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The executive profile of children with Benign Epilepsy of Childhood with Centrotemporal Spikes and Temporal Lobe Epilepsy

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ABSTRACT

Rationale: Benign Epilepsy of Childhood with Centrotemporal Spikes (BECTS) and temporal lobe epilepsy (TLE) represent two distinct models of focal epilepsy of childhood. In both, there is evidence of executive dysfunction. The purpose of the present study was to identify particular deficits in the executive function that would distinguish children with BECTS from children with TLE.

Methods: We prospectively evaluated 19 consecutive children and adolescents with TLE with hippocampal sclerosis (HS) (57.9% male; mean 11.74 years [SD 2.05]; mean IQ 95.21 [SD 15.09]), 19 with BECTS (36.8% male; mean 10.95 years [SD 2.33]; mean IQ 107.40 [SD 16.01]), and 21 age and gender-matched controls (33.3% male; mean 11.86 years [SD 2.25]; mean IQ 108.67 [15.05]). All participants underwent a neuropsychological assessment with a comprehensive battery for executive and attentional functions. We used ANOVA and chi-square to evaluate differences on demographic aspects among groups (BECTS, TLE-HS, and control groups). Group comparisons on continuous variables were complemented by MANOVA and Bonferroni posthoc comparisons.

Results: Patients with BECTS had worse performance than controls in: Matching Familiar Figures Test, time ($p = 0.001$); Matching Familiar Figures Test, time × errors index ($p < 0.001$); Verbal Fluency for foods ($p = 0.038$); Trail Making Test, part B time ($p = 0.030$); Trail Making Test, part B number of errors ($p = 0.030$); and WCST, number of categories achieved ($p = 0.043$). Patients with BECTS had worse performance than patients with TLE-HS on Matching Familiar Figures Test, time ($p = 0.004$), and Matching Familiar Figures Test, time × errors index ($p < 0.001$). Patients with TLE-HS had worse performance than controls on the following tests: Verbal Fluency for foods ($p = 0.004$); Wisconsin Card Sorting Test, the number of categories achieved ($p < 0.001$); and Wisconsin Card Sorting Test, the number of perseverative errors ($p = 0.028$). Patients with TLE-HS had worse performance than patients with BECTS on Digit Backward ($p = 0.002$); and the Wisconsin Card Sorting Test, the number of perseverative errors ($p < 0.001$).

Conclusions: Patients with TLE and BECTS present distinct cognitive profiles. Patients with TLE-HS had worse performance in mental flexibility, concept formation, and working memory compared to BECTS. Patients with BECTS had worse inhibitory control compared to children with TLE-HS. Both TLE-HS and BECTS had a higher number of errors on an inhibitory control test. However, patients with BECTS had a slower mental processing even when compared to patients with TLE-HS. Rehabilitation programs for children with epilepsy must include children with benign epilepsies and must take into account the epileptic syndrome and its particular neurocognitive phenotype.

1. Introduction

Cognitive impairments are frequently observed in different epileptic syndromes and, as such, the current definition of epilepsy encompasses the occurrence of cognitive deficits associated with this brain disorder [1]. It is well established that different epileptic syndromes are associated with specific cognitive deficits [2,3]. In children and adolescents, the study of neuropsychological impairments is of particular importance due to the impact of epileptiform discharges in a developing brain. Besides, children and teenagers face the first years of formal education and even mild cognitive impairments may have a major effect on academic performance with enduring and long-term impact [4,5].

Benign Epilepsy of Childhood with Centrotemporal Spikes (BECTS) is a focal epilepsy, previously classified as idiopathic, and currently

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categorized as a syndrome of unknown etiology [6–9]. For many years, BECTS was known as a benign form of childhood epilepsy due to the lack of neurological deficits and structural lesions on routine neuroimaging exams. Also, BECTS is a pharmacoresponsive form of epilepsy that spontaneously remits during a predictable age range, usually during adolescence [6,10]. However, the term "benign" has been questioned due to the presence of cognitive deficits and behavioral disorders that may negatively impact the quality of life, social adaptation, and academic performance [6,9,11–13].

Temporal lobe epilepsy (TLE) is another form of focal epilepsy in which seizures can originate in one or both temporal lobes and may occur in the presence or absence of a lesion. Therefore, considering etiology, it may be classified as lesional or undetermined. Lesional TLE encompasses hippocampal atrophy, tumors, cortical developmental malformations, cysts, vascular malformations, and gliosis. Patients with lesional TLE usually present a higher degree of drug resistance and are frequently referred to surgery [14]. TLE caused by hippocampal sclerosis (TLE-HS) is the most frequent cause of drug-resistant TLE in adults [15]. Although HS is not the most common cause of TLE in childhood, this condition is highly associated with memory loss, executive dysfunction, and underachievement in school performance [15,16].

Executive functions (EF) refer to a set of cognitive and metacognitive functions related to self-directed behavior. This complex system is composed of different skills, allowing individuals to receive stimuli, monitor their responses, and behave in an integrated manner. Moreover, the planning of sequential responses, alternating attention to stimuli of different sources, resistance to distraction, and sustaining behaviors for extended periods also comprise the EF [17]. People with a malfunctioning of the EF often have difficulties completing their daily activities or adjusting socially.

Children and adolescents with BECTS have impairments in different areas of EF [18–24], including attention [18,25–28]. Still, there is no consensus on an executive and attentional profile for these children. Some studies show impairments in alternate attention [24] and inhibitory control [22,25,26,28–30]. Others identify impairments in other executive abilities such as working memory, verbal fluency, organization, and planning [20,31].

The EF in children and adolescents with TLE have been less investigated compared to adult literature. Rzezak et al. [32] show executive and memory deficits in a sample of children and adolescents with TLE. The main findings observed in previous studies with children with TLE [32–35] are impairments in distinct executive domains such as inhibitory control, alternate attention, working memory, mental flexibility, and concentrated attention.

At the moment, most studies comparing EF of children and adolescents with distinct epilepsy syndromes do not include a sample of BECTS patients [21,36]. Culhane-Shelburne et al. [36], comparing frontal lobe epilepsy (FLE) and TLE, observed that children with FLE have an impairment of executive functioning but not memory, while patients with TLE have the opposite pattern. Hernandez et al. [37] compared lesional epilepsy (FLE and TLE) with childhood absence epilepsy and showed that children with FLE had worse performance in a broader category of tests that evaluate executive functions, which is highly expected. The only study that compared the performance of patients with TLE and BECTS evaluated cognitive functions related to reading (i.e. oral language, visuospatial capacities, phonological awareness) and reading ability itself. Chaix et al. [38] observed with a small sample size (12 children with BECTS and ten children with TLE) that patients with TLE had worse performance on reading and lexical skills.

BECTS and TLE represent two distinct models of focal epilepsy of childhood. The authors believe that both groups show some level of executive dysfunction. However, these epilepsies are likely to be associated with different executive/attentional profiles since they are related to distinct neuroanatomical regions, etiology of the seizures (undetermined vs lesional), electroclinical profile, outcome, and drug susceptibility [14,6–10]. Previous studies have already delineated different patterns of impairments in other cognitive domains for these epilepsies, with memory being the function most often affected in TLE and language in BECTS [13,32,38].

To our knowledge, no study conducted a direct comparison between TLE and BECTS with a comprehensive battery of executive functions. In the present study, we aimed to verify whether specific executive function impairments could distinguish children with BECTS from children with TLE caused by hippocampal sclerosis (HS).

2. Methods

2.1. Patients and controls

2.1.1. Patients with TLE and HS

We prospectively evaluated 19 consecutive children and adolescents with TLE and hippocampal sclerosis documented by MRI; they were followed in a tertiary epilepsy center.

2.1.2. Patients with BECTS

We included 20 children with BECTS, diagnosed by history and corroborated by current and previous interictal EEG.

2.1.3. Controls

We recruited 21 healthy volunteers among students from a public state-sponsored school located in the same neighborhood of the university hospital. These children were matched to the patients regarding age, socio-demographic, and educational backgrounds and had neither psychiatric disorders based on DSM-IV-TR criteria [39] nor a previous or current history of neurological disorders.

The clinical and demographic information for these three groups (TLE-HS; BECTS and controls) is summarized in Tables 1 and 2.

We excluded patients and controls with an estimated IQ lower than 80, who had a diagnosis of a psychiatric disorder, who abused alcohol or drugs, who had had any surgical brain interventions (including epilepsy surgery), and with a lack of school attendance. Clinical signs of drug intoxication or any other condition that could lead to cognitive impairment other than epilepsy in the patient group was also an exclusion criterion. We also excluded patients with epilepsy presenting with moderate/severe learning disabilities that might impair neuropsychological performance. In addition, we excluded patients with attention deficit/hyperactivity disorder and patients using psychoactive drugs.

In both groups with epilepsy, we had patients who were controlled with AEDs (at least one-year freedom from seizures before assessment) and patients with pharmacoresistant epilepsy. In the latter, the time

Table 1
Clinical description of patients with epilepsy.

Clinical epilepsy variables	TLE	BECTS
Age of onset, μ (SD)	4.36 (3.16)	6.55 (2.95)
Epilepsy duration, μ (SD)	6.79 (3.66)	3.26 (2.28)
Status epilepticus		
Present, n (%)	6 (31.6%)	0 (0%)
Absent, n (%)	13 (68.4%)	20 (100%)
Seizure control		
Present, n (%)	6 (31.57%)	14 (70%)
Absent, n (%)	13 (68.42%)	6 (30%)
Seizure frequency		
No seizures, n (%)	6 (31.57%)	14 (70%)
Daily, n (%)	6 (31.57%)	0 (0%)
Weekly, n (%)	5 (26.31%)	2 (10%)
Monthly, n (%)	1 (5.26%)	0 (0%)
Sporadic n (%)	1 (5.26%)	3 (15%)
Number of AEDs		
No AED	0 (0%)	6 (30%)
Monotherapy	10 (52.63%)	13 (65%)
Polytherapy	9 (47.36%)	1 (5%)

Legend: μ: mean; SD: Standard Deviation; n: number; TLE: temporal lobe epilepsy; BECTS: Benign Epilepsy of Childhood with Centrotemporal Spikes; AED — antiepileptic drugs.