ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803–5253

REGULAR ARTICLE

Cognitive and linguistic abnormalities in benign childhood epilepsy with centrotemporal spikes

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Keywords
Antiepileptic treatment, Expressive vocabulary, Global intelligence, Neuropsychological impairments, Rolandic epilepsy

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Received
29 August 2010; revised 23 December 2010; accepted 11 January 2011.

DOI:10.1111/j.1651-2227.2011.02159.x

ABSTRACT

Aim: To assess the cognitive function and language ability in children with benign partial epilepsy with centrotemporal spikes.

Methods: Twenty-five patients with benign partial epilepsy with centrotemporal spikes were included. They were divided into two subgroups. Group I: 10 patients with rolandic focus who were not treated. Group II: 15 patients with rolandic focus receiving treatment. A third Group of 12 healthy subjects have been studied. All children underwent standardized neuropsychological testing: electroencephalogram recording, Wechsler Intelligence Scale for Children-revised, Peabody Picture Vocabulary Test-III (PPVT-III) and Boston Naming Test (BNT), both during active disease (T1) and 2 years after recovery from epilepsy (T2).

Results: At T1 evaluation, no significant differences in group I and II patients about general intelligence, when compared with controls, were found. Group I and II patients were impaired with respect to controls in the receptive and expressive vocabulary evaluated with PCVT-III and BNT, respectively. At T2 evaluation, group I and II patients showed a normalization of the language abnormalities.

Conclusion: Deficits of speech-related abilities can be detected in children with this type of epilepsy: these dysfunctions seem to be independent of the effects of antiepileptic treatment and are reversible after remission of epilepsy.

INTRODUCTION

Benign rolandic epilepsy of childhood with centrotemporal spikes (BECTS) is the most common form of epilepsy in childhood. Its onset is between the ages of 2 and 13 years, with a peak at 7–8 years, usually followed by recovery during adolescence (1). Seizures predictably occur during sleep, often in the early morning hours.

Benign rolandic epilepsy of childhood with centrotemporal spikes can be associated with mild cognitive and learning difficulties; poor performance is reported in a number of functional domains including language (2–5), attention (6,7), spatial perception (8), memory (9), executive function (2,10) and academic achievement (11). Despite many studies, there are conflicting data in neuropsychological function of these patients and it is still unclear if epileptiform activity might be an important determinant of cognitive difficulties in BECTS. In addition, there are very few longitudinal studies evaluating the patients after resolution of epilepsy.

Our prospective study aimed to characterize neuropsychological function in a sample of children followed at the same institutions since their diagnosis, to assess the relationship between electroencephalogram (EEG) findings and the neurocognitive function explored and to evaluate whether the abnormal neuropsychological findings were transient.

MATERIALS AND METHODS

Subjects

In our prospective study, we enrolled 26 children (age range from 7.5 to 11.3 years) affected by BECTS, as followed up, at the Department of Paediatrics, University of Chieti, University of Rome and at the Department of Child Neuropsychiatry, University of Naples. The study began in April 2005, and the children were followed by periodical clinical and EEG evaluations from the onset of epilepsy.

Parents of the participants provided informed consent, and the study was approved by the ethical committee of the University of Chieti.

Inclusion criteria were as follows: (i) age over 6 years; (ii) uneventful pregnancy and delivery, normal neonatal status and early psychomotor development; (iii) normal

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intelligence (full-scale intelligence quotient above 80); (iv) normal neurological examination and brain MRI; (v) right handedness and no family history of left handedness; (vi) normal auditory functioning. Diagnosis of BECTS was made according to criteria defined by the International Classification of Epilepsy and Epileptic Syndromes (12). The typical seizures were hemifacial, characterized by clonic manifestations involving the hemiface, sometimes preceded by unilateral paresthesia involving tongue, lips, gums and cheek; the jerks were often associated with a lateral tonic deviation of the mouth involving lips and tongue, resulting in drooling. The seizures lasted from less than a minute to 5 min and spread to the homolateral arm and, rarely, to the leg. In all patients, EEGs were recorded during wakefulness with hyperventilation and photic stimulation and during drowsiness and sleep (stages 1–4); all patients showed a normal, well-organized and symmetrical background activity. We recorded only interictal EEGs: in all patients, we found typical centrotemporal spikes, clearly localized in the central regions; the main spikes component was diphasic with a maximum surface, negative, rounded peak followed by a smaller positive peak; this was followed by a negative or negative–positive slow wave. A relatively minute positive spike often preceded this spike slow wave complex. The spikes significantly increased in frequency during drowsiness and throughout all sleep stages. Subjects studied were divided into three groups, and patients were not randomized to treatment. Group I consisted of 10 patients (four boys and six girls) aged between 8.0 and 11.2 years [mean standard deviations (SD) ± 9.6 ± 1.6] at the onset of the first seizure. They all had a rolandic focus, and were not given any treatment, having experienced only one seizure (seven patients) or very rare seizures, not more than three per year (three patients). Group II consisted of 16 patients (seven boys and nine girls); age of the onset of the first seizure was between 7.8 and 11.3 years (mean ± SD 9.5 ± 1.8). They had a rolandic focus and were treated with various antiepileptic drugs (AEDs) monotherapy: carbamazepine in six cases, valproic acid in seven cases and levetiracetam in three cases. After the first seizure, the patients of this group suffered from very frequent seizures (two or three seizures in the first week from the onset); therefore, after the third seizure, we began antiepileptic therapy in all patients of this group. All patients showed an excellent response to therapy: after at least 5 months from the beginning of therapy, all children were seizure-free. The duration of treatment ranged from 2.0 to 3.1 years (mean ± SD 2.5 ± 0.6). Control group (group III) comprised 12 healthy subjects aged from 7.5 to 11.2 years (mean ± SD 9.3 ± 1.8) of the same sex and socioeconomic status with no known learning, language or neurological problems. Each control participant underwent the same EEG recordings and neuropsychological evaluations as the group I and group II patients to rule out neurological and sensory impairment, as well as undiagnosed seizure disorders or EEG abnormalities. All subjects studied attended normal schools and their school records were within the average range for their class.

Diagnostic workup

All patients underwent clinical neurological examinations, brain MRI and EEG evaluations. Awake and sleep EEG recordings were performed. Electrodes were placed according to the International 10–20 System. EEGs were analysed visually by the senior author and scored according to Bast et al. (13) and Aebyet al. (14). Five grades were defined (grade 0 = normal EEG; grade 1 = normal background, unilateral centro-temporo-parietal sharp wave focus; grade 2 = normal background, bilateral independent sharp waves located in the centro-temporo-parietal electrodes; grade 3 = destructured background, intermittent slow wave focus, sharp waves diffusing to one hemisphere or multiregional sharp waves; grade 4 = destructed background, intermittent slow wave focus, sharp waves diffusing to both hemispheres). Only patients with EEG grades 1 and 2 were included, those with grades 3 and 4 were considered atypical and, therefore, excluded from the study; one patient of group II was excluded from the study for this reason.

Neuropsychological assessment

General intelligence was measured with the Wechsler Intelligence Scale for Children-revised (WISC-R) to verify cognitive performance in both qualitative and quantitative terms and it covers a total intelligence quotient (TIQ) consisting of two types of evaluation: that of cognitive performance related to verbal aspect (verbal intelligence quotient, VIQ) and that of cognitive performance related to nonverbal and, therefore, to performance (performance intelligence quotient, PIQ). With respect to language, receptive vocabulary was evaluated with the Peabody Picture Vocabulary Test-III (PPVT-III) (15); moreover, Boston Naming Test (BNT) was used to identify naming deficiencies and impaired word-retrieval capacities (16). Neuropsychological tests were given to all participants within 7 days after their EEG recordings.

Study design

All children were carefully evaluated from the onset of the epilepsy (periodical clinical and EEG evaluations have been performed in all children) for at least 4 years; the two assessments that are subjects of this report have been carried out after 1 year from the onset of the disease (**T1**) and 2 years after the remission (after at least 8 months from the withdrawal of AED treatment in the Group II patients) (**T2**). All patients were treated with AED-monotherapy: 6 patients with carbamazepine, 7 with valproic acid and 3 with levetiracetam.

At T1 complete diagnostic workup, complete cognitive assessment was performed. Re-evaluation at T2 consisted of complete clinical neurological and psychiatric investigations, as well as EEGs including sleep.

Statistical analyses

Means and SD were calculated. The Statistical Package (IBM, Somers, NY, USA) for the Social Sciences version for Windows 10.0 was used, and the level of significance considered was $p < 0.05$. Chi-square test, *T* test, ANOVA and

nonparametric tests for independent samples were carried out depending on the situation under analysis. Statistical analysis of the data was performed using means and their corresponding relative SDs; raw scores were converted into age-based normalized *T* scores (mean 50, SD 10), and then means were obtained. A test for independent samples was conducted to compare the performance of subjects with BECTS and control subjects and a *T* test for paired samples to compare data within subjects. A one-way ANOVA was used to compare neuropsychological performance according to EEG features and a least significant difference post hoc analysis to investigate which groups differed from each other (patients were grouped by side of epileptic spikes).

RESULTS

Intake data (T1)

A total of 25 patients were studied; the relevant data of the three groups are shown in Table 1. EEG recordings were grade 1 in 9 (36%) patients with right hemispheric foci and in 7 (28%) patients with left hemispheric foci. Independent bilateral foci (EEG grade 2) were found in 9 (36%) patients.

Cognitive performance

Our results did not show a significant difference in the general intelligence of the three groups, which was measured with TIQ, VIQ and PIQ. Furthermore, these parameters appeared to be independent **of** AED treatment, age of patients and age of onset; moreover, no significant difference was found between patients with right unilateral, left unilateral or bilateral foci.

Receptive and expressive vocabulary

Group I and II patients displayed significantly lower results than controls (group III) in their ability to recognize and express interpersonal relations, measured by PPVT and BNT. They did not differ according to their EEG focus, AED treatment, age of onset, age of patients and EEG grade. Furthermore, group I showed data similar to those of group II for PPVT and BNT. Again, no significant differences were found according to the focus side, AED treatment, age of patients and age of onset.

Results at T2

No patient and control was lost at follow-up. All 25 children showed normal EEG during wakefulness and sleep.

Cognitive performance

Group I and group II patients continued to show normal performance with regard to TIQ, VIQ and PIQ, when compared with healthy subjects. Moreover, comparison between group I and group II patients showed no significant difference.

Receptive and expressive vocabulary

No significant difference in PPVT and in BNT was recorded either between group I and group II subjects, or between the two groups and healthy controls.

Table 1 Neuropsychological results as mean (standard deviations) for patients (group I and group II) and for the control subjects (group III), at the first (T1) and second (T2) evaluation

Group	Sex	Age (year, month) (range)	Side of focus	TIQ		VIQ		PIQ		PPVT-III		BNT	
				T1	T2	T1	T2	T1	T2	T1	T2	T1	T2
I (10)	F/M (6/4)	8.0–11.2	Right (4)	108.72 (14.96)	107.56 (13.49)	104.78 (10.95)	105.67 (10.49)	117.94 (16.22)	118.33 (20.97)	80.14 (18.46)*	100.87 (16.44)	28.65 (11.57)*	40. 67 (10.26)
			Left (2)	110.54 (16.86)	110.73 (16.74)	106.25 (11.57)	106.84 (10.99)	115.68 (20.07)	116.68 (19.76)	80.56 (16.78)*	100.34 (16.14)	29.37 (11.53)*	40.21 (10.66)
			Bilateral (4)	105.11 (14.23)	106.56 (13.78)	107.35 (11.59)	108.25 (11.83)	114.55 (17.96)	115.46 (20.64)	79.97 (18.26)*	99.75 (16.35)	28.68 (11.73)*	40.13 (10.78)
II (15)	F/M (7/8)	7.8–11.3	Right (6)	105.93 (14.78)	105.27 (15.17)	106.65 (11.33)	106.89 (11.23)	115.83 (18.12)	116.45 (19.56)	80.76 (17.68)*	99.23 (16.53)	27.77 (11.72)*	40.55 (10.48)
			Left (6)	106.83 (13.56)	107.34 (13.58)	105.87 (11.25)	106.56 (11.36)	110.76 (17.56)	110.45 (17.69)	79.29 (16.91)*	99.62 (16.71)	27.39 (11.96)*	40.17 (10.77)
			Bilateral (3)	106.82 (13.98)	106.97 (13.61)	106.64 (11.62)	106.98 (11.71)	109.26 (16.37)	110.77 (17.83)	80.48 (16.74)*	98.15 (17.10)	27.22 (12.26)*	39.85 (11.35)
III (12)	F/M (5/7)	7.5–11.2		118.70 (11.14)	117.58 (11.24)	113.70 (11.62)	112.32 (11.74)	117.34 (10.69)	118.57 (11.52)	102.3 (16.84)	102.46 (16.82)	40.82 (10.33)	40.69 (10.47)

TIQ = Total Intelligence Quotient; VIQ = Verbal Intelligence Quotient; PIQ = Performance Intelligence Quotient; PPVT-III = Peabody Picture Vocabulary Test-III; BNT = Boston Naming Test.
*$p < 0.05$ vs. group III (controls) and vs. T2 evaluation.

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DISCUSSION

In general, evaluating the relationship between epilepsy and disorders of cognitive function is complex because of the different factors involved, such as age-at-onset, type, frequency and severity of seizures, the existence of underlying lesions, focus side, AED treatment and the amplitude of the discharges. BECTS is a good model for such an evaluation as age-at-onset is fairly homogeneous, there are few seizures, treatment is not systematic and of short duration when given and there are no underlying cerebral lesions.

This study analyses intelligence and language competence in a sample of children with BECTS: we did not find a significant difference between patients and controls in terms of WISC-R test, in accordance with some studies (3,17–19) but in contrast with others (2,20–22); in particular, Vago et al. (19) demonstrated that children with BECTS had a TIQ and a VIQ within the normal range.

In the area of verbal abilities, our study showed that during the active disease, impairments in expressive and receptive vocabulary can be detected. Some studies have shown significantly greater impairment in cognitive function, particularly in the areas of language ability, in patients on AEDs treatment compared with those untreated (7); this could be attributed to two reasons: the disease is more severe and requires treatment; therefore, it is this severity of the seizures that makes the difference between treated and untreated patients. This hypothesis is supported by works reporting that the higher spike frequency on EEG appeared to correlate with poorer neuropsychological performance (2,19,23,24). The second reason is that changes in cognitive abilities are because of adverse effects of AEDs. In fact, drug treatment is often considered as a potential bias in the interpretation of the existence of effects of epilepsy on cognitive function, because several researchers have demonstrated cognitive deficits in children taking AEDs (25). In our study, there were no differences in cognitive abilities between children taking AEDs and those not taking AEDs. The absence in our study of a significant difference between treated and untreated groups does not support a relationship between AED treatment and the occurrence of neuropsychological disorders. These results are in agreement with other data reported in literature (8,11,23). In particular, a recent study assessed prospectively language and speech ability in children with BECTS: mild deficits in both receptive and expressive grammar and in vocabulary were found, and no significant difference between patients with and without AED treatment concerning speech and school performance was observed, suggesting that an improvement in cognitive abilities examined cannot be explained as the result of AED treatment (26).

With regard to the effects of epilepsy on cognitive disorders, our experience suggests a role of the epilepsy *per sè*. In fact, some authors have suggested that paroxysmal abnormalities may alter cerebral mechanisms underlying cognitive activity and that the pattern of functional cerebral representation in patients with focal epilepsy depends on the focus side (27); paroxysmal abnormalities might be responsible for an impairment of brain maturation even in regions distant from discharges.

In our study, the laterality of the EEG focus was not related to performance in tests, as was already found in earlier works that considered this variable (8,23,25). In contrast, some studies have reported side-specific deficits: impairment in attention and visuospatial tests, but not in verbal span, in the case of prevalently right-sided anomalies (7,24) or in language tests in the case of left-sided prevalence (5).

Finally, our results at T2, after complete recovery from BECTS, demonstrated that impairments PPVT and BNT were no longer found. Accordingly, in previous studies (2,6,8), at remission, patients exhibited a normalization of neuropsychological anomalies. In contrast, other authors (24) found residual deficit even in patients whose seizures and EEGs had been resolved. Because in our study, both group I and group II patients, after remission of seizures, returned to show normal results, and it seems that language defects are reversible whether patients are treated or not; the reversibility of the deficiencies is not related to the withdrawal of therapy but to the disappearance of the seizures.

A relatively brief, limited test battery was used in this study, and it is possible that a more comprehensive evaluation could have uncovered other areas of cognitive or behavioural concern. However, our study has compared the performance results of the patients with normative data, using a control group.

In conclusion, in patients with BECTS, cognitive defects in receptive and expressive vocabulary can be detected, and these problems appear both in treated patients and untreated patients; at remission from BECTS, both **deficiencies** are no longer present; **therefore**, the deterioration of some cognitive abilities may be explained as the result of a negative impact of the BECTS itself on neuropsychological function.

References

1. Shields WD, Snead OC. Benign epilepsy with centrotemporal spikes. *Epilepsia* 2009; 50: 10–5.
2. Baglietto MG, Battaglia FM, Nobili L, Tortorelli S, De Negri E, Calevo MG, et al. Neuropsychological disorders related to interictal epileptic discharges during sleep in benign epilepsy of childhood with centrotemporal or Rolandic spikes. *Dev Med Child Neurol* 2001; 43: 407–12.
3. Monjauze C, Tuller L, Hommet C, Barthez Ma, Khomsi A. Language in benign childhood epilepsy with centro-temporal spikes abbreviated form: rolandic epilepsy and language. *Brain Lang* 2005; 92: 300–8.
4. Riva D, Vaga C, Franceschetti S, Pantaleoni C, D'Arrigo S, Granata T, et al. Intellectual and language findings and their relationship to EEG characteristics in benign childhood epilepsy with centrotemporal spikes. *Epilepsy Behav* 2007; 10: 278–85.
5. Wolff M, Weiskopf N, Serra E, Preissl H, Birbaumer N, Kraegeloh Mann I, et al. Benign partial epilepsy in childhood: selective cognitive deficits are related to the location of focal spikes determined by combined EEG/MEG. *Epilepsia* 2005; 46: 1661–7.

6. D'Alessandro P, Piccirilli M, Tiacci C, Ibba A, Maiotti M, Sciarma T, et al. Neuropsychological features of benign partial epilepsy in children. *Ital J Neurol Sci* 1990; 11: 265–9.
7. Piccirilli M, D'Alessandro P, Sciarma T, Cantoni C, Dioguardi MS, Giuglietti M, et al. Attention problems in epilepsy: possible significance of the epileptogenic focus. *Epilepsia* 1994; 35: 1091–6.
8. Völkl-Kernstock U, Willinger U, Feucht M. Spacial perception and spatial memory in children with benign childhood epilepsy with centro-temporal spikes (BCECTS). *Epilepsy Res* 2006; 72: 39–48.
9. Croona C, Kihlgren M, Lundberg S, Eeg-Olofsson O, Eeg-Olofsson KE. Neuropsychological findings in children with benign childhood epilepsy with centrotemporal spikes. *Dev Med Child Neurol* 1999; 41: 813–8.
10. Metz-Lutz MN, Kleitz C, de Saint Martin A, Massa R, Hirsch E, Marescaux C, et al. Cognitive development in benign focal epilepsies of childhood. *Dev Neurosci* 1999; 21: 182–90.
11. Vinayan KP, Biji V, Thomas SV. Educational problems with underlying neuropsychological impairment are common in children with Benign Epilepsy of Childhood with Centrotemporal spikes (BECTS). *Seizure* 2005; 14: 207–12.
12. Commission on Classification Terminology of the ILAE. Proposal for revised classification of epilepsies and epileptic syndrome. *Epilepsia* 1989; 30: 389–99.
13. Bast T, Völp A, Wolf C, Rating D, Sulthiame StudyGroup. Sulthiame Study Group. The influence of sulthiame on EEG in children with benign childhood epilepsy with centrotemporal spikes (BECTS). *Epilepsia* 2003; 4: 215–20.
14. Aeby A, Poznanski N, Verheulpen D, Wetzburger C, Van Bogaert P. Levetiracetam efficacy in epileptic syndromes with continuous spikes and waves during slow sleep: experience in 12 cases. *Epilepsia* 2005; 46: 1937–42.
15. Dunn LM, Dunn LM. Peabody Picture Vocabulary Test-III. Circle Pines, MN: American Guidance Service, 1997.
16. Riva D, Nichelli F, Devoti M. Developmental aspects of verbal fluency and confrontation naming in children. *Brain Lang* 2000; 71: 267–84.
17. Giordani B, Caveney AF, Laughrin D, Huffman JL, Berent S, Sharma U, et al. Cognition and behavior in children with benign epilepsy with centrotemporal spikes (BECTS). *Epilepsy Res* 2006; 70: 89–94.
18. Pinton F, Ducot B, Motte J, Arbuès AS, Barondiot C, Barthez MA, et al. Cognitive functions in children with benign childhood epilepsy with centrotemporal spikes (BECTS). *Epileptic Disord* 2006; 8: 11–23.
19. Vago C, Bulgheroni S, Franceschetti S, Usilia A, Riva D. Memory performance on the California Verbal Learning Test of children with benign childhood epilepsy with centrotemporal spikes. *Epilepsy Behav* 2008; 13: 600–6.
20. Duman O, Kizilay F, Fettahoglu C, Ozkaynak S, Haspolat S. Electrophysiologic and neuropsychologic evaluation of patients with centrotemporal spikes. *Int J Neurosci* 2008; 118: 995–1008.
21. Papavasiliou A, Mattheou D, Bazigou H, Kotsalis C, Paraskevoulakos E. Written language skills in children with benign childhood epilepsy with centrotemporal spikes. *Epilepsy Behav* 2005; 6: 50–8.
22. Riva D, Nichelli F, Devoti M. Developmental aspects of verbal fluency and confrontation naming in children. *Brain Lang* 2000; 71: 267–84.
23. Deonna T, Zesiger P, Davidoff V, Maeder M, Mayor C, Roulet E. Benign partial epilepsy of childhood: a longitudinal neuropsychological and EEG study of cognitive function. *Dev Med Child Neurol* 2000; 42: 595–603.
24. Yung AW, Park YD, Cohen MJ, Garrison TN. Cognitive and behavioral problems in children with centrotemporal spikes. *Pediatr Neurol* 2000; 23: 391–5.
25. Deltour L, Quaglino V, Barathon M, Vernier MP, Despretz P, Bouvart M, et al. Clinical evaluation of attentional processes in children with benign childhood epilepsy with centrotemporal spikes (BCECTS). *Epileptic Disord* 2007; 9: 424–31.
26. Völkl-Kernstock S, Bauch-Prater S, Ponocny-Seliger E, Feucht M. Speech and school performance in children with benign partial epilepsy with centro-temporal spikes (BCECTS). *Seizure* 2009; 18: 320–6.
27. Hommet C, Billard C, Motte J, Passage GD, Perrier D, Gillet P, et al. Cognitive function in adolescents and young adults in complete remission from benign childhood epilepsy with centro-temporal spikes. *Epileptic Disord* 2001; 3: 207–16.