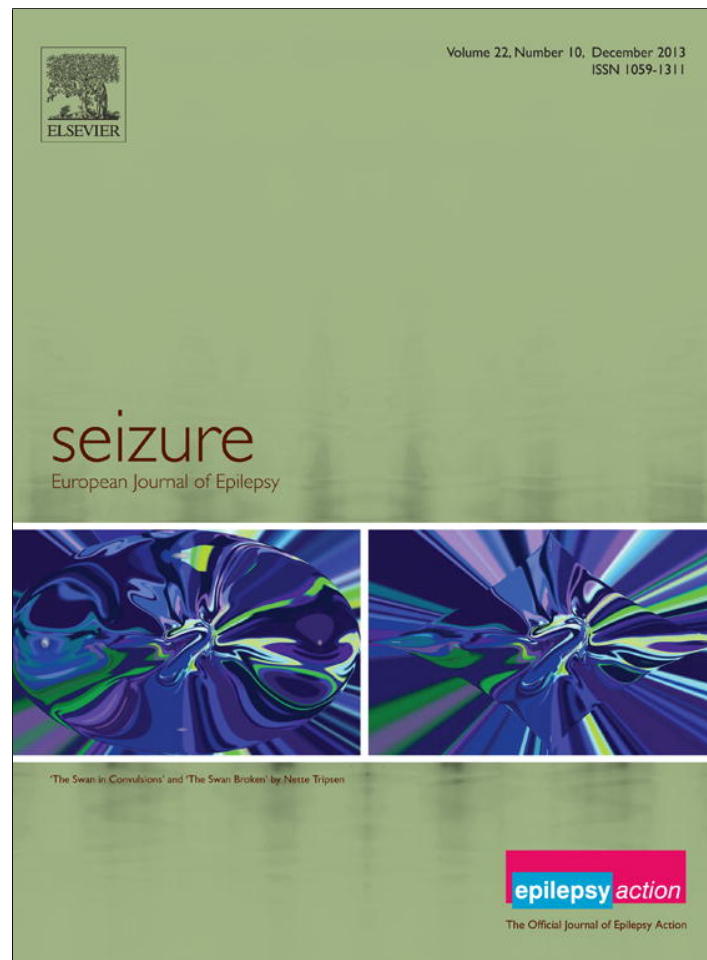


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Intellectual functioning in children with epilepsy: Frontal lobe epilepsy, childhood absence epilepsy and benign epilepsy with centro-temporal spikes



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ABSTRACT

Purpose: The purpose of our study is to describe intellectual functioning in three common childhood epilepsy syndromes – frontal lobe epilepsy (FLE), childhood absence epilepsy (CAE) and benign epilepsy with centro-temporal spikes (BECTS). And also to determine the influence of epilepsy related variables, type of epilepsy, age at epilepsy onset, duration and frequency of epilepsy, and treatment on the scores.

Methods: Intellectual functioning was examined in a group of 90 children with epilepsy (30 FLE, 30 CAE, 30 BECTS), aged 6–15 years, and compared with a control group (30). All subjects obtained a Full Scale IQ ≥ 70 and they were receiving no more than two antiepileptic medications. Participants completed the Wechsler Intelligence Scale for Children – Third Edition. The impact of epilepsy related variables (type of epilepsy, age at epilepsy onset, duration of epilepsy, seizure frequency and anti-epileptic drugs) on intellectual functioning was examined.

Results: Children with FLE scored significantly worse than controls on WISC-III Verbal IQ, Full Scale IQ and Processing Speed Index. There was a trend for children with FLE to have lower intelligence scores than CAE and BECTS groups. Linear regression analysis showed no effect for age at onset, frequency of seizures and treatment. Type of epilepsy and duration of epilepsy were the best indicators of intellectual functioning.

Conclusion: It is crucial that children with FLE and those with a longer active duration of epilepsy are closely monitored to allow the early identification and evaluation of cognitive problems, in order to establish adequate and timely school intervention plans.

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1. Introduction

Many children and adolescents with epilepsy have normal general intellectual functioning,^{1–3} however a lowered intelligence quotient (IQ) is a main consequence of epilepsy in some cases. In a representative community-based study by Anne Berg's team⁴ 26% of the children identified when first diagnosed with epilepsy had a subnormal cognitive function. Most studies using intelligence scales have documented low average range IQ's.^{5–7}

The cause of cognitive problems in epilepsy seems to be multifactorial, that is several intercorrelated factors contribute for deficits in intellectual functioning. Such epilepsy related variables

include: type of epilepsy and underlying aetiology, age at onset, frequency of seizures, duration of epilepsy and treatment (anti-epileptic drugs). The type of epilepsy is considered an important predictor of intellectual functioning. Studies have described below average performances for partial epilepsies and in idiopathic generalized epilepsies.^{8–12} It is well known that children with generalized symptomatic epilepsy are at a higher risk for lower intellectual functioning.^{13–15} In fact in severe epilepsies, like Lennox–Gastaut and West syndromes, mental retardation is seen as part of the syndrome. Age at seizure onset seems to be one of the most important predictors of cognitive outcome. Several studies have identified an increased risk of cognitive dysfunction on children that had an early onset of epilepsy. The study by Cormack et al.¹¹ identified 82% of intellectual impairment in children with epilepsy onset in the first year of life. In the community-based sample of Berg et al.⁴ the most significant factor contributing to IQ impairment was seizure onset before 5 years of age. The negative impact of a longer duration of epilepsy on intellectual performance

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has been described in several types of epilepsy.^{7,10,13} Frequency of seizures is also an important factor that can influence intellectual functioning as several authors have described that children with a history of higher seizure frequency tend to present lower IQ scores.^{6,9,12,15} Finally, polytherapy (taking more than one anti-epileptic drug) seems to have a significant impact on IQ.^{8,15–17}

Intelligence scales, such as the Wechsler Scales gives us a global measure of intellectual abilities, and at the same time they cover different aspects of cognitive functioning (namely, verbal, visuo-spatial, processing speed, attention tasks). Using an intelligence scale may be the first step on neuropsychological assessment of children with epilepsy. The information coming from these scales can help neuropsychologists to identify the cognitive domains which needs further assessment (i.e. language, memory, attention, executive functions, motor functions). Also performance on intelligence scales may facilitate the understanding of academic and behavioural problems^{18,19} and can be used as a baseline for later comparison, depending on the evolution of the epileptic syndrome.

The intelligence scales are probably the instrument most often included in neuropsychological studies of children with epilepsy, but most times their scores are merely used as exclusion/inclusion criteria and only global cognitive measures are reported. The purpose of our study is to compare the WISC-III performance in children with frontal lobe epilepsy (FLE), usually considered to cause problems on cognitive functioning, and children with childhood absence epilepsy (CAE) and benign epilepsy with centro-temporal spikes (BECTS), often considered as benign disorders. We also investigated the influence of epilepsy related variables on intellectual functioning, including type of epilepsy, age at epilepsy onset, duration and frequency of epilepsy, and treatment.

2. Methods

2.1. Participants

The clinical sample included 90 children with epilepsy [30 with frontal lobe epilepsy (FLE); 30 with childhood absence epilepsy (CAE); 30 with benign epilepsy with centro-temporal spikes (BECTS)] and 30 controls. Children with epilepsy were recruited from neuropaediatric units of the Hospital Garcia de Orta and Coimbra's Paediatric Hospital. All children with epilepsy from these geographic areas are referred to these tertiary care paediatric epilepsy outpatient clinics for neurological and neuropsychological care, and therefore they seem representative samples of children and adolescents with FLE, CAE and BECTS.

The child neurologists (i) classified the participants with epilepsy based on the International League Against Epilepsy criteria^{20,21} and (ii) provided for each child information regarding age at epilepsy onset, date of last seizure, frequency of seizures and present treatment. Children with epilepsy were selected based on the following inclusionary criteria: (1) children had to be between 6 and 15 years of age; (2) diagnosis of FLE, CAE or BECTS; (3) they were administered the Wechsler Intelligence Scale for Children – Third Edition (WISC-III)²² to obtain a Full Scale IQ ≥ 70 (WISC-III); and (4) they were receiving no more than two antiepileptic medications.

The group of healthy control children was chosen, from the group that was previously used to standardise the Portuguese version of the WISC-III, to match the experimental group for socio-economic level, age and gender.

2.2. Intelligence assessment

Intellectual functioning was assessed using the Portuguese version of the Wechsler Intelligence Scale for Children – Third

Edition (WISC-III).²² The Portuguese version of the WISC-III was normed on 1354 children aged 6–16 years of age. The sample was stratified according to gender, age, years of education and geographic regions. Geographic regions were based on the 1998 Portuguese Census. This scale allows the calculation of six composite scores: Verbal IQ (VIQ), Performance IQ (PIQ), Full Scale IQ (FSIQ), Verbal Comprehension Index (VCI), Perceptual Organization Index (POI), Processing Speed Index (PSI) (see [Table 1](#)); each with a mean of 100 and a standard deviation of 15. There are 13 subtests (10 core and 3 supplemental) that are transformed in scaled scores with a mean of 10 and standard

Table 1
Description of WISC-III composite scores and subtests.

| Composite scores | Description |
|-------------------------------|--|
| Verbal IQ | Verbal IQ reflects the child's verbal ability and is a good predictor of school achievement. The Information, Similarities, Arithmetic, Vocabulary, Comprehension subtests comprises the Verbal IQ. |
| Performance IQ | Performance IQ is not as good a predictor of school achievement as the VIQ. This composite score provides a better estimate of fluid activity and is not as loaded with verbal and cultural content as the Verbal IQ. The Picture Completion, Coding, Picture Arrangement, Block Design and Object Assembly subtests comprises the Performance IQ. |
| Full Scale IQ | Full Scale IQ is a measure of general intellectual functioning. The Information, Similarities, Arithmetic, Vocabulary, Comprehension, Picture Completion, Coding, Picture Arrangement, Block Design and Object Assembly subtests comprises the Full Scale IQ. |
| Verbal Comprehension Index | Verbal Comprehension Index assesses verbal knowledge and comprehension. The Information, Similarities, Vocabulary and Comprehension subtests comprises the Verbal Comprehension Index. |
| Perceptual Organization Index | Perceptual Organization Index is a measure of perceptual and organizational dimension. The Picture Completion, Picture Arrangement, Block Design and Object Assembly subtests comprises the Perceptual Organization Index. |
| Processing Speed Index | Processing Speed Index is a measure of processing speed of nonverbal information. The coding and Symbol Search subtests comprises the Processing Speed Index. |
| Verbal subtests | |
| Information | Information assesses the general cultural knowledge and acquired facts. |
| Similarities | Similarities is a measure of logical abstract thinking and reasoning. |
| Arithmetic | Arithmetic is a measure of mental arithmetic ability and problem solving. |
| Vocabulary | Vocabulary assesses verbal fluency, word knowledge and language development. |
| Comprehension | Comprehension is a measure of social knowledge and practical judgement in social situations. |
| Digit Span | Digit Span assesses short-term verbal memory and attention. |
| Performance subtests | |
| Picture Completion | Picture Completion assesses visual alertness and visual long-term memory. |
| Coding | Coding is a measure of visual-motor dexterity, associative nonverbal learning and speed. |
| Picture Arrangement | Picture Arrangement assesses visual comprehension, planning and social intelligence. |
| Block Design | Block Design is a measure of spatial analysis and nonverbal reasoning. |
| Object Assembly | Object Assembly assesses perception, assembly skills and flexibility. |
| Symbol Search | Symbol Search is a measure of perception, speed, attention and concentration. |

deviation of 3. Information, Similarities, Arithmetic, Vocabulary, Comprehension, Picture Completion, Coding, Picture Arrangement Block Design, Object Assembly are the 10 core subtests. Digit Span, Symbol Search and Mazes are the 3 supplemental tests. In the present study the Mazes subtest was not administered.

2.3. Procedure

This study was approved by the institutional review boards of both institutions. Also families and children gave their consent to participate. Children and adolescents that met the inclusion criteria were identified by the responsible neuropsychiatrician or paediatrician, and during the medical appointment they would briefly explain the aim and procedures of the study. After the consent of the families, we approached children and their families, and with more detail explained the goals and procedures of the study, and scheduled the day of the assessment. Each participant was assessed individually by one of the investigators of this study (AFL). Prior to the assessment an interview with the parents was conducted, to acquire information regarding the developmental history, children's behaviour and school performance. Children had two neuropsychological assessment sessions – one in the morning, followed by a lunch break, and another on the afternoon. A feedback session was provided for each family, as well as a written report and whenever necessary a telephone conversation was held with the responsible teacher.

2.4. Statistical analysis

The statistical analysis was performed with the assistance of the program *Statistical Package for the Social Sciences* (SPSS, Chicago, IL, USA – Version 17.0). Associations between categorical variables were analysed using Chi-Square Test. Analysis of variance (ANOVA) was used to test mean differences in demographic and clinical variables, and in intelligence scores across the three types of epilepsy (FLE, CAE, BECTS), with post hoc analysis using *Tukey HSD*. To analyse the effects of epilepsy related clinical variables (type of epilepsy, age at onset, active duration, frequency of seizures and treatment) on intellectual functioning (WISC-III composite scores and subtests) simple regression analysis was

used. In all analysis results were judged statistically significant if the *p*-value was identical to or smaller than .05.

3. Results

We assessed 90 children and adolescents with epilepsy and 30 controls, between the ages of 6 and 15 years old. The main demographic (age at testing, gender and parental education) and clinical characteristics (age at epilepsy onset, seizure frequency, active duration – i.e. time interval between age at onset of epilepsy and the last episode of seizure –, and treatment) for the 3 experimental groups and control group are presented in **Table 2**. There were no significant differences between the clinical groups and controls for age at testing and parental education. However for the variable gender the FLE group differed from the CAE, BECTS and control groups. These can be explained by the fact that FLE seems to be more frequent on male gender.⁹ We tested for gender differences on the intelligence scale results, and no differences were found between boys and girls. On the neurological characteristics of the experimental samples no significant differences were observed between the groups for any of the epilepsy-related variables (age at onset of epilepsy, active duration of epilepsy, seizure frequency and treatment). The FLE group consisted of 7 participants with structural aetiology and 23 with unknown aetiology. The analysis revealed no differences on WISC-III performance between FLE with structural and unknown aetiology.

3.1. WISC-III composite scores results

Global intellectual functioning was normal (FSIQ scores \geq 90) for 53% (*N* = 48) of the clinical sample [FLE 47% (*N* = 14); CAE 43% (*N* = 13), BECTS 70% (*N* = 21)], and for 88% (*N* = 24) of the control group. 28% (*N* = 25) of the children and adolescents with epilepsy presented a low average (FSIQ scores between 80 and 89) FSIQ [FLE 30% (*N* = 9), CAE 37% (*N* = 11), BECTS 17% (*N* = 5)] and 19% (*N* = 17) borderline (FSIQ scores between 70 and 79) [FLE 23% (*N* = 7), CAE 20% (*N* = 6), BECTS 13% (*N* = 4)], whereas in the control group 13% (*N* = 4) had a low average FSIQ and 7% (*N* = 2) borderline (see **Fig. 1**).

Table 2
Demographic and neurological features.

| | FLE (<i>N</i> =30) | CAE (<i>N</i> =30) | BECTS (<i>N</i> =30) | Control (<i>N</i> =30) | <i>p</i> -Value |
|-----------------------------|--|--|--|---|-----------------|
| Age | <i>M</i> = 10.13 (<i>SD</i> = 2.73) | <i>M</i> = 9.93 (<i>SD</i> = 2.54) | <i>M</i> = 9.77 (<i>SD</i> = 2.43) | <i>M</i> = 10.13 (<i>SD</i> = 2.73) | .937 |
| Gender | | | | | |
| Boys | 77% (<i>N</i> = 23) | 30% (<i>N</i> = 9) | 33% (<i>N</i> = 10) | 50% (<i>N</i> = 15) | .001 |
| Girls | 23% (<i>N</i> = 7) [*] | 70% (<i>N</i> = 21) | 67% (<i>N</i> = 20) | 50% (<i>N</i> = 15) | |
| Years of education (mother) | | | | | |
| Up to 9th grade | 17% (<i>N</i> = 5) | 23% (<i>N</i> = 7) | 20% (<i>N</i> = 6) | 10% (<i>N</i> = 3) | .702 |
| 9th grade | 30% (<i>N</i> = 9) | 30% (<i>N</i> = 9) | 47% (<i>N</i> = 14) | 43% (<i>N</i> = 13) | |
| 12th grade | 30% (<i>N</i> = 9) | 20% (<i>N</i> = 6) | 20% (<i>N</i> = 6) | 30% (<i>N</i> = 9) | |
| Superior | 23% (<i>N</i> = 7) | 27% (<i>N</i> = 8) | 13% (<i>N</i> = 4) | 17% (<i>N</i> = 5) | |
| Age at onset (years) | <i>M</i> = 6.40 (<i>SD</i> = 3.10) | <i>M</i> = 6.83 (<i>SD</i> = 2.32) | <i>M</i> = 6.77 (<i>SD</i> = 2.43) | | .792 |
| Seizure frequency | | | | | |
| No seizures (last 6 months) | 57% (<i>N</i> = 17) | 70% (<i>N</i> = 21) | 60% (<i>N</i> = 18) | | .177 |
| <1 a month | 30% (<i>N</i> = 9) | 13% (<i>N</i> = 4) | 37% (<i>N</i> = 11) | | |
| \geq 1 a month | 13% (<i>N</i> = 4) | 17% (<i>N</i> = 5) | 3% (<i>N</i> = 1) | | |
| Active duration (months) | <i>M</i> = 27.57 (<i>SD</i> = 36.24) | <i>M</i> = 22.63 (<i>SD</i> = 17.95) | <i>M</i> = 20.90 (<i>SD</i> = 26.44) | | .632 |
| Treatment | | | | | |
| No medication | 7% (<i>N</i> = 2) | 13% (<i>N</i> = 4) | 27% (<i>N</i> = 8) | | |
| Monotherapy | 80% (<i>N</i> = 24) | 73% (<i>N</i> = 22) | 73% (<i>N</i> = 22) | | .087 |
| Duotherapy | 13% (<i>N</i> = 4) | 13% (<i>N</i> = 4) | – | | |

^{*} Differs from control (*p* = .032), from CAE (*p* = .000) and from BECTS (*p* = .001).

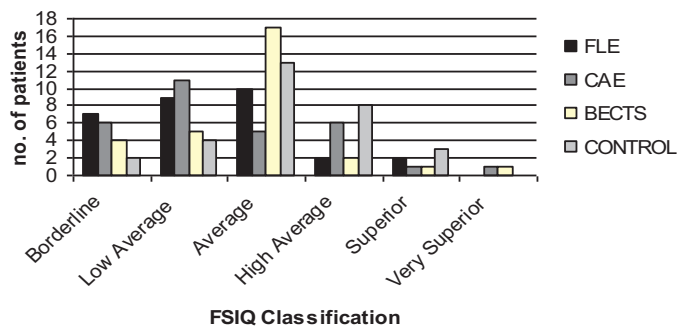


Fig. 1. The distribution of Full Scale IQ on the four samples studied.

The results of the comparison between the 3 groups of children with epilepsy and the control group are presented in Table 3. We found significant differences for VIQ [$F(3,116) = 3.600, p = .016$], FSIQ [$F(3,116) = 3.256, p = .024$] and PSI [$F(3,116) = 4.768, p = .004$]. Post hoc analysis indicated that children with FLE scored significantly worse than controls on the following WISC-III composite scores: VIQ ($p = .014$), FSIQ ($p = .016$) and PSI ($p = .001$). There was no significant difference in the PIQ, VCI and POI.

Given the fact that 7 children from the FLE group had structural lesions, a second analysis including only the other 23 cases with unknown cause was performed. Significant differences were still found for VIQ [$F(3,109) = 3.242, p = .025$] and PSI [$F(3,109) = 3.681, p = .014$]. A tendency towards statistical significance was observed for FSIQ results [$F(3,109) = 2.558, p = .059$]. Post hoc analysis revealed that children with FLE performed worse than controls on the VIQ ($p = .033$) and PSI ($p = .007$).

Although the other two clinical groups (CAE and BECTS) did not differ statistically from controls, their mean results on the six composite scores were systematically lower compared to the controls' scores.

3.2. WISC-III subtests results

The results for the 12 WISC-III subtests are shown in Table 3. Significant differences were observed for the following subtests: Information [$F(3,116) = 5.966, p = .001$], Arithmetic [$F(3,116) = 4.470, p = .005$], Digit Span [$F(3,116) = 9.149, p = .000$] and Coding [$F(3,116) = 4.856, p = .003$]. For the Information and Digit Span subtests all the three clinical groups differed from the control group, presenting significantly lower results: Information [FLE ($p = .004$), CAE ($p = .002$), BECTS ($p = .015$)]; Digit Span [FLE ($p = .000$), CAE ($p = .000$), BECTS ($p = .002$)]. FLE children also differed from the Control group on Arithmetic ($p = .002$) and Coding subtests ($p = .001$).

The analysis without the 7 children with FLE with structural lesions revealed significant differences for the same subtests: Information [$F(3,109) = 6.391, p < .001$], Arithmetic [$F(3,109) = 5.480, p = .002$], Digit Span [$F(3,109) = 8.973, p < .001$] and Coding [$F(3,109) = 4.099, p = .008$]. For the Information and Digit Span subtests all the three clinical groups showed an inferior performance compared to the control group: Information [FLE ($p = .004$), CAE ($p = .001$), BECTS ($p = .011$)]; Digit Span [FLE ($p < .001$), CAE ($p < .001$), BECTS ($p = .002$)]. FLE children also performed worse than controls on Arithmetic ($p = .001$) and Coding subtests ($p = .005$).

3.3. Results related to epilepsy variables (Regression)

In the linear regression analysis (Table 4), intelligence scores were correlated to type of epilepsy and active duration of epilepsy. There was no significant effect for age at onset of epilepsy, frequency of seizures and treatment (p -values $>$ than .052). Lower scores on VIQ ($p = .022$), on FSIQ ($p = .018$) and VCI ($p = .009$) were all associated with a longer active duration of epilepsy. Lower results on PSI were associated with a longer active duration of epilepsy ($p = .005$) and type of epilepsy: PSI was higher for children with BECTS when compared with FLE ($p = .032$). A lower result on the subtest Similarities was associated to a longer active duration

Table 3
WISC-III composite and subtest scores.

| | FLE (N=30) M (SD) | CAE (N=30) M(SD) | BECTS (N=30) M (SD) | CONTROL (N=30) M (SD) | F | df | p-Value (ANOVA) |
|-----------------------------|----------------------|---------------------|------------------------|--------------------------|-------|-------|--------------------|
| Composite scores | | | | | | | |
| Verbal IQ | 92.97 (14.29)** | 94.83 (15.71) | 97.97 (12.28) | 103.90 (12.75) | 3.600 | 3.116 | .016 |
| Performance IQ | 92.40 (14.26) | 95.10 (16.34) | 95.30 (13.45) | 101.30 (15.19) | 1.921 | 3.116 | .130 |
| Full Scale IQ | 90.40 (14.22)** | 93.63 (17.47) | 95.10 (13.24) | 101.97 (13.89) | 3.256 | 3.116 | .024 |
| Verbal Comprehension | 95.93 (15.54) | 95.93 (15.50) | 99.37 (13.21) | 104.63 (12.52) | 2.494 | 3.116 | .063 |
| Perceptual Organization | 95.70 (14.66) | 95.63 (17.20) | 96.27 (14.51) | 101.20 (14.64) | .922 | 3.116 | .432 |
| Processing Speed | 88.30 (11.19)** | 95.27 (17.80) | 96.30 (11.87) | 102.57 (15.88) | 4.768 | 3.116 | .004 |
| Verbal subtests | | | | | | | |
| Information | 8.90 (2.87)** | 8.70 (2.74)** | 9.20 (2.93)** | 11.50 (3.10) | 5.966 | 3.116 | .001 |
| Similarities | 10.43 (2.75) | 9.87 (3.59) | 10.37 (2.71) | 10.33 (2.50) | .236 | 3.116 | .871 |
| Arithmetic | 7.47 (2.65)** | 8.87 (3.43) | 9.07 (2.73) | 10.17 (2.60) | 4.470 | 3.116 | .005 |
| Vocabulary | 9.43 (3.13) | 10.20 (3.04) | 10.20 (2.86) | 10.83 (2.63) | 1.155 | 3.116 | .330 |
| Comprehension | 9.10 (3.18) | 8.97 (2.14) | 10.13 (2.64) | 10.63 (2.87) | 2.620 | 3.116 | .054 |
| Digit Span | 7.67 (2.28)** | 7.93 (2.39)** | 8.30 (2.61)** | 10.79 (2.96) | 9.149 | 3.116 | .000 |
| Performance subtests | | | | | | | |
| Picture Completion | 10.70 (3.13) | 9.90 (2.90) | 10.73 (3.14) | 10.23 (2.96) | .496 | 3.116 | .686 |
| Coding | 7.83 (2.51)** | 8.87 (2.84) | 9.27 (2.78) | 10.47 (2.69) | 4.856 | 3.116 | .003 |
| Picture Arrangement | 8.80 (2.86) | 8.90 (3.86) | 9.33 (2.66) | 10.27 (3.44) | 1.279 | 3.116 | .285 |
| Block Design | 9.03 (2.33) | 9.77 (2.62) | 9.03 (2.71) | 10.40 (3.78) | 1.535 | 3.116 | .209 |
| Object Assembly | 9.23 (3.55) | 9.47 (2.69) | 9.23 (2.94) | 10.03 (2.09) | .520 | 3.116 | .669 |
| Symbol Search | 8.00 (2.49) | 9.50 (4.12) | 9.23 (2.98) | 10.25 (3.44) | 2.335 | 3.116 | .078 |

** Differs from control ($p \leq .01$).
*** Differs from control ($p \leq .001$).

Table 4
WISC-III composite scores and subtests: linear regression analysis.

| Dependent variables | Independent variables included in the model | | | | | | | | | | | | | | | |
|---------------------|---|------|---------------|------|---------------|------|--------------|------|-----------------|------|-----------------------|------|-----------|------|----------------|-------|
| | FLE vs. CAE | | FLE vs. BECTS | | CAE vs. BECTS | | Age at onset | | Active duration | | Frequency of seizures | | Treatment | | r ² | F |
| | β | p | β | p | β | p | β | p | β | p | β | p | β | p | | |
| VIQ | 1.725 | .637 | 5.225 | .171 | 3.499 | .350 | -.835 | .179 | -.147 | .022 | .561 | .802 | 2.463 | .464 | .086 | 1.296 |
| PIQ | 2.461 | .522 | 2.544 | .524 | .083 | .983 | -.368 | .571 | -.124 | .063 | 2.000 | .395 | .211 | .952 | .055 | .803 |
| FSIQ | 2.975 | .444 | 4.471 | .269 | 1.497 | .706 | -.752 | .254 | -.161 | .018 | 1.302 | .584 | 1.184 | .740 | .085 | 1.282 |
| VCI | -.150 | .968 | 3.453 | .380 | 3.603 | .351 | -1.019 | .113 | -.173 | .009 | 1.366 | .554 | 1.844 | .596 | .095 | 1.460 |
| POI | -.321 | .937 | .114 | .978 | .435 | .916 | -.097 | .887 | -.112 | .109 | 2.809 | .257 | -.340 | .927 | .045 | .658 |
| PSI | 6.812 | .057 | 7.979 | .032 | 1.167 | .747 | -.994 | .099 | -.174 | .005 | 1.621 | .454 | 1.681 | .606 | .153 | 2.502 |
| INF | -.267 | .718 | .369 | .632 | .637 | .402 | .055 | .659 | -.021 | .104 | .190 | .675 | .611 | .372 | .053 | .778 |
| SIM | -.596 | .441 | -.052 | .948 | .544 | .491 | -.256 | .053 | -.036 | .008 | .079 | .867 | .454 | .523 | .102 | 1.578 |
| ARIT | 1.421 | .072 | 1.786 | .030 | .365 | .648 | -.063 | .632 | -.004 | .759 | -.324 | .498 | .701 | .331 | .075 | 1.117 |
| VOC | .782 | .307 | .731 | .358 | -.051 | .948 | -.235 | .071 | -.032 | .016 | .745 | .114 | -.016 | .982 | .108 | 1.675 |
| COMP | -.156 | .824 | .976 | .181 | 1.132 | .116 | -.176 | .140 | -.019 | .114 | -.072 | .866 | .047 | .942 | .083 | 1.245 |
| DS | .210 | .745 | .616 | .358 | .407 | .537 | .054 | .622 | -.007 | .541 | -.135 | .732 | .198 | .739 | .026 | .369 |
| PC | -.868 | .296 | -.005 | .995 | .863 | .310 | .115 | .414 | -.013 | .375 | .367 | .469 | .118 | .877 | .047 | .676 |
| COD | 1.001 | .161 | 1.425 | .056 | .424 | .559 | -.131 | .277 | -.017 | .162 | -.222 | .609 | .262 | .688 | .084 | 1.261 |
| PA | -.013 | .987 | .148 | .862 | .161 | .848 | -.064 | .647 | -.018 | .218 | .054 | .915 | -.896 | .239 | .056 | .826 |
| BD | .684 | .308 | -.036 | .959 | -.720 | .294 | .059 | .602 | -.014 | .213 | .423 | .302 | .077 | .900 | .058 | .852 |
| OA | .316 | .692 | .218 | .793 | -.098 | .905 | -.184 | .175 | -.023 | .091 | .774 | .115 | .610 | .407 | .059 | .874 |
| SS | 1.485 | .073 | 1.217 | .155 | -.268 | .749 | -.237 | .090 | -.043 | .003 | .792 | .117 | .233 | .757 | .151 | 2.468 |

VIQ: Verbal IQ; PIQ: Performance IQ; FSIQ: Full Scale IQ; VCI: Verbal Comprehension Index; POI: Perceptual Organization Index; PSI: Processing Speed Index; INF: Information; SIM: Similarities; ARIT: Arithmetic; VOC: Vocabulary; COMP: Comprehension; DS: Digit Span; PC: Picture Completion; COD: Coding; PA: Picture Arrangement; BD: Block Design; OA: Object Assembly; SS: Symbol Search.

of epilepsy ($p = .008$), as well as a lower result on Vocabulary ($p = .016$) and Symbol Search ($p = .003$). Lower results on the subtest Arithmetic were related to type of epilepsy: BECTS showed a better performance than FLE ($p = .030$) on the Arithmetic.

4. Discussion

The aim of our study was to describe the intellectual performance in three common groups of childhood epilepsies [frontal lobe epilepsy (FLE), childhood absence epilepsy (CAE) and benign epilepsy with centro-temporal spikes (BECTS)] and to determine the influence of epilepsy related variables (type of epilepsy, age at onset, duration of epilepsy, frequency of seizures and treatment).

Following results were observed: first, children with FLE did significantly less well than controls with respect to the following WISC-III Composite Scores: Full Scale IQ (FSIQ), Verbal Comprehension Index (VCI), Processing Speed Index (PSI), as well as on the subtests related to school performance (Information, Arithmetic, Digit Span and Coding). Excluding children with structural lesions from the FLE group did not change these results. Second, children with CAE and BECTS performed significantly lower than controls on Information and Digit Span subtests. Third, linear regression analysis revealed that type and duration of epilepsy were the best indicators of intellectual functioning. Finally results showed no effect for age at onset, frequency of seizures and treatment.

In this study we did not include more severe syndromes of infancy and early childhood, also children with IQ's below 70 were excluded, and in spite of that we still found that 28% of the children with epilepsy had a low average FSIQ and 19% borderline. More specifically, our results show that FLE group exhibited lower FSIQ scores, when compared with the control group. Also there was a trend for children with FLE to have lower intelligence scores than CAE and BECTS groups. The impact of FLE on intelligence is still controversially discussed in the literature, as some authors report impairments on IQ scores^{9,15} and others do not.^{23,24} Our results, together with recent studies^{9,13,15} shows that children with FLE have lower IQ scores than the general population. Future studies,

with large samples, are needed to specify which specific subgroups of children with FLE are at risk, considering aetiology, age at onset, duration of epilepsy, frequency of seizures and treatment.

In this study, for the children with FLE differences were more marked on processing speed tasks and in subtests that are thought to influence school performance – Information, Arithmetic, Digit Span and Coding –, which compose the so called ACID pattern previously identified in children with learning problems.^{25–27} Gottlieb's²⁸ group recent work considered working memory and processing speed tasks together as an integrated component of mental ability called Cognitive Proficiency. In this study 90 patients with paediatric epilepsy were examined and the relationship between cognitive proficiency and general ability and seizure focus was analysed. The authors concluded that deficits in cognitive proficiency are a neurocognitive marker of paediatric epilepsy, as children presented more problems on cognitive proficiency than in general ability. When seizure focus was analysed, deficits on cognitive proficiency were especially noted if patients presented frontal lobe epilepsy or right temporal lobe epilepsy. Also, in a recent validity study of WISC-IV for the paediatric population with epilepsy, children with epilepsy scored lower on Processing Speed and Working Memory Indexes than on Verbal Comprehension and Perceptual Organization Indexes.²⁹ Other investigations have outlined that children with FLE have impaired results on processing speed tasks.^{9,13,30,31} Difficulties in processing speed are relevant, especially in school aged children, as they may impact on general cognition. In fact, some authors^{32–34} describe processing speed as a fundamental property of the central nervous system that provides a foundation for the efficient implementation of other cognitive functions, supporting learning and classroom performance. This way cognitive performance and school achievement may be impaired when processing is slow. The classroom setting tasks may not be successfully completed as there is a limited time, and this way simultaneity may be hard to achieve, as early processing may no longer be available when late processes are complete. More rapid processing seems to increase working memory capacity, which impacts on inductive reasoning and mathematical problem solving.³⁵

A lot has been said about the effect of treatment on intellectual functions in children, specially regarding processing speed tasks.^{3,14,36–39} However in our study no considerable difference was noted between intelligence scores of children in monotherapy, duotherapy, or with no medication. However, note that participants were not equally distributed over the groups, with most subjects on monotherapy (75%) and only 9% on duotherapy and 16% with no medication. This result was corroborated by other studies that also found no effects for treatment. Berg and colleagues⁴⁰ demonstrated that processing speed was slower even in a group of children with epilepsy with 5 years seizure free and off anti-epileptic drugs. In addition, recent studies have demonstrated that these deficits may precede seizure onset. Fastenau et al.¹⁴ identified several neuropsychological deficits, including on processing speed, in a sample of children assessed at the time of the first recognized seizure. As Kwan and Brodie⁴¹ have noted it seems that the negative effects of anti-epileptic drugs on neuropsychological functioning may have been over-rated in the past. However, our study was not designed to address this aspect, so results need to be interpreted with caution.

The children with CAE and BECTS showed difficulties on Information and Digit Span subtests. So although their global intellectual functioning was intact, they can have specific cognitive deficits that may impact on their school performance. In fact, several studies reported that children with CAE^{42,43} and BECTS^{44–46} show school problems. More specifically, neuropsychological deficits in the domains of attention for CAE^{47–49} and language functions for BECTS^{50–52} seems to be associated to academic achievement problems, that intelligence scales are not able to capture.

In this study age at epilepsy onset, frequency of seizures and treatment did not affect intellectual functioning. We highlight that the mean age at onset of the sample studied was 6 years of age, which can explain the absence of impact of this epilepsy-related variable on intellectual functioning. As some authors have shown that onset of epilepsy in the first three years of life is the most significant risk factor for intellectual disabilities.^{11,53,54}

Active duration of epilepsy was the strongest predictor of intellectual problems. A longer active duration of epilepsy was associated with lower scores on four composite scores (FSIQ, VIQ, VCI and PSI) and three subtests (Similarities, Vocabulary and Symbol Search). The adverse effect of a longer duration of epilepsy on intellectual functioning has been reported on adults⁵⁵ and children with epilepsy.^{7,10,13,29} This data captures our attention towards the risk of cognitive decline. There are only a few longitudinal studies that addressed the investigation of cognitive change in epilepsy. In a review of cognitive longitudinal studies in children and adults, Dodrill⁵⁶ reported a mild but real relationship between seizures and mental decline, and these seems to be more evident on children than on adults.⁵⁷ In addition in the last ten years several studies have documented that cognitive problems may be present at the beginning of the epilepsy.^{14,43,58–61.}

Future research work needs to analyse longitudinally the performance of these patients (starting their follow-up at time of diagnosis and grouping patients in specific epilepsy syndromes), especially those that have a longer duration of epilepsy, in order to establish the stability of their IQ's. But one must keep in mind that intellectual deterioration may be real or apparent.^{62–64} The intelligence scores are related to age-related norms, this way a child with slow progressing or stagnation will show a decline of IQ, but in fact there is no real decline or regression. The best way to distinguish these situations is to analyse raw subtests results, rather than the scaled scores.

Intelligence tests are widely used to assess cognitive problems in children as they help to guide diagnosis, treatment and educational intervention. But IQ measures were not designed to investigate brain-behaviour relationships and sometimes can be

relatively insensitive, as a normal IQ does not exclude other specific cognitive deficits. Many children with normal IQ still experience difficulties at school. The present study results demonstrate the strengths and limitations of Wechsler Scales, as IQ results do not reflect all domains of cognitive functioning. If other cognitive functions, such as attention or language, had been tested then children with CAE and BECTS may have presented different results. For this reason assessments must be more comprehensive, a complete analysis of specific cognitive functions (memory, language, attention, executive functions, visuospatial and visuoconstructional functions, motor functions), complemented with the assessment of academic achievement and socio-emotional status is necessary to identify which factors are contributing for academic vulnerability and to better understand how each child perceives and processes information.

Conflict of interest

None of the authors has any conflict of interest to disclosure.

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