

BENIGN CHILDHOOD EPILEPSY WITH CENTRO-TEMPORAL SPIKES

Correlation between clinical, cognitive and EEG aspects

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ABSTRACT - Benign childhood epilepsy with centro-temporal spikes (BECTS) is a form of epilepsy with no demonstrable anatomical lesion showing spontaneous seizure remission. During the active phase of the disease the children may show cognitive deficits. The objective of this study was to assess, in children with BECTS, the relationship between clinical-EEG aspects and performance in the school performance test (SPT), Raven's progressive matrixes test and the Wechsler Intelligence Scale for Children (WISC-III). Forty-two 7 to 11 year old children were included and the following tests carried out: anamnesis, neurological examination, electroencephalogram (EEG), SPT, Raven's test and WISC-III. The children with BECTS had normal IQ values but showed inferior performance in the SPT more frequently than "healthy" children, paired with respect to age and maternal scholastic level. There was moderate positive correlation between WISC-III results and the age when the seizures started and the educational level of the parents. On the other hand, aspects linked to the epileptic nature of BECTS, such as the number of seizures, time since last seizure and the number and lateralization of the centro-temporal spikes on the EEG, showed no correlation with the neuropsychological tests.

KEY WORDS: benign childhood epilepsy, epileptiform activity, electroencephalogram, cognition.

Epilepsia benigna da infância com pontas centrotemporais: correlação entre aspectos clínicos, eletrencefalográficos e cognitivos

RESUMO - A epilepsia benigna da infância com pontas centrotemporais (EBICT) é uma forma de epilepsia na qual não existem lesões anatômicas demonstráveis e há remissão espontânea das crises. Na fase ativa da epilepsia as crianças podem apresentar déficits cognitivos. O objetivo deste estudo foi avaliar, em crianças com EBICT, a relação entre aspectos clínico-eletrencefalográficos e o desempenho no teste de desempenho escolar (TDE), no teste das matrizes progressivas de Raven e na Escala Wechsler de Inteligência para Crianças (WISC-III). Foram incluídas 42 crianças de 7 a 11 anos de idade. Foram realizados: anamnese, exame neurológico, eletrencefalograma (EEG), TDE, teste de Raven e WISC-III. As crianças com EBICT tiveram valores normais de QI e apresentaram desempenho inferior no TDE mais frequentemente que crianças "sadias" pareadas quanto à idade e à escolaridade materna. Houve correlação positiva moderada entre idade de início das crises e escolaridade dos pais com resultados do WISC-III. Por outro lado, aspectos ligados à natureza epiléptica da EBICT como número de crises, tempo decorrido da última crise, número e lateralidade das pontas centrotemporais ao EEG não mostraram correlação com os resultados dos testes neuropsicológicos.

PALAVRAS-CHAVE: epilepsia focal benigna, atividade epileptiforme, eletrencefalograma, cognição.

Benign childhood epilepsy with centro-temporal spikes (BECTS) is the most common form of focal idiopathic epilepsy in childhood, showing no demonstrable anatomical lesions. In general the progno-

sis is good and the seizures disappear by 15 years of age, with normalization of the electroencephalogram (EEG)¹. During the interictal period, the baseline brain electrical activity is normal, showing epileptiform ac-

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Received 16 January 2007, received in final form 27 March 2007. Accepted 4 May 2007.

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tivity (EA) characterised by spikes located mainly in the central and midtemporal regions – centro-temporal spikes (CTS). CTS are unilateral in 60% of the cases and activated during sleep. There is no correlation between the number of CTS and seizure frequency¹.

Approximately a quarter of the children show some degree of cognitive deficit during the active epilepsy phase². Slight neuropsychological alterations have been described for language³⁻⁹, attention^{7,10}, executive functions¹¹, memory^{7,11,12}, visuospatial orientation⁴, phonological processing¹² and school performance¹³. It has been discussed in the literature whether the cognitive deficit occurs due to the location of the EA in the centro-temporal region, side of the CTS, the number of CTS or even to a deficit in brain maturity, which interferes with the functional organization of the developing brain, or if it is due to activity of the focus^{3,4,6,8,14-17}. A previous study showed a relationship between immaturity in the development of brain electrical activity in children with BECTS¹⁸, represented by findings in the quantitative EEG, and inferior cognitive performance in the WISC-III. However, few studies have widely investigated the relation between clinical aspects of this epileptic syndrome, such as the age when the seizures started, the total number and type of seizure and the duration of the epilepsy phase, and the observed cognitive deficits. Thus greater knowledge of possible correlations between the clinical aspects and performance in neuropsychological tests could provide subsidies for a better knowledge of the factors related to the neuropsychological alterations observed in this syndrome.

The objective of this study was therefore to assess the relationship between clinical, EEG and neuropsychological aspects in children with BECTS, as assessed by the school performance test (SPT), Raven's progressively coloured matrix test and the Wechsler Intelligence Scale for Children (WISC-III).

METHOD

Forty-two 7 to 11 year old children diagnosed with BECTS according to the International Classification of Epilepsies and Epileptic Syndromes¹⁹ and the Dalla Bernardina et al.²⁰ criteria, were included in this study. The children were sent by the Child Neurology Outpatients Department and the Electroencephalography Department of The Celso Pierro General Hospital and Maternity, PUC-Campinas. Children were only included after the parents and/or guardians gave their consent.

The following procedures were carried out:

1. Medical history and examination of the medical file with the clinical and laboratory data.
2. Traditional neurological examination.
3. School Performance Test (SPT)²¹ - a standardized psychometric instrument, favourably considered by the Psychological Tests Evaluation System (Brazilian Federal Council Of Psychology), which offers an evaluation of the fundamental capacities for school performance in writing, reading, arithmetic and overall ability, per school year, classifying the performance as superior, average or inferior.
4. The Raven test for progressively coloured Matrixes, Special Scale - a standardised instrument adapted to Brazilian reality, destined to measure overall intelligence. The results were expressed in percentages and grades that varied from 1 to 5, grade 1 being obtained by intellectually superior subjects and grade 5 by intellectually deficient subjects.
5. Assessment of lateral dominance using the Edinburgh Inventory - an instrument that assesses the lateral specificity of the examinee.
6. The Wechsler Intelligence Scale for Children (WISC-III) - widely used measure of general intelligence for children aged 6-16 years. The WISC-III is organized into three IQ scores (Verbal, Performance, and Full Scale) and further divided into four factorially derived index scores including the Verbal comprehension, Processing Speed, Freedom from Distractibility and Perceptual Organization. Each of the IQ scores and factor indexes yield standard scores with a mean of 100 and a S. D. of 15.
7. Digital Electroencephalogram - brain electrical activity was recorded using the Braintech 3.0 equipment (EM-SA Equipamentos Médicos), with a resolution of 12 bits, 0.5 and 35 Hz filters, analysing 200 samples per second. Impedance was maintained below 10kΩ. The electrodes were placed according to the 10-20 international system and the reference consisted of inter-connected auricular electrodes. The recording was carried out while resting, hyperventilation for three minutes and, when possible, during spontaneous sleep.

The location and the side of the EA was assessed and also the number of CTS per minute.

The project was approved by the Ethics in Research with Human Beings Committee of PUC-Campinas.

Data analysis – The relationship between the clinical and electroencephalographic aspects and cognitive aspects obtained using SPT, Raven's test and the WISC-III, was studied.

Chi-Square test, Spearman rank correlation, and T Student's test were used for statistical analysis; p values less than 0.05 were considered significant.

With the objective of making a comparative analysis of the SPT results of the children with BECTS, a control group was formed, consisting of 42 children paired with respect to age and maternal scholastic level, presenting no antecedents suggestive of pathologies involving the CNS or alterations in the neurological examination or EEG.

RESULTS

Clinical aspects – Of the 42 children studied (24 female), 5 had only had one seizure, 24 had had from two to five seizures and 13 more than six seizures.

The epileptic seizures were focal in 35 cases, with oro-pharyngeal manifestation in 28, motor in 4, ver- sive in 3 and generalised tonic-clonic with no descrip- tion of initial focal aspects in 7 cases. The seizures only occurred while sleeping in 16 cases.

Twenty-five children were using anti-epileptic drugs (carbamazepine, phenobarbital or valproic acid).

Five (11.9%) children presented a prior history of febrile seizures.

The scholastic level of the fathers was variable, with 27 fathers (64.3%) having up to 8 years of school- ing (complete or incomplete basic education), 10 (23.8%) with up to eleven years of schooling (second- ary education) and 5 (11,9%) with higher education. For maternal scholastic level, one mother was illiterate (2.4%), 23 (54.7%) had complete or incomplete basic education, 15 (35.7%) with secondary education and 3 (7.1%) had completed higher education.

Electroencephalographic aspects – At rest, all the children showed normal EEG baseline activity. CTS were centrally located in one case, mid-temporal in 10 cases and central and mid-temporal in 27 cases. On the day of the cognitive assessment, four children showed no CTS on the EEG. The CTS were exclusively or predominantly in the right hemisphere in 17 cas- es, in the left hemisphere in 16 cases, bilateral with no predominance in 3 cases and median in 2 cases.

The number of CTS per minute was from 1 to 6 in 27 children and more than 6 in 11 cases.

Cognitive aspects – Table 1 shows the distribu- tion of the children according to the WISC-III classi- fication.

Their performance in the Raven progressive ma- trix test was superior or average in 31 (73.8%) cas- es and inferior in 11 (26.2%) cases.

When the SPT results for the children with BECTS were compared with those of the control group, it was shown that the children with BECTS showed in- ferior performance more frequently, and in a statis- tically significant way, in the overall SPT and in the reading and writing subtests (χ^2 ; $p < 0.01$) (Table 2).

Relationship with WISC-III – There was no correla- tion between the results of the WISC-III and the gen- der or age of the children.

Statistically significant (Spearman's test) positive cor- relation was found between the age when the first ep- ileptic seizure occurred and performance IQ ($p=0.013$), full-scale IQ ($p=0.013$), processing speed ($p=0.023$) and perceptual organization ($p=0.026$) (Table 3). Thus for these variables, the later the start of the seizures, the higher the values observed in the WISC-III.

No statistically significant relationship was found between the WISC-III values and the time since the last

Table 1. Distribution of the children according to the WISC-III classification.

WISC-III classification	Intelligence quotient			Factor-based indexes			
	verbal	performance	full-scale	VC	PO	FD	PS
Superior	11	8	9	10	10	7	1
Average	26	28	28	30	26	29	33
Inferior	5	6	5	2	6	6	8

Superior, very superior and superior; Average, above average, average and below average; Inferior, inferior and limitrophe; IQ, intelli- gence quotient; VC, verbal comprehension; PO, perceptual organization; FD, freedom from distractibility; PS, processing speed.

Table 2. Distribution of the individuals in the BECTS and control groups according to the School Performance Test.

SPT	Performance in SPT	BECTS N° of cases	Control group N° of cases
Reading*	Superior or average	16	29
	inferior	26	13
Writing*	Superior or average	21	35
	inferior	23	7
Arithmetic	Superior or average	23	29
	inferior	19	13
Overall SPT*	Superior or average	20	33
	inferior	22	9

Chi-Square Test: *significant, $p < 0.01$

Table 3. Correlation between the intelligence quotients and factor-based indexes obtained in WISC-III and the age at the first seizure, the number of seizures and the number of centro-temporal spikes in the EEG (Spearman's correlation coefficient and value for p).

	Age at 1 st seizure		Total n° of seizures		N° of CTS in the EEG	
	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	p
Intelligence quotient						
Full-scale	0.338	0.031*	-0.206	0.190	0.07	0.650
Verbal	0.220	0.167	0.086	0.585	0.084	0.616
Performance	0.384	0.013*	-0.259	0.097	0.055	0.741
Factor-based indexes						
Verbal comprehension	0.128	0.422	-0.094	0.554	-0.012	0.941
Freedom from distractibility	0.1693	0.290	-0.155	0.327	0.204	0.218
Processing speed	0.353	0.023*	0.086	0.585	-0.038	0.820
Perceptual organization	0.347	0.026*	-0.288	0.064	0.057	0.732

Spearman rank correlation: *significant correlation, $p < 0.05$; CTS, centro-temporal spikes.

Table 4. Correlation between the WISC-III results and the mother and father's scholastic levels (Spearman's correlation coefficient and value for p).

	Scholastic level father		Scholastic level mother	
	Correlation coefficient	p	Correlation coefficient	p
Intelligence quotient				
Full-scale	0.309	0.052	0.353	0.023*
Verbal	0.393	0.012*	0.313	0.046*
Performance	0.209	0.194	0.357	0.022*
Factor-based indexes				
Verbal comprehension	0.380	0.016*	0.263	0.96
Freedom from distractibility	0.405	0.010*	0.361	0.020*
Processing speed	0.165	0.308	0.255	0.107
Perceptual organization	0.247	0.124	0.392	0.011*

Spearman rank correlation: *significant correlation, $p < 0.05$.

seizure, total number and type of seizure, prior febrile seizures, CTS lateralisation and number of CTS on the EEG, or with the use of anti-epileptic drugs (Table 3).

Statistically significant correlation (Spearman's correlation coefficient) was found between higher scholastic level of the father and better performance of the child in the verbal IQ ($p=0.012$), in the factor-based indexes for verbal comprehension ($p=0.016$) and freedom from distractibility ($p=0.010$), and also between higher maternal scholastic level and full-scale ($p=0.023$), verbal ($p=0.046$) and performance ($p=0.022$) IQ values and in the factorial indexes (FI) for freedom from distractibility ($p=0.020$) and perceptual organization ($p=0.011$) (Table 4).

There was a significant association between better performance in the Raven test and the WISC-III quotients and indexes (Spearman's correlation coefficient; $p < 0.001$).

In the relationship between WISC-III and the SPT test, on comparing the results of the WISC-III for the

children with higher or average performance in the SPT with those of the group showing inferior performance, the subjects with inferior performance in the subtest for writing in the SPT showed statistically significantly lower values for verbal IQ (T test, $p=0.038$), whilst inferior performance in the arithmetic subtest was associated with a lower value in the freedom from distractibility index (T test, $p=0.027$) (Table 5).

There was no statistically significant correlation between the other IQ values and factor-based indexes and the SPT values (overall and subtests).

Relationship with SPT – There was no statistically significant difference between the results for SPT and the age when the first seizure occurred, the time since the last seizure, the total number of seizures, the number of CTS on the EEG and the use of anti-epileptic drugs (AED) (T test).

The children with mothers who studied for more than 8 years, showed median and superior perfor-

Table 5. Values for *p* for the correlation between the IQ values and factor-based indexes and performance in the School Performance Test.

SPT	Performance in SPT	Intelligence quotients means and values for <i>p</i>			Factor-based indexes means and values for <i>p</i>			
		Full-scale	Verbal	Performance	Verbal comprehension	Freedom from distractibility	Progressing speed	Perceptual organization
Writing	Superior or average	108.6	112.5	104.1	110.7	106.8	98.6	105.0
	Inferior	96.3	98.5	94.9	99.4	96.6	93.7	94.1
	<i>Value for p</i>	0.063	0.038*	0.164	0.079	0.602	0.233	0.106
Reading	Superior or average	107.4	112.6	101.6	112.1	105.3	98.1	102.3
	Inferior	98.5	100.0	97.6	99.9	98.7	94.6	97.0
	<i>Value for p</i>	0.197	0.072	0.548	0.063	0.344	0.408	0.457
Arithmetic	Superior or average	107.7	110.1	104.3	108.6	107.8	99.0	104.5
	Inferior	94.7	98.4	92.8	99.5	93.2	92.1	92.4
	<i>Value for p</i>	0.051	0.084	0.078	0.160	0.027*	0.092	0.071
Overall	Superior or average	107.4	109.9	103.8	108.7	105.9	98.7	105.8
	Inferior	96.8	100.2	94.9	100.7	96.9	93.3	92.9
	<i>Value for p</i>	0.113	0.155	0.175	0.220	0.175	0.190	0.055

Two sample T test, *significant difference, $p < 0.05$.

mance in the sub-test for reading and the overall score in the SPT (χ^2 , $p=0.039$ and $p=0.039$, respectively). There was no significant correlation between the scholastic level of the father and the SPT performance.

DISCUSSION

Clinical, EEG and cognitive aspects – The present patients studied showed clinical and electroencephalographic characteristics suggestive of a typical BECTS population, with a low seizure frequency, predominance of focal seizures with sensitive/motor oro-pharyngeal manifestation, an age for the appearance of the first seizure between 2 and 10, brain activity with a normal base response and no serious behavioural or cognitive complaints⁷.

With respect to the WISC-III results, more than 10% of the children assessed in the present study showed values slightly below those expected for their age.

In comparative studies of the WISC-III results between children with BECTS and healthy controls, although within the normal limits, some authors found a significant reduction in IQ for children with BECTS^{6,10}, although others did not^{4,22}.

Weglage et al.¹⁰ showed a reduction in performance IQ in children with BECTS, but not in verbal IQ. In the majority of the studies, no abnormalities were observed in the verbal tasks of WISC².

Scholastic difficulties, although cited in the initial description of BECTS¹, have only recently been recog-

nised and approached. Greater attention has been given to specific neuropsychological tests such as language, attention and visuospatial perception¹⁶.

Learning difficulties in children with BECTS have been pointed out by their teachers^{3,23,24} and transitory stagnation or regression in cognitive abilities such as reading and writing, have also been described¹⁶. In BECTS children with a high proportion of atypical epileptic seizures, educational problems were reported in about 50% of the cases⁹.

In earlier studies¹³, the SPT instrument was applied to evaluate fundamental abilities in school performance. Frequently and in a statistically significant way, inferior performance was observed in the reading subtest as compared to a control group paired for age and maternal scholastic level. There was also a statistical tendency for lower performance in writing and overall SPT score.

In the present study, with different patients, the inferior performance was statistically significant for reading, writing and overall SPT, similar to the observations made by Misiara²⁵.

Correlation of the EEG and cognitive aspects – Similar to observations made by other authors^{2,5,10,25}, no significant association was observed in the present study between inferior performance in the WISC, in the Raven and SPT tests and the total number and type of epileptic seizure. In addition, no significant relationship was observed between inferior performance and the use of AED, this being in agreement

with various studies on cognition in children with BECTS^{2,3,16,26}.

Correlation was encountered between the age of the child when he had his first seizure and performance in the performance and full-scale IQ, and also with processing speed and perceptual organization (WISC-III). One hypothesis that may explain this correlation is that an earlier start to epilepsy could coincide with the period in which certain abilities are starting to be acquired¹⁶. One factor affecting the finding of a correlation between age for the first seizure and performance IQ, but not with verbal IQ, could be the fact that the verbal tasks making up the verbal IQ use material that is learnt and highly consolidated, which is less vulnerable to brain alterations, whilst the non-verbal tasks used in the performance IQ use material that demands strategy formulation to emit an adequate response²⁷.

Monjauze et al.²⁶ found no correlation between age at first seizure and specific language aspects such as morpho-syntax and special reading abilities, and raised the hypothesis that this did not occur because these abilities were acquired later in life. In idiopathic epilepsy, the functional alterations, when intense, can lead to important cognitive impairment²⁸.

In the present study, there was no significant correlation between low SPT scores and the age of the child at the first seizure, a result in agreement with Mizziara²⁵.

The mother and father's scholastic levels were an important factor in performance in the WISC-III test. Correlation was found between lower paternal scholastic level and inferior performance of the child in the verbal IQ and in the factor-based index for verbal comprehension and freedom from distractibility, as also between lower maternal scholastic level and inferior performance in the IQs (full-scale, verbal and performance) and in factor-based indexes (resistance to distraction and perceptual organization). These findings suggest that cultural limitations of the parents can be additional adverse factors for children with BECTS, and can influence in the formation of their perceptive abilities, in the processing of activities and in performance.

With respect to the relationship between EA and cognitive performance, greater numbers of CTS are also associated with a lower IQ^{6,10} and inferior performance in reading in the School Performance Test¹³. However, the relationship between the number of CTS and cognition did not reach statistical significance³ or there was no assessment of specific neuropsychological aspects^{4,6}.

A possible mechanism for transitory cognitive difficulty during CTS in the genesis of cognitive difficulties and behaviour, has surprisingly been little assessed in the literature²³ and, in recent research, only 15% of the children showed alterations, and even this was limited^{29,30}.

In the present study, no relationship was found between the number of CTS and the results in the WISC-III and SPT.

With respect to CTS lateralization and neuropsychological aspects, involvement of the right hemisphere would be connected to difficulties in visuo-spatial processing, and of the left hemisphere with language dysfunctions^{4,17,31}.

As in other studies^{10,12,16}, there was no significant correlation in the present study between inferior performance in WISC-III and in the Raven test and CTS lateralization.

Final considerations – Inferior performance was found in the School Performance Test in important proportions in children with BECTS. The time for the first seizure was a factor in the neuropsychological results, as also with the parents scholastic level. On the other hand, factors connected to the epileptic nature of BECTS, such as the number of seizures, time since the last seizure and the CTS number and lateralization, showed no correlation with the results in the neuropsychological tests, suggesting the existence of other factors to be better investigated, such as an eventual immaturity or brain dysfunction¹⁴, which could be expressed in basal brain electrical activity elements¹⁸.

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