

# ADHD in idiopathic epilepsy

## TDAH em epilepsia idiopática

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### ABSTRACT

Our aim was to clarify the correlation of attention deficit hyperactivity disorder (ADHD) with epilepsy and behavior problems. This was a cross-sectional study. Sixty children with idiopathic epilepsy were interviewed using the MTA-SNAP IV Teacher and Parent Rating Scale, Vineland Adaptive Behavior Scales and Conners' Rating Scales. We used the chi-square test to analyze the correlation of epilepsy variables in patients with and without ADHD with a significance level of 0.05. Eight patients had ADHD symptoms (13%), seven had the inattentive ADHD subtype and only three had behavioral problems. When epileptic patients with and without ADHD symptoms were compared we found no significant difference in regard to epilepsy variables. All patients were controlled and 43% were either without AED or undergoing withdrawal. Our study revealed a low comorbidity of ADHD symptoms and epilepsy due to low interference of seizures and drug treatment on the comorbid condition.

**Keywords:** epilepsy, ADHD, childhood, psychosocial aspects, behavior.

### RESUMO

Nosso objetivo foi clarificar a correlação entre transtorno do déficit de atenção (TDAH) com epilepsia e problemas comportamentais. Este foi um estudo transversal. Sessenta crianças com epilepsia idiopática foram entrevistadas com a Escala para Pais e Professores MTA-SNAP IV, Escala de Comportamento Adaptativo Vineland e Escala Conners. Utilizamos o teste do qui-quadrado para analisar a correlação das variáveis de epilepsia em pacientes com e sem TDAH com um nível de significância de 0,05. Oito pacientes apresentaram sintomas de TDAH (13%), sete tiveram o subtipo inatento e três deles tinham problemas comportamentais. Quando os pacientes epiléticos com e sem TDAH foram comparados, não encontramos diferença significativa em relação às variáveis de epilepsia. Todos os pacientes estavam controlados e 43% deles estavam sem medicação ou em retirada da droga. O nosso estudo mostrou baixa comorbidade entre epilepsia e TDAH devido à baixa interferência de crises e tratamento na condição comórbida.

**Palavras-chave:** epilepsia, TDAH, infância, aspectos psicossociais, comportamento.

ADHD is three to five times more common in people with epilepsy than in the normal population<sup>1,2</sup>. It occurs in 14-31% of children with epilepsy<sup>3,4</sup>. It seems that the severity of epilepsy enhances the predisposition for having ADHD, since comorbidity is described in both benign and refractory childhood epilepsy<sup>1,5-7</sup>. Inattentive ADHD is appointed as the most common subtype in epileptic patients<sup>4,6-8</sup>.

Etiology, duration of epilepsy, seizure frequency, seizure control, and the use of antiepileptic drugs are important variables related to neuropsychological and behavioural problems in patients with epilepsy and ADHD. It seems that patients with idiopathic epilepsy presenting with few seizures or who are seizure-free with monotherapy have a low frequency of neuropsychological and behavioral problems<sup>8-12</sup>. Epileptiform discharges, particularly during the active phase

of the epilepsy, are also an important variable when neuropsychology and behavior are concerned<sup>6,8,11</sup>.

The correlation between the variables of epilepsy and ADHD has not yet been fully elucidated. This study aims to verify the occurrence of ADHD symptoms in a group of patients with idiopathic epilepsy and the relationship between clinical variables, electroencephalogram (EEG), treatment, and psychosocial and behavioral changes.

### METHODS

This is a cross-sectional study. We interviewed 60 patients who were diagnosed with idiopathic epilepsy according to the ILAE criteria<sup>13</sup>. Patients were followed at the Childhood

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Outpatient Clinic of our University Hospital. This study was approved by the Ethical Committee of our institution (protocol 309/2009).

Patients and/or their guardians were invited to sign an informed consent form. The interview was based on a questionnaire asking for detailed characterization of the epileptic seizures, personal histories and morbidities, including previous ADHD symptoms. Patients underwent a clinical and neurological exam.

Seizure frequency was classified as: sporadic (less than one or one seizure a month), frequent (from one to four seizures a month) and very frequent (more than four seizures a month)<sup>14</sup>.

The following tests were applied: to investigate ADHD symptoms<sup>15</sup> we utilized the MTA-SNAP IV Teacher and Parent Rating Scale<sup>16</sup> to assess inattention, hyperactivity and impulsivity symptoms; the Conners' Parent Rating Scale Revised Long Version<sup>17</sup> to assess behavioral problems, including inattention, impulsivity and hyperactivity; and, the Vineland Adaptive Behavior Scale<sup>18</sup> to assess abilities in communication, daily activities and sociability. In patients with ADHD symptoms, the Wechsler Intelligence Scale for Children - WISC III<sup>19</sup> - was administered by an experienced professional.

Every patient underwent a digital EEG, with electrodes positioned according to the International 10-20 system, in resting position, during wakefulness and spontaneous sleep, in hyperventilation, and with intermittent photic stimulation. The visual analysis of the EEG sought to characterize the background activity and, when epileptiform discharges occurred, analyze the morphology, amplitude and duration, location, laterality and, when bilateral, the synchrony, distribution and frequency. The findings were categorized as: (1) normal during wakefulness, drowsiness and/or sleep; (2) abnormal with non-epileptiform disturbance: focal or generalized slow waves in the theta or delta range; (3) abnormal with focal epileptiform discharges: spikes or focal

sharp waves or spike-slow wave; (4) abnormal with generalized epileptiform discharges: spikes or focal sharp waves or spike-slow wave; (5) abnormal with both epileptiform and non-epileptiform disturbances.

We used the chi-square test to analyze the correlation of epilepsy variables (age at seizure onset, epileptic syndrome, type of seizure, seizure frequency, period without seizures and abnormalities in the EEG) in patients with and without ADHD symptoms. We used a significance level of 0.05.

## RESULTS

Between September of 2008 and September of 2009, we assessed 60 patients diagnosed with idiopathic epilepsy, with age between six and 16 years of age ( $M=6.42\pm 2.6$ ), and half of them were girls. Brain MRIs were normal in all patients.

Benign epilepsy of childhood with centrotemporal spikes was the most frequent epileptic syndrome, occurring in 31 patients (51.6%). The age at seizure onset varied between one and 14 years ( $M=6.41\pm 2.5$ ). The distribution of patients in regard to epileptic syndrome, occurrence of ADHD symptoms, sex and age at seizure onset are presented in Table 1. Most of our patients (44=73.3%) received the diagnosis of epilepsy within the past five years ( $M=4.7\pm 2.2$ ). Most of our patients had focal seizures (44=73.3%). The distribution of patients in regard to epilepsy duration and seizure type is presented in Table 2. Most of our patients (32=53.3%) were seizure-free for more than two years and, of those, 26 patients were either without antiepileptic drug treatment or undergoing withdrawal.

Eight patients had ADHD symptoms (13.3%). Seven of these eight patients were girls. No patient had IQ scores under 79 ( $M=97.6\pm 8.3$ ). Benign childhood epilepsy with centrotemporal spikes occurred in five of the eight patients with ADHD symptoms. Five out of patients were not on

**Table 1.** Distribution of patients in regard to epileptic syndrome, the occurrence symptoms of ADHD, gender and age at seizure onset.

Epilepsy syndrome (n/%)	Symptoms of ADHD (SNAP IV /DSM IV)		Gender				Age at seizure onset (years)					
			Male		Female		< 6		6 to 11		> 11	
	n	%	n	%	n	%	n	%	n	%	n	%
BECT (31/51.6)	5	62.5	17	28.3	14	23.3	17	28.3	14	23.3	-	-
CAE (10/16.6)	2	25	6	10	4	6.6	6	10	4	6.6	-	-
LCOE (8/13.2)	1	12.5	3	5	5	8.3	3	5	5	8.3	-	-
JME (4/6.6)	-	-	3	5	1	1.6	-	-	-	-	4	6.4
PS (3/5)	-	-	-	-	3	5	3	5	-	-	-	-
ADNFLE (2/3.3)	-	-	-	-	2	3.3	-	-	2	3.3	-	-
EGTCSA (1/1.6)	-	-	1	1.6	-	-	-	-	1	1.6	-	-
JAE (1/1.6)	-	-	-	-	1	1.6	-	-	-	-	1	1.6
Total (60/100)	8	100	30	50	30	50	29	48.3	26	43.3	5	8.4

ADHD: attention deficit hyperactivity disorder; BECT: Benign epilepsy with centrotemporal spikes; CAE: Childhood absence epilepsy; LCOE: Late onset childhood occipital epilepsy; JME: Juvenile myoclonic epilepsy; PS: Panayiotopoulos syndrome; ADNFLE: Autosomal-dominant nocturnal frontal lobe epilepsy; EGTCSA: Epilepsy with generalized tonic-clonic seizures alone; JAE: Juvenile absence epilepsy.

antiepileptic drugs at the time of the assessment, whereas most patients without ADHD (68.4%) were on antiepileptic drugs (Table 3). All patients with ADHD symptoms were seizure-free in the past year.

The distribution of patients in regard to the period of time in which their seizures were controlled, the seizure frequency, the use of antiepileptic drugs, current EEG and the occurrence of ADHD symptoms are presented in Table 3.

**Table 2.** Distribution of patients in regard to epilepsy duration and seizure type.

Characteristics	Frequency	
	n	%
Epilepsy duration (years)		
< 1	–	–
1-5	28	46.7
> 5	32	53.3
Seizure type		
Focal	44	73.3
Generalized	16	26.7

Among the patients with ADHD symptoms, the current EEG was normal in four patients, abnormal with focal epileptiform activity in four and abnormal with generalized epileptiform activity in one.

When epileptic patients with ADHD symptoms were compared with epileptic patients without ADHD we found no significant difference in regard to age at seizure onset ( $p=0.073$ ), epileptic syndrome ( $p=0.924$ ), type of seizure ( $p=0.909$ ), seizure frequency ( $p=0.871$ ), period without seizures ( $p=0.202$ ) and abnormalities in the EEG.

Seven patients presented with the inattentive ADHD subtype on the Conners' Scale. One patient with ADHD symptoms also showed psychosomatic alterations on the Conners' Scale. The distribution of behavioral problems in the patients according to the Conners' Rating Scale is presented in Table 4.

Most patients with ADHD symptoms (75%) did not have problems on the Vineland Adaptive Behavioral Scale. The two patients with low scores on the communication domain of the scale were the same ones who did not have a passing grade at school. The distribution of patients according to the Vineland Adaptive Behavior Scale is presented in Table 5.

**Table 3.** Distribution of patients in regard to the seizure-free period, seizure frequency, use of antiepileptic drugs, current EEG and the occurrence symptoms of ADHD.

Symptoms of ADHD	Seizure free (months)			Seizure frequency			Use of antiepileptic drugs			**Current EEG		
	≥24	≥12	<12	*Sporadic	*Frequent	*Very Frequent	None	Monotherapy	Polytherapy	**1	**2	**3
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Presence	5 (8.3)	3 (5)	– (-)	4 (6.6)	2 (3.3)	2 (3.3)	4 (6.6)	3 (5)	1 (1.6)	4 (6.6)	4 (6.6)	– (-)
Absence	27 (45)	11 (18.4)	14 (23.4)	30 (50)	8 (13.3)	14 (23.5)	11 (18.4)	36 (60)	5 (8.4)	26 (43.3)	20 (33.3)	6 (10)
Total (%)	32 (53.3)	14 (23.4)	14 (23.4)	34 (56.7)	10 (16.6)	16 (26.7)	16 (26.7)	38 (63.3)	6 (10)	30 (50)	24 (40)	6 (10)

\*Sporadic: less than one or one seizure a month; frequent from one to four seizures a month; very frequent more than four seizures a month; \*\*1: normal during wakefulness, drowsiness and/or sleep; 2: abnormal with focal epileptiform discharges: spikes or focal sharp waves or spike-slow wave; 3: abnormal with generalized epileptiform discharges: spikes or focal sharp waves or spike-slow wave; EEG: electroencephalogram; ADHD: attention deficit hyperactivity disorder.

**Table 4.** Distribution of patients in regard to behavioral problems on the Conners' Scale.

Significance	Patients with symptoms of ADHD (n)									
	Normal		Very slightly atypical		Slightly atypical		Moderately atypical		Markedly atypical	
	Presence	Absence	Presence	Absence	Presence	Absence	Presence	Absence	Presence	Absence
Opposition	8	52	–	–	–	–	–	–	–	–
Cognitive problems/inattention	–	52	–	–	–	–	1	–	7	–
Hyperactivity	7	52	–	–	–	–	–	–	1	–
Anxiety	8	52	–	–	–	–	–	–	–	–
Perfectionism	8	52	–	–	–	–	–	–	–	–
Social problems	8	52	–	–	–	–	–	–	–	–
Psychosomatic	7	52	–	–	–	–	–	–	1	–
CGI: restlessness/impulsivity	4	52	1	–	3	–	–	–	–	–
CGI: emotional ability	8	52	–	–	–	–	–	–	–	–
Inattention (DSM IV)	–	52	–	–	–	–	–	–	8	–
Hyperactivity – impulsivity (DSM-IV)	7	52	–	–	–	–	–	–	1	–

CGI: Conner's Global Index; ADHD: attention deficit hyperactivity disorder.

**Table 5.** Distribution of patients according to the Vineland Adaptive Behavior Scale.

Scale	Patients with symptoms of ADHD											
	Communication				Day-to-day abilities				Sociability			
	Presence		Absence		Presence		Absence		Presence		Absence	
	n	%	n	%	n	%	n	%	n	%	n	%
Adequate	6	75	52	100	8	100	52	100	8	100	52	100
Moderately inferior	1	25	–	–	–	–	–	–	–	–	–	–
Inferior	1	25	–	–	–	–	–	–	–	–	–	–
Total	8	100	52	100	8	100	52	100	8	100	52	100

ADHD: attention deficit hyperactivity disorder.

## DISCUSSION

In this study the occurrence of ADHD symptoms among our patients was 13%, which is similar to other studies<sup>3,20,21</sup>. However, it is less than that described by Hermann et al.<sup>4</sup> who found an occurrence of ADHD symptoms in 31.5% of patients with idiopathic epilepsy. The authors included patients with diagnosis of epilepsy within the past 12 months; we might wonder that at least some of them were still in the active phase of the disease. Nevertheless, the majority of our patients had been diagnosed with epilepsy within the past five years, most of them were seizure-free for more than two years, and almost half of our patients were either without antiepileptic drug treatment or undergoing withdrawal. Therefore, we consider that our results reflect cleaner data with less interference of seizures and drug treatment on the presence of the comorbid condition.

Our results showed that ADHD symptoms occur more frequently in girls with epilepsy than in boys and most of our patients with ADHD symptoms fit into the inattentive subtype. Our data are in keeping with the findings of other authors<sup>4,7</sup> and point to the fact that there is a difference between ADHD features in patients with and without epilepsy, as ADHD in patients without epilepsy occur mostly in boys and the most common form is the hyperactive-impulsive subtype<sup>1,22,23</sup>.

Our study found that most of our patients did not have adaptive behavioral changes. Seven of our eight patients with ADHD symptoms did not present with any other behavioral abnormalities measured on the Conners' Rating Scale; this was also the case with the 52 patients without symptoms of ADHD. Besides, most of our patients with ADHD symptoms did not present with abnormalities in the adaptive behavior measured on the Vineland Scale; neither did the patients without symptoms of ADHD, which is distinct from the results described by others<sup>4,6,7,24</sup>. This discrepancy between our study and others' is probably due to the different inclusion criteria, because we included only patients with idiopathic

epileptic syndromes and other authors included patients with all types of epilepsy<sup>6</sup>, recently-diagnosed epilepsy<sup>4</sup> or even uncontrolled patients<sup>6,24</sup>. Our findings match with other studies that show that infrequent seizures and well-controlled patients on monotherapy are important variables to predict lower rates of ADHD symptoms and behavioral abnormalities<sup>8,10</sup>. Moreover, we did not find a positive correlation between clinical epilepsy variables and the occurrence of ADHD symptoms as described by others<sup>8-12</sup>. This is probably due to the benignity of our sample.

Behavioral problems, such as depression and anxiety, are important comorbid conditions when patients with ADHD without epilepsy are considered<sup>25,26</sup>. In our study most of the patients did not have behavior problems or adaptive behavioral changes, reinforcing that there is a difference between ADHD features in patients with and without epilepsy.

The presence of epileptiform activity was not found to be correlated with the occurrence of ADHD symptoms. There are many studies that analyze the relationship between epileptiform activity and patients with ADHD<sup>9,27,28</sup>.

The concern about the impact of epilepsy on cognitive development has been longstanding. It is well known that seizure itself and antiepileptic drugs may jeopardize cognition. Several reports, however, demonstrate that ADHD symptoms are present even before the onset of epilepsy<sup>1,29,30</sup>. The finding that half of our patients with ADHD symptoms were well controlled without antiepileptic drug suggests that ADHD symptoms may occur in epileptic patients independent of active seizures or treatment. Moreover, more recent studies have shown that structural abnormalities and cognitive development are present in children with new onset epilepsy, suggesting pre-existing abnormalities in brain development<sup>30-32</sup>.

To summarize, our data reinforce the idea that the brain of epileptic patients may harbor subtle abnormalities which are responsible for ADHD symptoms and epilepsy. This study also points to the existing difference between the ADHD features in patients with and without epilepsy.

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