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ARTICLE

Clinical and neuropsychological assessment of executive function in a sample of children and adolescents with idiopathic epilepsy

Avaliação clínica e neuropsicológica das funções executivas em uma amostra de crianças e adolescentes com epilepsia idiopática

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ABSTRACT

Objective: To compare the executive functions of children and adolescents with idiopathic epilepsy with a control group and to correlate with clinical data, intelligence and academic performance. **Method:** Cross-sectional, descriptive and analytical study. Thirty-one cases and thirty-five controls were evaluated by the WCST (Wisconsin Card Sorting Test).The results were compared with clinical data (seizure type and frequency, disease duration and number of antiepileptic drugs used), IQ (WISC-III) and academic performance (APT). **Results:** Patients with epilepsy had poorer executive function scores. There was no positive linear correlation between test scores and epilepsy variables. There was a positive association between academic performance and some executive function results. **Conclusion:** Children with well controlled idiopathic epilepsy may show deficits in executive functions in spite of clinical variables. Those deficits may influence academic performance.

Keywords: epilepsy, executive function, child, adolescent.

RESUMO

Objetivo: Comparar as funções executivas de crianças e adolescentes com epilepsia idiopática com um grupo controle e correlacioná-las com dados clínicos, nível intelectual, desempenho acadêmico. **Método:** Estudo transversal, descritivo e analítico. Foram avaliados 31 casos e 35 controles através do WCST (Wisconsin Card SortingTest). Os resultados foram comparados com dados clínicos (tipo e frequência de crises, duração da doença e número de drogas antiepilépticas utilizadas), QI (WISC-III) e desempenho acadêmico (TDE). **Resultados:** Pacientes com epilepsia tiveram piores resultados de funções executivas. Não houve correlação linear positiva entre a pontuação nos testes e as variáveis da epilepsia. Houve associação positiva entre desempenho acadêmico e alguns resultados de função executiva. **Conclusão:** Crianças com epilepsia idiopática bem controlada podem apresentar déficit de função executiva não relacionado a aspectos clínicos. Isso pode influenciar o rendimento acadêmico.

Palavras-chave: epilepsia, função executiva, criança, adolescente.

Epilepsy is a brain disorder caused by an enduring predisposition to generate epileptic seizures and its neurobiological, cognitive and psychosocial consequences, with the occurrence of at least one epileptic seizure[1]. Epilepsy is not a single disease, but a syndrome of varied etiology (genetic, vascular, neurometabolic, structural or traumatic), not always identified. It's the most common chronic neurological disease of childhood[2].

There is a high cognitive and behavioral comorbidity in childhood and adolescence epilepsy, even in individuals with normal intelligence. There is an increased frequency of learning disorders and attention deficit and hyperactivity disorder (ADHD) in idiopathic epilepsy. Several epilepsy variables seem to impact on cognition, behavior and academic skills, including age of onset, disease duration, seizure severity, seizure type and antiepileptic drugs[2]. Also, genetic and environmental influences the degree of cognitive impairment, academic, behavioral and social performance in individuals with epilepsy[3,4,5,6].

Executive functions (EF) are a set of cognitive skills that enable the individual performance of voluntary actions to orient goals[7], encompassing control processes in cognitive, emotional and social areas[8]. They are responsible for

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focusing, guiding, directing, managing and integrating cognitive functions, emotions and behaviors necessary to the active solution of new problems, resulting in effective and adaptive behaviors[7]. Deficits in EF reduces the capacity of one individual to successfully engage in important activities of daily life, including academic and occupational pursuits, social activities and self-care[9]. Executive functions play an important role in learning in childhood[10,11,12,13,14,15,16,17] and is compromised in specific or general aspects in several common neuropsychiatric epilepsy comorbidities, such as ADHD, learning disorders, intellectual deficiency and autism spectrum disorders, all of them common comorbidities in childhood epilepsy[18].

Executive function domains mature at different moments from childhood to adulthood[2]. An earlier developmental period occurs between birth and 3 years old (attentional control skills, inhibition and self-regulation) and more complex processes (planning, organization, cognitive flexibility and concept formation) show the most significant developmental increments between 7 and 9 years of age[19]. Such complex cognitive skills may be particularly susceptible to the early influence of epilepsy, due to their protracted development, with the full extent of deficits not apparent until well into adolescence, when these skills are expected to be mature[19].

Rzezack et al.[20,21] found deficits in temporal lobe epilepsy. Half the sample was free from seizures. Høie et al.[22,23] also found executive function deficits in several other epilepsy syndromes, with the exception of Rolandic epilepsy. One author found an association between low executive function scores and higher behavior problem scores[24] and another with poorer quality of life[25]. No studies addressed directly the relationship between executive function and academic performance in children and adolescents with epilepsy[22].

There are few studies about executive functions in patients with idiopathic well controlled epilepsy, even much more in Brazil. This study was carried out to know if and how epilepsy impacts on executive functions in children. It's important not only for better understanding, but also for proper treatment and provide a better quality of life for these patients. The objective of the present study is to analyze the executive function in a clinical sample of Brazilian children and adolescents with idiopathic epilepsy in relation to epilepsy clinical variables and school performance.

METHOD

Subjects

Thirty one, consecutively seen, pediatric patients treated at the clinic of Pediatric Neurology, *Hospital Universitário Antonio Pedro* of *Universidade Federal Fluminense*, located in a midsize city in Niterói, Rio de Janeiro Brazil, were selected by the following criteria: diagnosis of epilepsy and idiopathic epileptic syndrome established as clinical, electroencephalographic criteria of ILAE[1], aged between 6 and 16 years old, regular attendance at school (at least in 1st year of elementary school), normal neuroimaging and normal neurological examination. The caregivers must have intellectual conditions to respond (alone or with assistance) the instruments of research.

An equal number of healthy controls, matched for age and sex, were subjected to the same procedures, as well as their caregivers. The study was approved by the local Ethics Committee. All caregivers signed an informed consent form. Number difference between patients and controls was due to asymmetric losses because of low IQ.

Assessment

Patients underwent neuropsychological evaluation to determine intelligence (WISC-III), executive function profile (WCST) and academic performance (APT).

Wechsler Intelligence Scale Children (WISC-III) assesses the intellectual ability, consisting of several subtests, each measuring a different aspect of intelligence. The performance on these subtests is summarized in three composite measures (Verbal, Performance and Total IQ) and four index factors (Verbal Comprehension, Perceptual Organization, Freedom from Distractibility and Processing Speed). Some of the WISC subtests are high dependent on attention and are also analysed (Arithmetic, Digits, Coding)[26].

Wisconsin Card Sorting Test (WCST) is one of the most commonly used instruments for the assessment of executive function and is considered a significant measure of cognitive flexibility, attention, and impulsivity. The test assesses abstract reasoning, the subject's ability to generate problem, solving strategies in response to changing conditions, and may be regarded, therefore, as a measure of flexibility of thought. WCST enables sixteen indicators: number of trials administered, total number correct, total number of errors, percent errors, perseverative responses, percent perseverative responses, perseverative errors, percent perseverative errors, non-perseverative errors, percent non-perseverative errors, conceptual level responses, percent conceptual level responses, number of categories completed, trials to complete first category, failure to maintain set and learning to learn[26].

Academic Performance Test (APT) provides an objective assessment of the capabilities critical to school performance, specifically writing, arithmetic and reading, indicating which areas of school learning that are preserved or impaired. It's a Brazilian version of achievement tests[26].

Statistical analysis

It was used the Statistical Package for Social Sciences Release (SPSS 17.0) for Windows (SPSS, 2008). Data were presented in their basic aspects (demographic, clinical, neuropsychological assessment and scholastic performance)

using descriptive statistics. Qualitative variables (categorical dichotomous and polytomous) were described in simple frequencies and quantitative ones as mean, standard deviation and limits. The hypothesis tests were performed within the specific objectives and selected according to the type of variable used: categorical, continuous, quantitative and discrete ones. Whenever possible, the accuracy of estimates was expressed through the Confidence Interval (CI). The following non-parametric tests were used: Mann-Whitney (dichotomous categorical variables × numerical variables) and Spearman correlation coefficient (correlation between numerical continuous variables).

The following study hypotheses were tested: there was a greater prevalence of executive dysfunction in children and adolescents with epilepsy in comparison to a healthy control group, as measured by the mean score results of WCST; patients with executive dysfunction had worse academic achievement and there was an association between clinical characteristics of epilepsy (disease duration, seizure frequency, type of seizure and polytherapy) and executive function profile.

RESULTS

Clinical and sociodemographic data

There were no statistical differences in gender and caregiver educational level (patients 10.3±5.0 vs. controls 9.8±2.9 years of study) between cases and controls, only in age (patients 11.0±2.2 vs. controls 9.8±1.0 years old) and education (patients 5.1±2.4 vs. controls 4.0±1.0 years of study). This difference doesn't seem of clinical relevance. The duration of epilepsy ranged from 12 to 120 months, with a mean of 53.37 months (SD 30.7). Twenty-two (71%) patients had generalized epilepsy and 8 (25.8%) had focal epilepsy. Thirty-one (67.7%) patients were on monotherapy, 6 (19.4%) were on polytherapy and 3 (9.7%) patients discontinued antiepileptic drugs in the last year. 23 patients (74.2%) had no seizures in the last year and 8 patients (25.8%) had less than 3 seizures in the same period. The family history of epilepsy was negative in 23 patients (74.2%).

Neuropsychological results

Table 1 describes the average IQ results of children and adolescents with epilepsy compared to the control group. Significant difference was found only in the processing speed factor, with the worst results for children and adolescents with epilepsy.

Table 2 describes APT subtests. There was no statistically significant difference in reading, writing and total subtests scores between the groups.

Table 3 describes WCST subtests. Poorer results of patients with epilepsy occurred in the following categories: number of administered trials, perseverative responses, percent perseverative responses and conceptual level responses.

Table 1. Intelligence of the samples (mean and SD).

	Patients with epilepsy	Healthy controls	p*
Fullscale IQ	90.7±17.9	99.1±17.6	0.116
Verbal IQ	94.3±19.07	99.2±19.7	0.591
Performance IQ	86.2±22.4	95.5±20.2	0.116
Processing speed factor	83.8±24.4	100.5±18.9	0.004
Freedom from distractibility factor (FDF)	93.1±20.9	97.5±17.1	0.258

*p<0.05. SD: Standard deviation; IQ: Intelligence quocient.

Table 2. Academic Performance Test (means and SD).

	Patients with epilepsy	Healthy controls	p*
Reading	49.9±23.9	53.1±19.02	0.957
Arithmetics	16.2±9.4	13.9±7.3	0.396
Writing	20.5±11.7	23.0±15.8	0.791
Total	86.6±43.3	88.0±32.2	0.624

*p<0.05. SD: Standard deviation.

Comparison between WCST and clinical variables

There were no statistical differences between WCST and clinical variables such as disease duration, seizure type and number of antiepileptic drugs.

Table 3. WCST subtests (means and SD).

	Patients with epilepsy	Healthy controls	p*
Number of trials administered	113.2±19.8	121.5±13.1	0.021
Total number correct	72.1±15.6	72.7±14.4	0.554
Total number of errors	52.06±13.3	52.4±10.5	0.888
Percent errors	52.9±12.4	52.4±10.9	0.709
Perseverative responses	50.7±12.9	43.1±9.02	0.010
Percent perseverative responses	51.6±14.4	44.0±12.2	0.032
Perseverative errors	46.25±13.58	40.1±12.2	0.136
Percent perseverative errors	48.8±14.09	42.14±11.7	0.126
Non-perseverative errors	45.87±14.4	30.2±27.15	0.005
Percent non-perseverative errors	44.8±11.73	45.6±15.5	0.612
Conceptual level responses	58.2±19.8	53.02±10.8	0.043
Percent conceptual level responses	51.1±13.08	58.3±30.7	0.315
Number of categories completed	4.22±1.7	41.7±11.05	0.000
Trials to complete first categorie	23.7±23.7	4.8±9.9	0.082
Failure to mantain set B	1.58±1.8		0.391
Learning to learn B	2.5±6.2		

WCST: Wisconsin Card Sorting Test; SD: standard deviation.

Comparison between WCST and academic achievement

Table 4 shows the comparison between WCST and APT results of children and adolescents with epilepsy. Positive correlation was observed in the following items: Number of trials administered, total number of errors, perseverative errors, percent perseverative errors, non-perseverative errors, percent non-perseverative errors, number of categories completed, trials to complete first category, failure to maintain set and learning to learn. There was a negative relationship in the following items: total number correct and perseverative responses.

DISCUSSION

Our patients had a benign profile of epilepsy, with most patients presenting few or no seizures. We found poorer results in patients with epilepsy, with no correlation with clinical variables (type of epilepsy, duration of illness, seizure frequency, number of antiepileptic drugs), and a positive relation to academic performance.

Table 4. Comparison between WCST and APT.

WCST	APT reading		APT aritmethics	
	p	r_s	p	r_s
Number of trials administered	0.050	0.361	0.001	0.574
Total number correct	0.617	0.095	0.880	0.029
Total number of errors	0.105	0.302	0.006	0.493
Percent errors	0.418	0.154	0.117	0.292
Perseverative responses	0.862	0.033	0.194	0.244
Percent perseverative responses	0.737	0.064	0.363	0.172
Perseverative errors	0.298	0.197	0.021	0.419
Percent perseverative errors	0.292	0.199	0.023	0.414
Non-perseverative errors	0.158	0.264	0.029	0.398
Percent non-perseverative errors	0.159	0.264	0.038	0.380
Conceptual level responses	0.177	0.253	0.361	0.173
Percent conceptual level responses	0.378	0.167	0.154	0.267
Number of categories completed	0.009	0.468	0.001	0.565
Trials to complete first category	0.006	0.486	0.010	0.462
Failure to mantain set	0.045	0.369	0.070	0.335
Learning to learn	0.827	0.048	0.379	0.193
Number of trials administered	0.001	0.559	0.001	0.580
Total number correct	0.663	0.083	0.892	0.026
Total number of errors	0.008	0.476	0.007	0.484
Percent errors	0.111	0.297	0.103	0.304
Perseverative responses	0.418	0.153	0.464	0.139
Percent perseverative responses	0.718	0.069	0.638	0.090
Perseverative errors	0.016	0.437	0.040	0.377
Percent perseverative errors	0.018	0.428	0.045	0.369
Non-perseverative errors	0.050	0.361	0.025	0.410
Percent non-perseverative errors	0.040	0.376	0.027	0.404
Conceptual level responses	0.092	0.314	0.186	0.248
Percent conceptual level responses	0.145	0.273	0.122	0.288
Number of categories completed	0.000	0.600	0.000	0.602
Trials to complete first category	0.004	0.506	0.002	0.533
Failure to mantain set	0.179	0.252	0.062	0.345
Learning to learn	0.221	0.265	0.271	0.239

WCST: Wisconsin Card Sorting Test; APT: Academic performance.

We found impairment in some WCST categories (perseverative errors, number of categories completed, trials to complete the first category and failure to maintain set). Only two other study groups used the same instrument for executive function analysis. Høie et al.[22,23], in population studies of more than a hundred children with epilepsy also found changes on WCST categories for several epilepsy syndromes, with the exception Rolandic epilepsy: number of trials administered, the total number correct, the total number of errors, perseverative responses, perseverative errors, non-perseverative errors and number of categories completed. Our results were not related to seizure type; both generalized and focal epilepsy showed poor EF results, but we didn't analyzes epilepsy syndromes.

A Brazilian group studied EF in patients with temporal lobe epilepsy[20,21] and found changes in the number of categories completed, number of perseverative and non-perseverative errors, perseverative responses and failure to maintain set. In one of the studies they found a relationship between EF and memory skills. The authors raises critics to the use of WCST as the single test to analyze EF. Although WCST is considered the "gold standard" for assessing executive dysfunction in patients with epilepsy, the classic concept of EF as a multidimensional construct makes a single measure to evaluate all processes insufficient. Subjects may present impairment in some, but not all functions of the executive and attentional domains.

Other studies used different tests to analyze EF. Parrish et al.[27] studied a similar sample, children with a more benign profile of epilepsy, using different tests of EF and also found results consistent with ours.

We didn't find any correlation with clinical variables (type of epilepsy, duration of illness, seizure frequency, number of antiepileptic drugs). Gelzinienė et al.[28], found changes in cognitive flexibility and susceptibility to interference without correlation with clinical aspects of epilepsy. They analyzed a short duration group of idiopathic generalized epilepsies in adolescence (mainly juvenile myoclonic epilepsy) by means of verbal fluency test, five, point test, trail, making test and Stroop test. Høie et al.[22] found poorer results related to early epilepsy onset, high seizure frequency and polytherapy.

Although we didn't find differences between groups in relation to academic achievement, there was a positive correlation between APT and some WCST categories, which may explain poorer results at least for some patients. Høie et al.[22] found that adjustment for executive function explained most of the poorer school performance, followed by cognitive function, and depression and that socioeconomic status did not explain this difference. This study

defined poor academic performance by means of parental report on Child Behavior Checklist List (CBCL) and not by direct measurement.

Some variables not addressed in this study must explain executive dysfunction irrespective of clinical variables. In another study from our group[26], using the CBCL for behavior problem analysis, we found worse results in psychopathology in children with epilepsy with certain psychopathological variables related to IQ (sluggish cognitive time, aggressive behavior, attention problem and activities) and academic performance (conduct, breaking rule behavior and school), also with no relation to clinical variables. Such results are probably related to the impact of psychological distress on cognitive performance and greater chance of absenteeism and poor compliance to studies. Høie et al.[23] found a combined burden of cognitive, EF and psychosocial problems in children with epilepsy. We also analyzed the ADHD comorbidity in this sample, which was higher in patients with epilepsy. ADHD is a prototype of developmental executive dysfunction.

In conclusion, children and adolescents with well controlled idiopathic epilepsy may show deficits in EF not influenced by number of seizures, but that correlates to academic performance.

This study reinforces the importance of a thorough neuropsychological examination of children and adolescence with epilepsy. Further studies should address other influences such as cognitive comorbidities, subtle electroclinical dysfunction and social issues.

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