Executive functions of children with attention deficit hyperactivity disorder with or without benign rolandic epilepsy.

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ABSTRACT

Introduction: *The relationship between ADHD and epilepsy, although very frequent, is not clear. Clinical studies in neuropsychology and neurology (neuropsychiatry) can provide valuable information for assessment, intervention and treatment.* ***Method:*** *A non-experimental design, quantitative approach, descriptive level and cross-sectional study was carried out with the aim of comparing the executive functioning of a group of children with ADHD and a group of children with ADHD and CPSDD. A convenience sample of 40 matched children (all males) grouped in two groups of 20 children between 7 and 13 years of age was formed. In order to evaluate executive functioning, some tests of the Neuropsychological Battery of Executive Functions and Frontal Lobes - BANFE were applied.* ***Results:*** *According to the bilateral asymptotic significance values, statistically significant differences were found in the variables Stroop A - Hits, Stroop B - Hits, Self-directed Signaling (Hits, Planning and Time), and Visuospatial Working Memory (Maximum Level, Perseverations and Order Errors).* ***Conclusions:*** *The results of the present study coincide with the failures in inhibitory control and sustained attention problems reported in the literature. Children with EBPCT and ADHD have a different and more impaired executive functioning profile than children with ADHD alone.*

Key words: *epilepsy, neuropsychology, frontal lobes.*

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in childhood and is twice as common in boys as in girls[1]. It is characterized by inability to maintain attention, easy distraction, frequent forgetfulness, difficulties to organize activities, excessive movement, difficulty to control oneself, frequent interruptions, need to be doing something permanently, among other symptoms that define its type. ADHD has a clinical diagnosis, but psychological (qualitative and psychometric), neuropsychological and neurological evaluations provide essential information to confirm and characterize it. It is a disorder with a very high prevalence at school age, with estimates between 8 - 11 %[1], although the figures vary depending on the country. Colombia, in particular, has one of the highest prevalences in the world, reaching 17.1%[2], which has led it to be considered a public health problem.[3]

ADHD regularly occurs along with other psychological, neuropsychological or neurological conditions. Some authors claim that pure ADHD is an exceptional condition(4). It is estimated that 60-100% of children with ADHD also present one or more comorbid disorders[5], such as autism spectrum disorders, insomnia, learning disabilities, obsessive compulsive disorder, oppositional defiant disorder, disruptive mood dysregulation disorder, intermittent explosive disorder, self-injurious behavior, depression, anxiety, bipolar disorder, among others[6]. Neurologically, headache diagnoses, specifically migraine and tension headache[7]; Tourette syndrome[8], chronic tic disorders[9] and epilepsy are some of the most frequent[10,11]. Particularly in children with ADHD, a high frequency of spikes of rolandic epilepsy has been detected.[11]

Benign epilepsy with centrotemporal spikes (BECTS), or benign rolandic epilepsy, is the most common form of epilepsy in childhood and accounts for approximately one quarter of epilepsies in school-aged children[13]. The characteristic spikes over the rolandic area (central sulcus of the brain) are considered neurobiological markers of BECTS. For this reason it is included in the group of localization-related epilepsies. The electroencephalogram (EEG) shows slow, biphasic, high-voltage, centrotemporal sharp spikes followed by a slow wave. These spikes are generated in repetitive bursts usually unilateral (corresponding to the focal nature of seizures) but may occur bilaterally[14]. This type of epilepsy is also more frequent in children.[12]

The relationship between ADHD and epilepsy, although very frequent, is not clear[15]. A prevalence of both conditions of 30 - 40%[11] and even 8 - 77%[16] has been reported. Most researchers in this area argue that it would be appropriate to consider ADHD in patients with epilepsy and not the reverse[11], since subclinical epileptiform activity, in itself, is associated with transient cognitive impairment and neuropsychiatric symptoms[16,17]. The second explanation suggests that both epilepsy and ADHD are generated by a common neurodevelopmental disorder possibly with genetic causes[18,19]. Thus, epilepsy and ADHD would be the manifestation of an underlying neurobiological disorder. This relationship can certainly be clarified by genetic and neurobiological analysis. However, clinical studies in neuropsychology and neurology (neuropsychiatry) can provide valuable information for evaluation, intervention and treatment.

One of the neuropsychological functions that has been most explored in ADHD is executive functions[20,21]. Assessments of these functions have also been performed in children with BECTS[22-25]. Here we show the results of a study in which the executive functioning performances of children with ADHD and BECTS and children with ADHD without BECTS were compared. To date, only one similar comparative study has been published recently in which two additional groups were included: a group of children with ADHD alone and a control group[26]. In that research it was found that children with BECTS and ADHD had worse executive performance compared to patients with ADHD alone, and that children with BECTS and ADHD had a different profile than the other groups.

METHOD

A non-experimental design, quantitative approach, descriptive level and cross-sectional study was carried out with the aim of comparing the executive functioning of a group of children with ADHD and a group of children with ADHD and BECTS. A convenience sample of 40 matched children (all males) grouped into two groups of 20 children aged 7 to 13 years was formed. The first group consisted of children with a diagnosis of ADHD of the combined type (without any comorbidity) applying the DSM-5 criteria. The second group consisted of children with the same diagnosis of ADHD and a clinical diagnosis of BECTS made by clinical neuropediatrics together with EEG analysis. The EEG recording was performed with a 26-channel digital Neurovirtual equipment, simultaneous filming during the whole recording, sensitivity of 7 mV, speed of 10 cm/s, LLF: 1 and HFF: 70 filters. The recommendations of the American Society of Neurophysiology and Electroencephalography and the International League Against Epilepsy were followed.

Seventy-five percent of these children have been treated with monotherapy and 25% with polytherapy. The most frequent drugs were non gabaergic such as: carbamazepine, oxcarbazepine, levetiracetam and lamotrigine. According to the literature, these drugs have the least effect on cognitive functioning. To control the effect of intellectual capacity on executive functions, only children without cognitive impairment, with normal intelligence, were included in both groups. To meet this inclusion criterion, the Reynolds Intelligence Scale - RIAS was applied and only children with a mean score of 80 participated. Four tests were applied: two of verbal intelligence and two of non-verbal intelligence, which compute a measure of general intelligence. Patients with cognitive disability, with other associated neurological or psychiatric disorders, with sensory compromises or patients medicated with valproic acid were excluded.

In order to evaluate executive functioning, some tests of the Neuropsychological Battery of Executive Functions and Frontal Lobes (Batería Neuropsicológica de Funciones Ejecutivas y Lóbulos Frontales – BANFE) were applied. Table 1 shows the tests, specifies the executive functions they evaluate and details the variables that were quantified. Because the neuropsychological evaluation process was conducted during one of the peaks of the COVID-19 pandemic, it was not possible to apply the complete BANFE because of difficulties with the attendance of the participants.

In total, seven executive functions were evaluated through 23 continuous quantitative variables, which were analyzed by means of tests of mean differences for non-parametric variables (Mann-Whitney U test for independent samples) in the IBM SPSS v.24 statistical package for social sciences. The $p < 0.05$ values were considered significant. All the children who participated in the study are part of the Centro de Atención Neuropediátrica Integral – CENPI, Medellín/Sabaneta, Colombia, where they participate in various psychological, neuropsychological and neurological intervention programs. The study complied with the ethical principles for medical research on human beings contemplated in the Declaration of Helsinki of the World Medical Association and was reviewed and approved by the ethics committee of the Universidad de San Buenaventura, Medellín, Colombia.

Table 1. Description of the neuropsychological assessment through the BANFE.

Test	Executive Function	Variables
Stroop Effect	Inhibitory control ability	Stroop A - Errors Stroop A - Time Stroop A - Successes Stroop B - Errors Stroop B - Time Stroop B - Successes
Mazes	Ability to respect boundaries and follow rules and ability to systematically anticipate (plan) visuospatial behavior	Through wall Planning Time
Self-directed pointing	Ability to use visuospatial working memory for self-directed pointing to a series of stimuli	Successes Perseverations Time
Visuospatial working memory	Ability to retain and actively reproduce the visuospatial sequential order of a series of stimuli	Maximum level Perseverations Order errors
Tower of Hanoi	Ability to anticipate sequenced actions in both progressive and regressive order (sequential planning).	Movements Time
Verbal fluency	Ability to produce fluently and within a short period of time as many verbs as possible.	Successes Perseverations
Semantic classifications	Abstraction skills, initiative and mental flexibility.	Categories Abstract categories Average animals Total score

RESULTS

Table 2 presents the participants' information. The mean age in both groups was nine years and a schooling of three years. The group of children with ADHD included two who had a high socioeconomic stratum and could not be matched with those in the group of children with ADHD and BECTS. All children had normal intellectual functioning.

Table 2. Sociodemographic and intelligence characteristics.

	ADHD + BECTS (*N*=20)	ADHD (*N*=20)
Sociodemographic		
Age M(SD)	8.9(1.6)	9.3(2.1)
Schooling M(SD)	3.0(1.9)	3.9(2.2)
Socioeconomic stratum	Lo (50%) – Med (50%)	Lo (55%) – Med (35%) – Hi (10%)
Intelligence		
Verbal Index M(SD)	88.9(10.5)	90.0(7.7)
Nonverbal Index M(SD)	86.5(9.7)	89.0(9.1)
Total Scale M(SD)	87.5(9.8)	88.6(7.9)
M: Media; SD: standard deviation; Lo: Low; Med: Medium; Hi: High.		

Table 3. Summary measures and mean comparison tests.

Test	Variables	ADHD + BECTS *M*(SD)	ADHD *M*(SD)	*U*	*p*
Stroop Effect	Stroop A - Errors	5.7(3)	5.4(3.7)	184,000	0.66
	Stroop A - Time	5.9(3)	7.7(2.3)	133,500	0.06
	Stroop A - Successes	5.4(2.2)	6.7(3.2)	128,500	0.05
	Stroop B – Errors	7.7(2.3)	7.1(3)	177,000	0.53
	Stroop B – Time	4.4(2.3)	6.2(3)	133,500	0.69
	Stroop B - Successes	6.6(1.1)	5.5(3.2)	151.500	0.17
Mazes	Through wall	6(3.4)	4.5(5.7)	176.500	0.51
	Planning	6.5(2.8)	6(2.6)	157.000	157.0
	Time	7.8(3)	8.1(2.3)	195.500	195.0
Self-directed pointing	Successes	5.1(2.0)	7.1(3.2)	113.000	0.017
	Perseverations	6.6(3.1)	7.3(2.0)	170.000	0.41
	Time	9.3(1.3)	6.8(2.7)	75.000	0.001
Visuospatial working memory	Maximum level	6.3(2.6)	7.7(2.2)	134.500	0.72
	Perseverations	7.8(2.4)	9.8(1.7)	100,000	0.006
	Order errors	4.7(1.7)	7.0(1.8)	60.000	0.000
Tower of Hanoi	Movements	6.0(4.0)	6(3.4)	180.000	196.0
	Time	6.1(4.1)	6.9(3.1)	196.000	180.0
Verbal fluency	Successes	7.0(2.6)	8.95(2.5)	112.500	112.5
	Perseverations	9.4(2.1)	8.95(2.8)	192.000	192.0
Semantic classifications	Abstract categories	6(2.2)	7.3(2)	134,500	0.07
	Categories	6.0(1.8)	7.45(2.4)	146.000	146.0
	Average animals	9.1(2.3)	8.4(3.5)	183.000	183.0
	Total score	6.2(2.1)	6.9(2.0)	162.000	162.0
U: **Mann-Whitney U value for independent samples;** ***p:*** **Bilateral asymptotic significance.**					

Table 3 shows the summary measures of the variables and the results of the mean comparison tests between both groups. According to the bilateral asymptotic significance values, statistically significant differences were found in the variables Stroop A - Hits, Stroop B - Hits, Self-directed Signaling (Hits, Planning and Timing), and Visuospatial Working Memory (Maximum Level, Perseverations and Order Errors). Thus, differences were found in only 8 of the 23 variables compared between the two groups. These variables correspond to three of the seven executive functions evaluated.

DISCUSSION AND CONCLUSIONS

The main finding of this comparison of executive functioning between a group of children with a diagnosis of ADHD and a clinical diagnosis of BECTS, and a group of children with a diagnosis of ADHD were differences in inhibitory control ability, the ability to use visuospatial working memory to self-directly cue a series of stimuli, and the ability to actively retain and reproduce the visuospatial sequential order of a series of stimuli. These functions are associated with the functioning of the Dorso Lateral Prefrontal Cortex (DLPFC).

In comparing the executive functioning and attentional skills of children with ADHD and BECTS, and children with ADHD without BECTS, Lima et al.[26] reported that children with BECTS (with or without ADHD) showed significantly more non-perseverative errors on the Wisconsin Card Sorting Test (WCST), while children with BECTS and ADHD (simultaneously) performed worse on Conners Continuous Performance Test (CPT) reaction time standard error, CPT variability, CPT number of perseverations, and CPT inter-stimulus reaction time.

For Lima et al.[26], the existence of severe executive dysfunction in children with BECTS is not clear, although there is subtle executive dysfunction, which had already been demonstrated in other studies[22,27,28] and attentional dysfunction. According to them, it has not been easy to define the executive and attentional functioning profile of these children because it is not always easy to purify the group and in many cases they have comorbidities with ADHD. According to them, children with BECTS and ADHD have worse performance in inhibitory control, impulsivity and different domains of sustained attention.

The results of the present study are consistent with the failures in inhibitory control and sustained attention problems reported in the literature[29]. Although attentional capacity was not directly assessed here, the ability to use visuospatial working memory to self-directly cue a series of stimuli and the ability to actively retain and reproduce the visuospatial sequential order of a series of stimuli have a high correlation with attentional capacities as they share the same processing resources and recruit overlapping brain regions[30]. Furthermore, working memory capacity and the ability to control attention have been linked to the same gene.[31]

Lee et al.[32] found no differences (statistically significant, although scores were lower in the comorbidity group) in visual short-term memory functioning when comparing children with focal epilepsy and ADHD to children with a diagnosis of ADHD alone. They suggest, based on the assessment of working memory performance, that the cognitive deficits shown by children with comorbidity are equivalent to those shown by children with ADHD alone[33], so that there would be a common neurobiological mechanism and neuroanatomical circuitry.

Indeed, children with ADHD (without BECTS) and children with BECTS (without ADHD) have neuropsychological impairments in their executive functioning. That has been reported in the literature. What was found here is that children with BECTS and ADHD have a different and more impaired executive functioning profile than children with ADHD alone. So, benign rolandic epilepsy does contribute to impaired executive function performance regardless of comorbidity with ADHD. This is an important finding since the scientific literature in this area regularly assumes the neuropsychological deficits of BECTS as a manifestation of the cognitive dysfunctions characteristic of ADHD.

However, this group of children was on monotherapy with non- GABAergic drugs, such as carbamazepine, oxcarbazepine, levetiracetam and lamotrigine. Each of these psychotropic drugs has a different effect on executive functioning. Levetiracetam is associated with a favorable effect[34], oxcarbazepine with a slight improvement[34], lamotrigine has no effect[35] and carbamazepine has a detrimental effect[34]. Thus, the effect of medications on executive functions must also be considered. So there would be three factors to evaluate: epilepsy, ADHD and medications. Not to mention family and social factors.

Historically, cognitive and behavioral problems in epilepsy have been conceived as consequences of electrophysiological alterations in the brain. However, seizures and neurobehavioral presentations are now considered as distinct biological components of specific types of epilepsy[36]. The results presented here, and despite some limitations (sample size and lack of control in the type of medications) contribute to the area with evidence suggesting that children with BECTS and ADHD face a neuropsychiatric condition of greater complexity that deserves a particularized approach.

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