

The intellectual profile of pediatric patients with posterior cortex epilepsy

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ARTICLE INFO

Article history:

Received 1 September 2021

Revised 27 October 2021

Accepted 12 November 2021

Keywords:

Pediatric epilepsy

Intelligence

Posterior cortex epilepsy

Neuropsychological assessment

ABSTRACT

Background: Cognitive functioning in epileptic syndromes has been widely explored in patients with temporal lobe epilepsy (TLE), but few studies have investigated the neuropsychological profile in posterior cortex epilepsy (PCE). In this study, we investigated the presurgical intellectual profile of children and adolescents with drug-resistant PCE.

Methods: Children and adolescents diagnosed with PCE ($n = 25$) participated in this study. The data were obtained from medical records, with assessments carried out between the years 2003 and 2019. To compare the intellectual profile, we also included patients diagnosed with frontal ($n = 26$) and temporal lobe epilepsy ($n = 40$). The Wechsler Intelligence Scales were used for the assessment of general intelligence. **Results:** There was an effect of the brain region on the Working Memory Index ($p < 0.01$), in which patients with TLE had significantly higher scores than groups with FLE ($p < 0.01$) and PCE ($p < 0.05$). We also demonstrated that patients with PCE tended to perform worse in the Processing Speed Index than patients with TLE ($p = 0.055$). The Full-Scale Intelligence Quotient, Verbal Comprehension, and Perceptual Reasoning indexes did not differ among the brain regions.

Conclusions: Children and adolescents with PCE demonstrated significant impairment in working memory and processing speed. The pattern of cognitive dysfunction in PCE was similar to that observed in FLE, which expands the evidence of the involvement of frontoparietal networks on cognitive proficiency.

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1. Introduction

Posterior cortex epilepsy (PCE) is characterized by recurrent epileptic seizures originating in the occipital, parietal and posterior temporal lobes or even in integrated regions of the posterior cerebral cortex [1,2]. There is no clear anatomical or neurophysiological distinction among these cortical areas, and the epileptogenic zones (EZ) are not always limited to the edges of the occipital, parietal and posterior temporal lobes. The surgical treatment for PCE is less common than for the frontal and temporal regions due to the lower frequency of this type of epilepsy and the difficulty locating the EZ [3].

Although focal or partial seizures in the posterior region are relatively less frequent among epilepsies considered for surgical

treatment, there is a propensity for these seizures to spread to anterior regions of the cortex [3]. In addition, the identification of EZ is particularly complex in PCE due to nonspecific clinical patterns of seizures [4], which require invasive investigation methods in some cases [5].

The posterior cortex is the region that involves some of the main primary sensory areas, which are responsible for the identification, integration, and response to visual, auditory, and tactile stimuli. Different functional systems are associated with the posterior regions of the brain, and impairment resulting from damage to these areas varies according to the extent of the injury [6,7]. In patients with epilepsy, cognitive deficits can arise from the interaction of the underlying pathology, the medical and surgical treatment, and the comorbidities associated with the clinical condition [8].

Cognitive functioning in epileptic syndromes has been widely explored in patients with temporal lobe epilepsy [9–11], but few studies have investigated the neuropsychological profile in PCE,

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more specifically in the parietal and occipital lobes [9,10,12]. In this study, we investigated the presurgical intellectual profile of children and adolescents with drug-resistant PCE, and compared the pattern of cognitive dysfunction to patients diagnosed with frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE).

2. Patients and methods

2.1. Patients

Children and adolescents aged 6–18 years, diagnosed with drug-resistant PCE that underwent surgery at the Epilepsy Surgery Center (CIREP), Hospital das Clínicas, Ribeirão Preto Medical School, University of São Paulo (Brazil) participated in this study. Data were obtained from medical records, with assessments carried out between the years 2003 and 2019. To compare the intellectual profile, we also included patients diagnosed with FLE and TLE.

The clinical investigation included a structured interview, detailed neurological examination, routine EEG, scalp and invasive video-EEG (when necessary), high-resolution MRI (3 Tesla), neuropsychological assessment, and ictal and interictal SPECT. The diagnosis of PCE followed the International League Against Epilepsy (ILAE) criteria for the classification of epileptic syndromes [13]. Engel's classification of postoperative clinical outcome was used as a reliability criterion for the diagnosis of PCE.

Inclusion criteria were: (1) diagnosis of focal epilepsy, based on V-EEG and MRI, agreed in a multi-professional clinical meeting, following ILAE classification; (2) assessment of the intellectual profile carried out using the Wechsler Intelligence Scales, age-appropriate. Neuropsychological assessment was performed during the period of V-EEG monitoring. The presence of secondary generalized tonic-clonic seizures (GTCS) was recorded in order to analyze possible effects on the intellectual profile. We excluded patients with severe cognitive impairment, who did not present minimally adequate receptive and expressive language for neuropsychological assessment through formal instruments, based on predefined protocols by CIREP.

From 286 patients who underwent epilepsy surgery between 2003 and 2019, 86 presented with PCE, 86 with FLE and 114 with TLE. After analyzing the medical records, 195 patients were excluded for being younger than 6 or older than 18 years, for not having the minimum cognitive conditions for a complete neuropsychological assessment, or for not meeting the other inclusion criteria. Ninety-one patients were included in this study, grouped according to the brain region: PCE ($n = 25$), FLE ($n = 26$), and TLE ($n = 40$). The study was approved by the Research Ethics Committee of the Hospital das Clínicas of Ribeirão Preto Medical School (# 3.454.604).

2.2. Assessment of intellectual profile

The assessment of the intellectual profile was carried out as part of CIREP pre-surgical investigation protocol, in a quiet, appropriate room, free from external interference. The examination was conducted by neuropsychologists with experience in the assessment of children and adolescents, in a single session.

Considering the retrospective nature of this study and the time of data collection (2003 to 2019), different versions of the Wechsler Intelligence Scale were used, according to the patient's age and period in which the assessment was performed. WISC-III was used in patients aged between 6 and 16 years evaluated until 2013, when WISC-IV became available in Brazil. WAIS-III remains the choice for individuals aged 16 and over.

In order to compare the intellectual profile between groups, we analyzed the results of the Full Scale Intelligence Quotient (FSIQ), the Verbal Comprehension (VCI), Perceptual Reasoning (PRI), Working Memory (WMI), and Processing Speed (PSI) indexes, as well as the performance in each subtest. Although WISC-III did not include the WMI, the scale presented the Freedom From Distractibility Index (FFD), which aggregates performance in the Digit Span and Arithmetic tasks. Because they are similar in their purpose to assess auditory-verbal attention and verbal working memory [14], the WMI and the FFD were analyzed together in this study.

Complementary analyses were performed using the SCAD profile [15], which aggregates the individual's performance in the Symbol Search (S), Coding (C), Arithmetic (A) and Digit Span (D) subtests.

2.3. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 23.0. Shapiro–Wilk was used to test for data distribution and the Levene test for homogeneity of variances. Continuous variables with normal distribution were assessed using a two-way ANOVA, in which the brain region and the presence of secondary GTCS were included as independent variables. In order to verify differences between groups, we used Bonferroni's post hoc. The Kruskal–Wallis test was used for continuous variables without normal distribution, with post hoc analysis by Mann–Whitney. The data are presented as mean (standard deviation) in variables with normal distribution and as median (interquartile range) for variables without normal distribution. Categorical data were analyzed using Fisher's exact test. In all analyses, the results were considered statistically significant at the level of 5% ($p < 0.05$).

3. Results

3.1. Sociodemographic data and clinical variables

Table 1 presents the sociodemographic and clinical profiles of the sample. The mean age at the assessment was 12.16 (SD = 2.90), 12.61 (SD = 3.61), and 13.30 (2.96) years for patients with PCE, FLE, and TLE, respectively. The median age at onset of epilepsy was 7.0 (IR = 6.50), 5.50 (IR = 5.50), and 4.50 (IR = 8.90) years for patients with PCE, FLE, and TLE, respectively. The lateralization of the EZ was in the left cerebral hemisphere (LH) in 60% of patients with TLE, 56% with PCE, and 46.2% of patients with FLE.

Fisher's exact test revealed an association between the seizure frequency and the brain region ($\chi^2 = 29.835$; $p = 0.000$), with a higher frequency of daily seizures in patients with FLE and a lower frequency of daily seizures in patients with TLE. We also observed an association between the etiology and the brain region ($\chi^2 = 47.471$; $p = 0.000$), with a higher frequency of malformations of cortical development (MCD) in patients with FLE, lower frequency of MCD in patients with TLE, and a higher frequency of gliosis in patients with PCE. Likewise, there was an association between the level of agreement of VEEG and MRI and the location of the EZ ($\chi^2 = 19.211$; $p = 0.005$), with greater agreement observed in patients with TLE, and less agreement in patients with PCE. There was no significant effect of the brain region concerning sex, age at assessment, age at onset of epilepsy, duration of epilepsy, laterality of EZ, and the presence of secondary GTCS.

3.2. Intellectual functioning and cognitive profile by brain region

Table 2 describes the results of the neuropsychological domains assessed, intellectual efficiency, and the effect of the brain region

Table 1
Sociodemographic and clinical characteristics of the sample.

	Mean (Standard Deviation)			Group Effect; Group Comparison
	PCE (n = 25)	FLE (n = 26)	TLE (n = 40)	
Patients Characteristics				
Gender (N Female)	7	10	14	$\chi^2 = 0.649$; $p = 0.723$
Age at Testing, Year (Mean, SD) [range]	12.16 (2.90) [8.00 – 18.00]	12.61 (3.61) [6.00 – 18.00]	13.30 (2.96) [8.00 – 18.00]	$F = 1.068$; $p = 0.236$
Age of Onset, Year (Median, IR)	7.00 (6.50)	5.50 (5.50)	4.50 (8.90)	$\chi^2 = 1.408$; $p = 0.495$
Duration of epilepsy (years) (Median, IR)	6.00 (5.50)	6.00 (5.00)	8.00 (8.75)	$\chi^2 = 2.582$; $p = 0.275$
% Left Hemisphere	56.0	46.2	60.0	$\chi^2 = 1.236$; $p = 0.539$
% Presence of Secondary GTCS	52.0	38.5	25.0	$\chi^2 = 4.928$; $p = 0.089$
% Seizure Frequency				
Daily	52.0	73.1 ⁽⁺⁾	22.5 ⁽⁻⁾	$\chi^2 = 29.835$; $p = 0.000^*$
At least once a week	36.0	19.2	30.0	
At least once a month	4.0 ⁽⁻⁾	3.8 ⁽⁻⁾	32.5 ⁽⁺⁾	
At least once every six months	4.0	0.0	0.0	
Seizure free for over six months	4.0	0.0	0.0	
Irregular	0.0	0.0	5.0	
Status epilepticus	0.0	1.1	1.1	
% Etiology				
MCD	28.0	57.7 ⁽⁺⁾	10.0 ⁽⁻⁾	$\chi^2 = 47.471$; $p = 0.000^*$
Gliositis	32.0 ⁽⁺⁾	15.4	10.0	
Tumor	28.0	23.1	17.5	
MTS	4.0 ⁽⁻⁾	0.0 ⁽⁻⁾	57.5 ⁽⁺⁾	
CVM	8.0	0.0	2.5	
Rasmussen	0.0	3.8	2.5	
% Agreement MRI × V-EEG				
Agree	48.0 ⁽⁻⁾	53.8	82.5 ⁽⁺⁾	$\chi^2 = 19.211$; $p = 0.005^*$
Disagree	16.0 ⁽⁺⁾	0.0	0.0	
Inconclusive	12.0	11.5	7.5	
Partially agree	24.0	34.6 ⁽⁺⁾	10.0 ⁽⁻⁾	

Abbreviations: PCE = Posterior Cortex Epilepsy; FLE = Frontal Lobe Epilepsy; TLE = Temporal Lobe Epilepsy; SD = Standard Deviation; IR = Interquartile Range; GTCS = Generalized Tonic-Clonic Seizures; MCD = Malformations of Cortical Development; MTS = Mesial Temporal Sclerosis; CVM = Cerebrovascular Malformations.

Note: ⁽⁺⁾Positive Adjusted Residual (>1.96); ⁽⁻⁾Negative Adjusted Residual (>-1.96); *Fisher's Exact Test.

Table 2
Means, SD, Group effects, Group comparisons, Minimum and Maximum scores across intelligence domains.

	Mean (Standard Deviation)			Group Effect; Group Comparison	Min.	Max.
	PCE (n = 25)	FLE (n = 26)	TLE (n = 40)			
Intellectual Domains (StS)						
Full Scale Intelligence Quotient (FSIQ)	78.40 (21.19)	79.58 (20.88)	86.35 (21.97)	F = 1.541; <i>p</i> = 0.220	45.00	135.00
Verbal Comprehension Index (VCI)	85.24 (20.43)	87.04 (21.26)	88.52 (18.75)	F = 0.320; <i>p</i> = 0.727	52.00	136.00
Perceptual Reasoning Index (PRI)	81.88 (20.49)	82.92 (18.36)	87.45 (20.93)	F = 1.046; <i>p</i> = 0.356	45.00	127.00
Working Memory Index (WMI)	76.40 (17.27)	72.69 (16.57)	88.67 (22.40)	F = 5.397; <i>p</i> = 0.006; T > F**, T > P*	45.00	153.00
Processing Speed Index (PSI)	76.88 (17.39)	77.85 (16.18)	88.02 (20.08)	F = 4.152; <i>p</i> = 0.019; T > P [#]	45.00	130.00
Clusters (StS)						
Visual Processing (Gv)	86.28 (18.28)	88.69 (20.68)	93.85 (19.15)	F = 2.143; <i>p</i> = 0.124	50.00	130.00
General Information (Gc-K0)	86.56 (18.98)	86.54 (20.18)	88.27 (19.19)	F = 0.134; <i>p</i> = 0.875	50.00	145.00
Long-Term Memory (Gc-LTM)	86.28 (18.74)	87.92 (18.27)	89.00 (16.65)	F = 0.201; <i>p</i> = 0.818	50.00	136.00
SCAD Profile	73.16 (18.50)	72.27 (17.50)	87.97 (22.74)	F = 5.915; <i>p</i> = 0.004; T > F**, T > P*	50.00	149.00
Subtests (SS)						
Block Design (Median, IR)	8.00 (5.00)	6.50 (3.50)	9.00 (4.00)	χ ² = 3.402; <i>p</i> = 0.183	1.00	17.00
Similarities	7.28 (3.62)	7.65 (3.95)	7.85 (3.41)	F = 0.190; <i>p</i> = 0.827	1.00	18.00
Digit Span	6.04 (2.80)	5.42 (2.83)	8.00 (3.83)	F = 5.530; <i>p</i> = 0.005; T > F**	1.00	19.00
Coding (Median, IR)	4.00 (3.50)	5.50 (3.25)	8.00 (4.75)	χ ² = 9.987; <i>p</i> = 0.007; T > P**	1.00	15.00
Vocabulary (Median, IR)	7.00 (4.50)	8.00 (7.25)	9.00 (4.50)	χ ² = 1.245; <i>p</i> = 0.537	1.00	16.00
Comprehension (Median, IR)	8.00 (6.00)	8.00 (7.00)	8.00 (5.00)	χ ² = 0.193; <i>p</i> = 0.908	1.00	19.00
Symbol Search	7.12 (3.77)	6.92 (3.50)	8.85 (4.10)	F = 2.552; <i>p</i> = 0.084	1.00	18.00
Picture Completion (Median, IR)	7.00 (6.50)	7.50 (9.00)	9.50 (6.75)	χ ² = 3.065; <i>p</i> = 0.216	1.00	19.00
Information (Median, IR)	6.00 (6.50)	7.00 (6.25)	8.00 (5.75)	χ ² = 0.393; <i>p</i> = 0.822	1.00	17.00
Arithmetic (Median, IR)	6.00 (5.50)	5.00 (6.00)	9.00 (6.00)	χ ² = 10.187; <i>p</i> = 0.006; T > F*, T > P*	1.00	19.00

Abbreviations: PCE = Posterior Cortex Epilepsy; FLE = Frontal Lobe Epilepsy; TLE = Temporal Lobe Epilepsy; StS = Standard Scores; SS = Scaled Scores; IR = Interquartile Range; Min. = Minimum; Max. = Maximum. For group comparison, consider: P = PCE; F = FLE; T = TLE.

Note: Asterisk indicates group contrasts observed with adjusted Bonferroni correction; * $p < 0.05$; ** $p < 0.01$; # $p = 0.055$.

on the cognitive profile. The standard score (mean = 100, SD = 15) expresses the Verbal Comprehension (VCI), Perceptual Reasoning (PRI), Working Memory (WMI), Processing Speed (PSI) indexes, Visual Processing (Gv), General Information (Gc-K0), Long-Term Memory (Gc-LTM) clusters, SCAD profile, and the Full Scale Intelligence Quotient (FSIQ). The scaled score (mean = 10, SD = 3)

expresses the subtests of the Wechsler Scales. Normative values adjusted for age were used as a reference.

Two-way ANOVA showed an effect of the brain region on the Working Memory Index (WMI) [$F(2.85) = 5.397$; $p < 0.01$]. Bonferroni's post hoc showed that the WMI of patients with TLE was significantly higher than that of the groups with FLE ($p = 0.005$) and

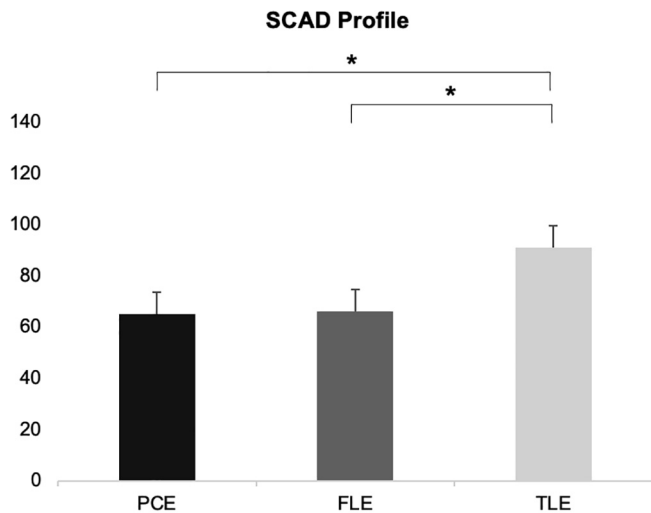


Fig. 1. Performance on the SCAD Profile. Note: PCE = Posterior cortex epilepsy; FLE = Frontal lobe epilepsy; TLE = Temporal lobe epilepsy; SCAD profile integrates the four subtests that compose the Working Memory and Processing Speed indexes (sums of Digit Symbol, Arithmetic, Coding and Symbol Search scaled scores converted to the composite score). Note that patients with FLE and PCE performed worse in the SCAD profile than patients with TLE; * $p < 0.05$.

PCE ($p = 0.048$). In addition, patients with FLE ($p = 0.008$) and PCE ($p = 0.015$) had lower performance on the SCAD profile compared to patients with TLE (Fig. 1). There was a trend toward significance on the Processing Speed Index (PSI), in which patients with PCE had lower performance compared to patients with TLE ($p = 0.055$). The Full Scale Intelligence Quotient (FSIQ), Verbal Comprehension (VCI), and Perceptual Reasoning (PRI) indexes did not differ in terms of brain regions.

We also analyzed the patients' performances on the subtests of Wechsler Intelligence Scales (Fig. 2). There was a significant effect of the brain region on the Digit Span, in which patients with TLE performed better than patients with FLE [$F(2.88) = 5.530$; $p = 0.005$]. The Kruskal–Wallis also showed worse performance of patients with PCE in the Coding [$\chi^2 = 9.987$; $p = 0.007$] and Arith-

metic [$\chi^2 = 10.187$; $p = 0.006$] subtests in relation to the group with TLE. Performance in Arithmetic was also impaired in patients with FLE. There was no effect of the brain region on the other subtests.

4. Discussion

This study analyzed the intellectual profile of children and adolescents with posterior cortex epilepsy, comparing their performance on the Wechsler Intelligence Scale to patients with frontal and temporal lobe epilepsies.

Although not significant, there was a higher prevalence of seizures in the left hemisphere (LH) in patients with TLE (60%) and PCE (56%). Another study described the predominance of EZ in the LH in 63.1% of adult patients with TLE [16]. Still, there is no consensus on a greater propensity for LH or brain lobes specific to epileptogenesis [17].

Seizure frequency is a risk factor for cognitive decline and is associated with brain damage [18]. Our study showed that patients with FLE had a higher frequency of daily seizures than TLE. Frontal injuries have been associated with a higher frequency of epileptic seizures [19]. Regarding the etiology, we found that 57.7% of patients with FLE had malformations of cortical development (MCD), including focal cortical dysplasias (FCD). Other authors have also found a higher prevalence of FCD in the frontal and temporal lobes [20–22]. A higher prevalence of gliosis is described in extratemporal epilepsies, especially in the posterior regions, which corroborates our results [23]. Regarding the degree of agreement between the VEEG and MRI, it was more difficult to locate the EZ in patients with PCE. A previous study found a more diffuse and less EEG-defined ZE in polymicrogyria [24].

Children with epilepsy have impaired working memory (WM) and processing speed (PS), even in patients with low IQ [25]. The brain areas directly involved in WM are the dorsolateral prefrontal cortex, the right parietal cortex, the anterior cingulate gyrus, and the medial occipital cortex [26,27]. Our patients with PCE presented deficits in the WMI similar to those with FLE [28], and this similarity may be due to: (1) ventral (for mesial temporal structures) or dorsal (for parietal and frontal structures) propagation of seizures originating in the posterior regions [29]; or (2) involve-

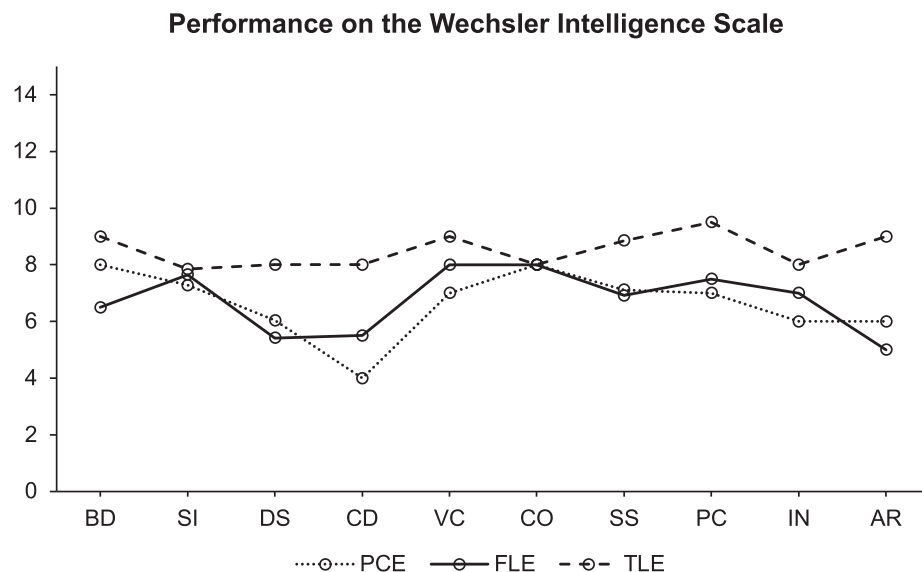


Fig. 2. Performance on the Wechsler Intelligence Scale. Note: PCE = Posterior cortex epilepsy; FLE = Frontal lobe epilepsy; TLE = Temporal lobe epilepsy; BD = Block Design^a; SI = Similarities^b; DS = Digit Symbol^b; CD = Coding^a; VC = Vocabulary^a; CO = Comprehension^a; SS = Symbol Search^b; PC = Picture Completion^a; IN = Information^a; AR = Arithmetic^a; a = Median; b = Mean.

ment of parietal regions in cognitive control, as previously demonstrated [30–32]. Our results expand the evidence that posterior cortical areas adjacent to the parietal lobe are also implicated in WM.

We also found that the PSI of children with PCE was lower than that of the TLE group [33]. Our patients with TLE and FLE showed no differences between the Coding and Symbol Search subtests, which compose the PSI. These results suggest that the motor component of the Coding task was not decisive for the losses in the PS, which are better explained by primary deficits in executive functioning [25].

The SCAD profile, initially proposed by Kaufman (1994) [15], is considered an integrative measure of WM and PS. WM has been directly related to acquiring basic academic skills [34,35] and is a better predictor of academic achievement than IQ [36]. Our results showed impairment of SCAD in children with FLE and PCE [37], suggesting that both groups may have worse school performance.

Some limitations of this study must be considered. The heterogeneity of clinical variables and cognitive deficits makes it difficult to understand specific profiles for each group of patients. Performance on some neuropsychological tasks is influenced by social, educational, and cultural factors, which have not been extensively investigated in this study. The difficulty in controlling seizures and the surgical indication for the patients in this study reflect the severity of their clinical condition, making it impossible to generalize our results to the pediatric population with epilepsy.

5. Conclusion

Although we did not evidence an effect of the epileptogenic region on IQ, children and adolescents with PCE demonstrated significant impairment in working memory and processing speed. The pattern of cognitive dysfunction in PCE was similar to that observed in FLE, which expands the evidence of the involvement of frontoparietal networks on cognitive proficiency. The early identification of deficits can guide educational policies that enable the better academic performance of patients with PCE. Future studies should investigate the impact of PCE on specific cognitive domains.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors gratefully acknowledge financial support from (a) Center for Interdisciplinary Research on Applied Neurosciences (NAPNA), Provost's Office for Research, University of São Paulo (USP), Grant# 2011.1.9333.1.3, and (b) the National Council for Scientific and Technological Development (CNPq, Brazil) by MSc. scholarship (Grant #134105/2019-2), and Postgraduate Program in Internal Medicine (CAPES). Ribeirão Preto Medical School, University of São Paulo, Brazil.

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