anita Datta, FRCPC, CSCN Diplomate (EEG), Department of Pediatrics, University of British Columbia, BC Children's Hospital, 4480 Oak Street, Vancouver, BC, Canada V6H 3N1. Email: anita.datta@cw.bc.ca

negativity in the centro-temporal regions and positivity in the frontal regions.[3,4] It is well established that this EEG pattern can occur in patients without clinical seizures.[5] Conversely, childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE) are the different forms of generalized epilepsies, accounting for 2%-10%[6] and 0.2%-3%[6–8] of childhood epilepsies, respectively. Characteristic EEG findings include synchronous and symmetrical spike-wave paroxysms of at least 3 Hz associated with brief impairment of consciousness.[9,10]

Although both EEG findings have age-dependent occurrence, absence of significant anatomic lesion on neuroimaging, multifactorial etiology, genetic predisposition and favorable long-term outcome, they are distinct electro-clinical entities that rarely overlap in the same individual. Some suggest that the conditions may be part of a continuum,[11] while others contend that their co-existence is coincidental.[12,13] We describe 20 patients with the co-existence of 3 Hz generalized spike-wave (GSW) and rolandic discharge on EEG over a period of 25 years. Three had BECTS and later developed absence epilepsy, whereas 17 had absence epilepsy with rolandic discharges on EEG, without typical rolandic seizures. This small fraction of patients with co-existence of both EEG findings is suggestive that they are distinct electro-clinical markers that likely do not share a common etiology.

## Methods

All EEG investigations at BC Children's Hospital (BCCH) are entered in a database, which included EEG findings and clinical data obtained by an EEG technologist at each visit. The database was queried for patients with both 3 Hz GSW discharges and benign rolandic discharges (centro-temporal spikes and sharp waves with centro-temporal negativity and frontal positivity) on simultaneous or separate EEGs between 1992 and 2017.

Clinical data, including demographics, seizure types and frequency, underlying and/or co-existing neurological diagnosis, medications, development and neuroimaging were obtained from the database and a retrospective review of medical records was conducted. Seizure type was classified according to 2017 International League Against Epilepsy as CAE, JAE or BECTS.[14] Clinical outcome was evaluated by reviewing developmental milestones, neurologic exam, seizure frequency and medications at presentation and follow-up.

## Results

Among the 43,061 patients in the EEG database from 1992 to 2017, 1426 patients were identified with benign rolandic discharges and 528 patients with 3 Hz GSW discharges on EEG, and 20 patients (0.05%) were found to have both EEG findings on the same or follow-up EEGs (Tables 1 and 2).

### Patients with BECTS Who Developed CAE

Of the 20 patients, three fulfilled the diagnostic criteria for BECTS and CAE (Table 1). In these patients, as BECTS resolved, they developed CAE. Age of onset of seizure ranged from 4 to 9 years of age. All patients presented with the characteristic seizure manifestation of BECTS, including symptoms of hemi-facial or hemi-body motor involvement, mainly affecting the face and orthopharynx with speech arrest and hyper-salivation accompanied by a typical EEG pattern with sharp waves in the centro-

**Table 1: Features of patients with BECTS who later developed CAE. Clinical features of patients with BECTS and absence epilepsy**

| Case | Gender | Age at seizure onset | Age at rolandic trait onset | Age at 3 Hz onset | Overlap in absence and rolandic trait? | Initial medication | Total no. of medications | GTCS? | Total length of follow-up (years) | Seizure-free at last follow-up? | Development | School assistance? | Other co-morbidities |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 9 | 10 | 14 | Yes | VPA | 1 | Yes | 12 | Yes | No | No | — |
| 2 | F | 4 | 7 | 13 | No | VPA | 3 | No | 9 | Yes | No | No | Anxiety |
| 3 | F | 6 | 6 | 9 | Yes | CLB | 4 | No | 12 | No | No | No | Anxiety |

AED = anti-epileptic drug; CLB = clobazam; DD = developmental delay; F = female; M = male; VPA = valproic acid



https://doi.org/10.1017/cjn.2018.364 Published online by Cambridge University Press

https://doi.org/10.1017/cjn.2018.364 Published online by Cambridge University Press



**Table 2: Features of patients with CAE who also had rolandic trait on EEG. Clinical features of patients with absence epilepsy and benign rolandic trait**

| Case | Gender | Age at seizure onset | Age at rolandic trait onset | Overlap in absence and rolandic trait? | Initial medication | Total no. of medications | Total length of follow-up (years) | Seizure-free at last follow-up? | Development delay? | School assistance? | Other comorbidities |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 4 | 9 | No | LEV | 2 | 1 | Yes | No | No | ADHD |
| 2 | F | 3 | 5 | Yes | ETX | 2 | 5 | Yes | Yes | Yes | — |
| 3 | M | 6 | 6 | Yes | ETX | 2 | 9 | Yes | No | No | ADHD |
| 4 | F | 4 | 5 | Yes | ETX | 1 | 4 | Yes | Yes | Yes | Fine motor |
| 5 | F | 3 | 4 | Yes | CLB/ETX | 4 | 14 | Yes | Yes | Yes | Anxiety |
| 6 | F | 4 | 9 | Yes | CLB | 2 | 11 | No | Yes | Yes | Autism |
| 7 | F | 6 | 6 | Yes | ETX | 1 | 1 | Yes | ? | ? | ? |
| 8 | M | 6 | 6 | Yes | VPA | 1 | 5 | Yes | Yes | Yes | — |
| 9 | M | 4 | 4 | Yes | NONE | 0 | 2 | Yes | No | No | — |
| 10 | M | 7 | 7 | Yes | ETX | 2 | 7 | Yes | Yes | Yes | ADHD |
| 11 | F | 2 | 7 | Yes | PHB | 10 | 15 | Yes | Yes | Yes | — |
| 12 | F | 3 | 5 | Yes | VPA | 4 | 13 | Yes | Yes | Yes | ADHD + anxiety |
| 13 | F | 7 | 8 | Yes | ETX | 1 | 0.5 | Yes | No | No | — |
| 14 | F | 5 | 9 | Yes | LAM | 2 | 9 | Yes | No | Yes | — |
| 15 | M | 3 | 5 | Yes | ETX | 2 | 6 | Yes | No | Yes | — |
| 16 | F | 1.5 | 6 | Yes | ETX | 6 | 16.5 | No | Yes | Yes | — |
| 17 | M | 7 | 7 | Yes | ETX | 1 | 0.5 | Yes | No | No | — |

AED = anti-epileptic drug; CLB = clobazam; DD = developmental delay; ETX = ethosuximide; F = Female; LAM = lamotrigine; LEV = levetiracetam; M = Male; PHB = phenobarbital; VPA = valproic acid.

temporal regions with characteristic of horizontal dipole and normal background. One had a family history of epilepsy and one had a family history of febrile seizures. Two had a history of febrile seizures before the onset of BECTS. Two patients had neuroimaging (MRI), which were normal. The conversion of one seizure type to another was not secondary to medications. Patient 1 had BECTS until 13 years of age and was not treated with any antiseizure medications. He developed CAE at 11, with an overlap of the seizure types for 2 years. Patient 2 had BECTS from 4 to 9 years of age and treated with valproic acid (VPA) and subsequently clobazam (CLB), which was weaned at 11. At 13 years of age, she developed absence epilepsy. Patient 3 was diagnosed with BECTS at 6 years of age and treated with CLB. After being seizure-free for 3 years, this medication was weaned. As she was weaning the medication, she developed CAE, which did not resolve with the reintroduction of CLB, but to ethosuximide (ETX). All patients had long-term follow-up, ranging from 9 to 12 years. Patients 1 and 2 were seizure-free at last follow-up and Patient 3 had rare seizures. One had a mood and anxiety disorder and another had severe anxiety. All three patients had normal intellectual functioning.

We provide a more detailed clinical description of an exemplary patient (Patient 3 in Table 1).

### Patient 3

At 6 years of age, a right-handed female was referred to the neurology clinic for a 3-minute seizure consisting of staring, speech arrest, rhythmic mouth movements, excessive drooling and hand fumbling, with relative preservation of consciousness. Electrocardiogram showed central temporal spikes and sharp waves with characteristic horizontal dipole. She was started on CLB and had no further seizures for 3 years and the medication was weaned at age 10. MRI brain, development and neurological examination were normal. She had a history of three febrile seizures from 2 to 3 years of age. There was no family history of seizures.

At the time of the discontinuation of CLB, it was noted that she started to have absence seizures, and EEG at the time confirmed absence epilepsy, with six clinical seizures captured associated with 3 Hz GSW discharges. She continued to have left central temporal spikes and sharp waves. Clobazam was re-initiated, but the absence seizures were not controlled. Subsequently, she was started on ETX and then lamotrigine (LAM). At last follow-up, she was seizure-free on LAM, developmentally normal, but had an anxiety disorder.

### Patients with Absence Epilepsy and Rolandic Trait on EEG

In addition, 17 patients were identified with absence epilepsy with 3 Hz GSW discharges and simultaneous rolandic trait, without having rolandic seizures (Table 2). Clinical and electroencephalographic features of the 17 patients were as follows: age at onset of seizures ranged from 1.5 to 7 years, with a mean of 4.5 years. All had the following ictal manifestations: abrupt loss of

**Table 3: Literature review: patients with history of rolandic trait and 3 Hz spike-wave discharges on simultaneous or subsequent EEGs**

| Clinical seizures | Author | No. of patients | Drug-related conversion? (Yes/No, drug) |
|---|---|---|---|
| Rolandic seizures only | Ramelli | 1 | Yes, CBZ |
| Absence seizures only | Dimova | 7 | No, all VPA, CLZ, ETX |
| | Rimelli | 2 | No, VPA, none |
| | Anyanwu | 1 | No, ETX |
| | Niedermeyer | 2 Dimova | |
| Concomitant rolandic and absence seizures | Montenegro | 1 | No, VPA |
| | Ramelli | 1 | No, VPA |
| | Verotti | 4 | No, 3 VPA; 1 LEV |
| | Echenne | 1 | No |
| Rolandic followed by absence seizures | Gambardella | 1 | No |
| | Catania[40] | 1 | Yes, VPA/LAM |
| | Ramelli | 1 | No, VPA |
| | Verotti | 2 | No, 1 VPA; 1 LEV |
| | Echenne | 1 | No |
| Absence followed by rolandic seizures | Dimovia | 1 | No, end of tx of PHB and CLZ |
| | Cerminara | 2 | No, as meds weaned VPA/LAM |
| | Verotti | 5 | No, LEV, VPA, ETX |
| Rolandic followed by "absence-like" seizures (not classic 3 Hz) | Dimova | 6 | Yes, (4 CBZ, 2 VPA) |
| | Hamano | 1 | Yes, PHB |
| | Beaumanoir | 6 | ? not described |
| | Grosso | 2 | Yes, OCBZ |

CBZ = carbamazepine; CLZ = clonazepam; ETX = ethosuximide; LAM = lamotrigine; LEV = levetiracetam; OCBZ: oxcarbamazepine; PHB = phenobarbital; VPA = valproic acid.



https://doi.org/10.1017/cjn.2018.364 Published online by Cambridge University Press

consciousness and quick recovery. Some had automatisms, fluttering of the eyelids and brief myoclonic jerks. All had bilateral synchronous symmetrical discharges of GSW at 3 cycles per second. Neurologic examination was normal in all and 12 had neuroimaging (11 with MRI and 1 with CT), of which 10 were normal, 1 showed non-specific delayed myelination. There was a family history of epilepsy in seven patients and family history of febrile seizures in one individual. The total number of medications each patient tried ranged from 0 to 10, with a mean of 2.53. Follow-up varied from 0.5 to 16.5 years, with a mean of 7.35 years. At the time of last follow-up 15 were seizure-free, one diagnosed with GLUT-1 deficiency continued to have daily absence seizures and one had occasional eyelid fluttering, but was not on any medications at last follow-up. Various co-morbidities were described, including attention deficit hyperactive disorder (ADHD) (four patients), anxiety (two patients), requirement of school assistance (11 patients) and developmental delay (nine patients).

## Discussion

We have described 20 patients with both 3 Hz GSW discharges and benign rolandic trait, representing 0.05% of patients in our EEG population. BC Children's Hospital is the only pediatric tertiary care center in British Columbia, Canada, serving a population of 4.7 million people. There are few reports of overlap of both EEG findings in the literature (Table 3).

Of our patients three were affected by BECTS, and upon remission of this idiopathic generalized epileptic syndrome with typical absences developed. Moreover, five patients with similar presentation, not thought to be drug-induced, have been previously described.[15–18] Gelisse et al reviewed patients over 11 years with rolandic EEG discharges. Of 66 patients identified with typical rolandic spikes, none of the patients had 3 Hz GSW. Therefore, they concluded that there is no continuum between the two EEG findings.[12] Others have described the conversion of benign rolandic to "absence-like epilepsy" that is likely drug-related.[11,19–21] Lamotrigine, phenobarbital (PHB) and carbamazepine (CBZ) have been implicated. None of our patients were on these medications at the time of onset of the absence epilepsy.

Dimova described six patients who developed "absence-like" seizures after a history of BECTS, of which four initially received CBZ, which is known to precipitate or aggravate absence seizures in epileptic patients. In their study, none of the children demonstrated the classic 3 Hz GSW discharge with their absence seizures and there was a strong laterality of the discharges, suggesting that the absences might be of a secondarily generalized origin, unlike that observed in idiopathic absence epilepsy.[19]

The transition from focal seizures to apparently generalized seizures is not a common phenomenon. There are several descriptions of "atypical partial benign epilepsy of childhood" or "pseudo-Lennox syndrome."[22,23] In this condition, children with focal epilepsy experience frequent atonic, atypical absence and myoclonic seizures, often with non-convulsive status epilepticus, as well as cognitive and behavioral disturbances. Some cases have been provoked by CBZ and other anti-seizure medications.[24]

Although 3 Hz GSW discharges are rare, brief subclinical bursts of bilateral abnormalities occur in about 25% of patients with BECTS.[12] Therefore, generalized GSW in BECTS has not been considered a specific marker for the continuum between focal and generalized epilepsies, as their appearance is likely the result of bilateral synchrony and not of generalized hyperexcitability.

In our study and in the literature, incidental rolandic spikes in patients with absence epilepsy were the most common finding in those with both types of EEG findings. We had 17 such patients and an additional 12 are collectively reported in the literature.[16,19,25,26] In general, typical rolandic discharges are seen in 0.7% of awake recordings or normal children without a history of seizures;[5] if recordings had sleep, this number may be higher. The percentage of children with rolandic discharge who develop clinically apparent seizures is unclear. The risk is probably $< 10\%$, on the basis of reported incidences of BECTS and of rolandic EEG discharges in normal children.[27] Therefore, rolandic discharges are considered most likely an incidental finding in children with seizures or spells whose semiology is not suggestive of BECTS. Benign rolandic trait could simply be a genetic expression and its overlap with CAE could be coincidental expression of two genetic predispositions.

Some have researched circuit mechanisms common to GSW discharges and focal discharges. One study demonstrated that the thalamic circuit, integral for 3 Hz generalized discharges, is capable of producing local recurrent activity that is highly organized and repetitive, such as rolandic discharges. Huntsman et al demonstrated that mutant mice that were devoid of a particular GABA, subunit (p3) lacked functional connectivity between TRN cells, which promote or desynchronize thalamocortical oscillations. These mice had absence seizures and widespread hypersynchrony in isolated thalamic slices. Of note, a small fraction (10%) of isolated thalamic slices from control animals demonstrated focal reverberant activity. Therefore, network responses that resembled the activity of absence seizures could evoke restricted activity in small regions of the thalamic slice, as seen in focal epilepsy.[28] Another study demonstrated that rolandic discharges in sleep have a high positive correlation with delta and spindle activity.[29] These suggest rolandic discharges may have a connection to thalamocortical activity, which is necessary for spindles and 3 Hz spike-wave discharges. Further evidence shows that the generation of 3 Hz GSW discharge relies on dual activation of the thalamus and cortex.[30,31]

Benign epilepsy of childhood with central temporal spikes and absence epilepsies have multifactorial etiology, with some genetic predilection, although unique from each other. As of yet, no overlapping genes have been described for both types of epilepsies. Rare cases associated with Elongator Protein Complex 4, which has roles in transcription and tRNA modification[32] and KCNQ2 and KCNQ3 mutations[33] have been described. In absence epilepsy, rare monogenetic etiology has been reported. Subunits of ion channels, GABRG2, CLCN2, GABRA1 and CACNA1H have been implicated.[34] Genetic studies in the patients with dual findings would be of great interest, to determine any link.

There are eight reported clinical cases with idiopathic generalized epilepsy onset: CAE or JAE, who, after a period of seizure freedom, experienced partial seizures with the electro-clinical characteristics of BECTS.[13,17,19] This was a common presentation described by Verotti in his multicenter trial of those with both seizure types.[17] We found no such cases in our population. There are seven cases in the literature of patients who simultaneously have both seizure types.[16–18,35] Again, this was not the cases in



https://doi.org/10.1017/cjn.2018.364 Published online by Cambridge University Press

our patients; as the first seizure type was remitting, the second seizure type developed. Patient 1 (Table 1) did have an overlap of both seizure types for 2 years.

Patients with GLUT-1 deficiency have a defect in the facilitative glucose transporter GLUT-1[37] and may present with focal[36] and/or generalized seizures in early infancy, including early-onset absence seizures (<4 years of age).[37,38] Multifocal or generalized discharges, including 3 Hz GSW discharges, often with background slowing, can be seen on EEG.[36,38] Early diagnosis is important, as GLUT-1 patients do not respond to anti-seizure medications, but to the ketogenic diet.[39] In our study, six patients presented with absence seizures under the age of 4 (Table 2). In 5/6 patients, good response to anti-seizure medications was not consistent with GLUT-1 deficiency. One patient was tested for GLUT-1 deficiency due to presentation at 1.5 years of age and the diagnosis was confirmed by cerebral spinal fluid profile. They were subsequently treated with the ketogenic diet. This patient had no history of focal seizure semiology and rolandic spikes had characteristic horizontal dipole formation.

Overall, despite having both EEG findings, the majority of our patients had good clinical outcome, regardless of clinical presentation or number of medications needed to control the seizures. At last follow-up, most patients were seizure-free or had rare seizures. This is similar to the patients reported by Verotti, where all patients with both clinical seizure types showed excellent clinical prognosis.[17]

To the best of our knowledge, this is the largest cohort of patients in one center with the co-existence of both EEG findings in the same individual that are not drug-induced. The rarity of the co-existence of these two EEG findings implicates a separate pathophysiology and genetic susceptibility. Further multicenter and genetic studies would contribute to our understanding. Ultimately, the majority of patients, regardless of clinical presentation, showed an improvement or normalization in their EEGs of both focal and generalized paroxysmal activity and had good seizure outcome, suggesting that the presence of dual findings does not alter the favorable prognosis of either type of epilepsy.

## Acknowledgments

The authors thank Jeffrey Zhi for his help in accessing archived EEGs and for his assistance with data entry. Also, thanks to Ruth Janke for helping to identify patients from the EEG database.

## Financial Support

This research received no specific grant from any funding agency in the public, or from commercial or not-for-profit sectors. All work was done at BCCH.

## Disclosures

AND, LW, and PKHW have no conflicts of interest to declare.

## Statement of Authorship

AND developed the original concept and study design of the manuscript. She obtained clinical data by performing a detailed chart review and entering the data in a spreadsheet. She did a literature review on the subject and created Table 3. She helped to analyze the data, drafted the manuscript, then reviewed and edited it for important intellectual content.

LW participated in identifying eligible patients. She helped obtain pertinent clinical information from the EEG database. She also helped to analyze the data. She prepared Tables 1 and 2, summarizing the clinical data. She reviewed and edited the manuscript for important intellectual content.

PKHW created the EEG database, which was crucial to identify patients. He provided guidance in study design and analysis. He reviewed and edited the manuscript for important intellectual content.

All authors gave approval to the final version of the manuscript to be submitted and are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Ethics Approval

Approved by University of British Columbia Ethics Board H17-01949.

## References

1. Cavazzuti GB. Epidemiology of different types of epilepsy in school age children of Modena, Italy. Epilepsia. 1980 Feb 1;21(1):57-62.
2. Kriz M, Gazdik M. Epilepsy with centrotemporal (Rolandic) spikes. A peculiar seizure disorder of childhood. Neurologia i neurochirurgia polska. 1978;12(4):413-9.
3. Gregory DL, Wong PK. Topographical analysis of the centrotemporal discharges in benign rolandic epilepsy of childhood. Epilepsia. 1984 Dec 1;25(6):705-11.
4. Gregory DL, Wong PK. Clinical relevance of a dipole field in rolandic spikes. Epilepsia. 1992 Jan 1;33(1):36-44.
5. Cavazzuti GB, Cappella L, Nalin A. Longitudinal study of epileptiform EEG patterns in normal children. Epilepsia. 1980 Feb 1;21 (1):43-55.
6. Jallon P, Latour P. Epidemiology of idiopathic generalized epilepsies. Epilepsia. 2005 Nov 1;46(s9):10-4.
7. Obeid T. Clinical and genetic aspects of juvenile absence epilepsy. J Neurol. 1994 Aug 1;241(8):487-91.
8. Loiseau P. Childhood absence epilepsy. In: Roger J, Bureau M, Dravet C, Dreifuss FE, Perret A, Wolf P editors Epileptic syndromes in infancy, childhood and adolescence. London: Libbey Eurotext; 1992, pp. 135-50.
9. Dravet C, et al. (eds) Epileptic syndromes in infancy, childhood and adolescence, 2nd ed. London: John Libbey & Company; 1992, pp. 135-50.
10. Wolf P. Juvenile absence epilepsy. In: Roger J, Bureau M, Dravet C, et al. (eds) Epileptic syndromes in infancy, childhood and adolescence, 2nd ed. London: John Libbey & Company; 1992:307-12.
11. Beaumanoir A, Ballis T, Varfis G, Ansari K. Benign epilepsy of childhood with rolandic spikes. Epilepsia. 1974 Sep 1;15 (3):301-15.
12. Gelisse P, Genton P, Bureau M, et al. Are there generalised spike waves and typical absences in benign rolandic epilepsy? Brain Dev. 1999 Sep 1;21(6):390-6.
13. Cerminara C, Coniglio A, El-Malhany N, Casarelli L, Curatolo P. Two epileptic syndromes, one brain: childhood absence epilepsy and benign childhood epilepsy with centrotemporal spikes. Seizure Eur J Epilepsy. 2012 Jan 1;21(1):70-4.
14. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: position paper of the ILAE commission for classification and terminology. Epilepsia. 2017;58:522-30.

15. Gambardella A, Aguglia U, Guerrini R, Morelli F, Zappia M, Quattrone A. Sequential occurrence of benign partial epilepsy and childhood absence epilepsy in three patients. Brain Dev. 1996 May 1;18(3):212-5.
16. Ramelli GP, Donati F, Moser H, Vassella F. Concomitance of childhood absence and Rolandic epilepsy. Clin Electroencephalogr. 1998 Oct;29(4):177-80.
17. Verrotti A, Casciato S, Spalice A, et al. Coexistence of childhood absence epilepsy and benign epilepsy with centrotemporal spikes: a case series. Eur J Paediatr Neurol. 2017 May 1;21(3):570-5.
18. Echenne B, Rivier F, Roubertie A, Touzery A, Humbertclaude V. Simultaneous occurrence of benign partial epilepsy and childhood absence epilepsy: report of 2 cases in 2 families. Epilepsia. 1997 Jan 1;38:120.
19. Dimova PS, Daskalov DS. Coincidence of rolandic and absence features: rare, but not impossible. J Child Neurol. 2002 Nov;17 (11):838-46.
20. Hamano SI, Mochizuki M, Morikawa T. Phenobarbital-induced atypical absence seizure in benign childhood epilepsy with centrotemporal spikes. Seizure Eur J Epilepsy. 2002 Apr 1;11 (3):201-4.
21. Grosso S, Balestri M, Di Bartolo RM, et al. Oxcarbazepine and atypical evolution of benign idiopathic focal epilepsy of childhood. Eur J Neurol. 2006 Oct 1;13(10):1142-5.
22. Aicardi J, Chevrie JJ. Atypical benign partial epilepsy of childhood. Dev Med Child Neurol. 1982 Aug 1;24(4):281-92.
23. Hahn A, Pistohl J, Neubauer BA, Stephani U. Atypical "benign" partial epilepsy or pseudo-Lennox syndrome. Part I: symptomatology and long-term prognosis. Neuropediatrics. 2001 Feb;32 (01):1-8.
24. Guerrini R, Belmonte A, Genton P. Antiepileptic drug-induced worsening of seizures in children. Epilepsia. 1998 Mar 1;39(S3.
25. Anyanwu C, Ghavami F, Schuelein M, Motamedi GK. Ethosuximide-induced conversion of typical childhood absence to rolandic spikes. J Child Neurol. 2013 Jan;28(1):111-4.
26. Niedermeyer E. Complexities of primary generalized epilepsy. Clin Electroencephalogr. 1981 Oct;12(4):177-91.
27. Wirrell E, Camfield CS, Camfield PR. Idiopathic and benign partial epilepsies of childhood. In: Wyllie's treatment of epilepsy: principles and practice, 5th ed. 2012 Feb 17. Wolters Kluwer Health.
28. Huntsman MM, Porcello DM, Homanics GE, DeLorey TM, Huguenard JR. Reciprocal inhibitory connections and network synchrony in the mammalian thalamus. Science. 1999 Jan 22;283 (5401):541-3.
29. Nobili L, Baglietto MG, Beelke M, et al. Modulation of sleep interictal epileptiform discharges in partial epilepsy of childhood. Clin Neurophysiol. 1999 May 1;110(5):839-45.
30. Aghakhani Y, Bagshaw AP, Benar CG, et al. fMRI activation during spike and wave discharges in idiopathic generalized epilepsy. Brain. 2004 May 1;127(5):1127-44.
31. Gotman J, Kobayashi E, Bagshaw AP, Bénar CG, Dubeau F. Combining EEG and fMRI: a multimodal tool for epilepsy research. J Magn Reson Imaging. 2006 Jun 1;23(6):906-20.
32. Strug LJ, Clarke T, Chiang T, et al. Centrotemporal sharp wave EEG trait in rolandic epilepsy maps to elongator protein complex 4 (ELP4). Eur J Hum Genet. 2009 Sep;17(9):1171.
33. Neubauer BA, Waldegger S, Heinzinger J, et al. KCNQ2 and KCNQ3 mutations contribute to different idiopathic epilepsy syndromes. Neurology. 2008 Jul 15;71(3):177-83.
34. Lu Y, Wang X. Genes associated with idiopathic epilepsies: a current overview. Neurol Res. 2009 Mar 1;31(2):135-43.
35. Montenegro MA, Guerreiro MM. Coexistence of childhood absence and rolandic epilepsy. J Child Neurol. 2006;21:535-6.
36. Wolking S, Becker F, Bast T, et al. Focal epilepsy in glucose transporter type 1 (Glut1) defects: case reports and a review of literature. J Neurol. 2014 Oct 1;261(10):1881-6.
37. De Vivo DC, Trifiletti RR, Jacobson RI, Ronen GM, Behmand RA, Harik SI. Defective glucose transport across the blood-brain barrier as a cause of persistent hypoglycorrhachia, seizures, and developmental delay. N Engl J Med. 1991 Sep 5;325 (10):703-9.
38. Klepper J, Willemsen M, Verrips A, et al. Autosomal dominant transmission of GLUT1 deficiency. Hum Mol Genet. 2001 Jan 1;10(1):63-8.
39. Klepper J, Scheffer H, Leiendecker B, et al. Seizure control and acceptance of the ketogenic diet in GLUT1 deficiency syndrome: a 2- to 5-year follow-up of 15 children enrolled prospectively. Neuropediatrics. 2005 Oct;36(05):302-8.
40. Catania S, Cross H, De Sousa C, Boyd S. Paradoxic reaction to lamotrigine in a child with benign focal epilepsy of childhood with centrotemporal spikes. Epilepsia. 1999;40: 1657-60.



https://doi.org/10.1017/cjn.2018.364 Published online by Cambridge University Press