

## INTERNALIZING SYMPTOMS IN CHILDREN AFFECTED BY CHILDHOOD ABSENCE EPILEPSY: A PRELIMINARY STUDY

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### ABSTRACT

**Introduction:** Childhood absence epilepsy (CAE) is a common type of pediatric idiopathic generalized epilepsy, characterized by multiple seizures of typical absence, with typical EEG pattern consisting in bilateral synchronous and symmetrical discharges of generalized 3 Hz spike-wave (SWDs).

Recently, some researchers have suggested that the underlying epileptogenic mechanism of absence seizures selectively involves the frontal cortical circuits, also supported by video-electroencephalography data<sup>(3)</sup>. These data may be considered as a new window in CAE comprehension and management, particularly about symptoms different from seizure that children affected may present.

In this light, aim of the present study is evaluating the presence of internalizing problems in prepubertal children affected by CAE.

**Material and methods:** 18 patients (10 females, 8 males) ranging age from 8-11 years (mean age  $9.36 \pm 1.32$ ) affected by typical CAE were recruited. Control group was composed by 43 subjects (32 females, 11 males) (mean age  $8.54 \pm 2.01$ ). All subjects were screened for internalizing symptoms with SAFA-A scale and CDI test.

**Results:** The two groups were comparable for age ( $p=0.117$ ) and sex distribution ( $p=0.251$ ). CAE children showed significantly higher score than controls for anxiety ( $p<0.001$ ) and depressive symptoms screening tests ( $p<0.001$ ) (Table 1).

**Conclusions:** Results of present study suggest the importance of screening for anxiety and depressive signs in CAE children, in order to optimize their management beyond the exclusive idea to control and stop epileptic seizure only.

**Keywords:** Childhood Absence Epilepsy, CAE, SAFA-A, Children Depression Inventory, Internalizing symptoms.

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### Introduction

Childhood absence epilepsy (CAE) is a common type of pediatric idiopathic generalized epilepsy, corresponding to 10%-17% of all cases of epilepsy diagnosed in school-age children<sup>(1)</sup>. Typically is characterized by multiple seizures of typical absence, with typical EEG pattern consisting in bilateral synchronous and symmetrical discharges of generalized 3 Hz spike-wave (SWDs).

CAE tend to be more frequent in girls than in boys (11.4% vs. 2.5%), occurring, usually, between 4-10 years with a peak at 5-7 years<sup>(2)</sup>.

Clinically, CAE is characterized by frequent absence seizures even up to 100 daily and the sudden consciousness suspension/lost is essential feature, with contact loss from the surrounding environment, the absence of response to the calls and psychomotor stop<sup>(2)</sup>.

Moreover, many children may interrupt their activity, but some may continue to perform their duties in an altered manner. Another important clinical feature associated ictal, consists of fixed gaze, regular movements of the eyes to 3 Hz and eye opening in cases in which they are initially closed, although frequently automatisms during long seizures and during performing hyperventilation<sup>(2)</sup>.

Recently, some researchers have suggested that the underlying epileptogenic mechanism of absence seizures selectively involves the frontal cortical circuits, also supported by video-electroencephalography data<sup>(3)</sup>. These data may be considered as a new window in CAE comprehension and management, particularly about symptoms different from seizure that children affected may present.

In this light, aim of the present study is evaluating the presence of internalizing problems in prepubertal children affected by CAE.

## Material and Methods

### Population

18 patients (10 females, 8 males) ranging age from 8-11 years (mean age  $9.36 \pm 1.32$ ) affected by typical CAE were recruited. Control group was composed by 43 subjects (32 females, 11 males) (mean age  $8.54 \pm 2.01$ ).

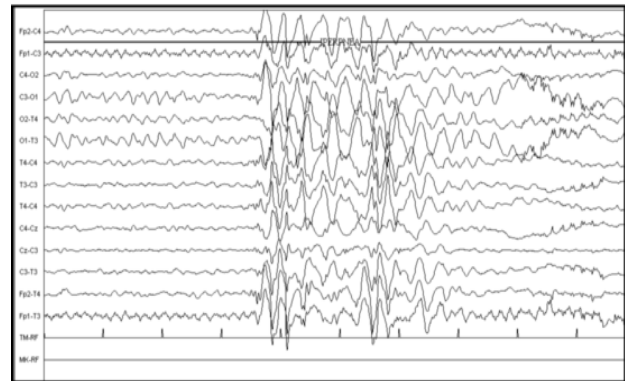
All subjects of both groups were recruited within the same urban area, all were Caucasian and homogeneous for socioeconomic status

Ethical approval from the local Research Ethics Center and informed parental consent were obtained.

### EEG evaluation

As reported by Rotondi et al.<sup>(4)</sup>, EEG was recorded in a dimly lit room by means of 21 Ag/AgCl surface electrodes placed according to the 10-20 International System, and acquired using a computerized system (Micromed System Plus, Mogliano Veneto (TV), Italy) (sampling frequency 256 Hz; band pass filter 1-120 Hz, 12 dB/octave). All of the EEG signals were recorded using a linked-ear reference. EEG data were transferred from head box (battery powered) to EEG machine using optical fiber connections. Before the recordings, the electrode impedances were checked and maintained their values below 5 kX until the end of the recording. A long lasting baseline eyes-closed EEG was recorded for all CAE and CTRL subjects in awake state.

The EEG recordings used for this study started between 9:20 and 10:30 AM and lasted at least 40 min (for both patients and controls). In all CAE typical sharp-waves discharges (SWDs) were recorded, occurring spontaneously or during hyperventilation. The typical EEG patterns was characterized by SWDs 3.5-4Hz (Figure 1).



**Figure 1:** Shows the typical EEG pattern consisting in bilateral synchronous and symmetrical discharges of generalized 3 Hz spike-wave (SWDs) of childhood absence epilepsy (CAE).

### Anxiety assessment

As reported by Esposito et al. in 2014 (5), all subjects filled out the SAFA - Anxiety (SAFA-A) scale, a self-administered questionnaire providing an emotional profile in children. The SAFA-A scale was created to assess internalizing problems and comprises a specific subscale for 8- to 10-year old children (SAFA A/e), for 11- to 13-year-old children (SAFA A/m), and for 14- to 18-year-olds (SAFA A/s). The SAFA A/e scale consists of 42 items (40 negative and two positive affirmations) grouped into four subscales: Generalized Anxiety (ten items); Social Anxiety (ten items); Separation-Loss Anxiety (ten items); and School-Related Anxiety (ten items). The scale is characterized by good reliability in healthy subjects (Cronbach's  $\alpha = 0.857$ ).

### Screening for depressive symptoms

As previously reported<sup>(6)</sup>, all children filled out the Italian version of the CDI, in order to evaluate depressive symptoms. The CDI is widely used to assess depressive symptomatology in children and adolescents aged 8-17 years, providing good internal consistency (Cronbach's  $\alpha = 0.80$ ). The scale is composed of 27 Likert-like items scored from 0 to 2, with higher scores reflecting more important depressive symptomatology. According to the Italian validation criteria, a score of 19 is considered suggestive of depressive symptoms.

### Statistical analysis

For comparison between the two groups (CAE and controls) t- testing and Chi-square test, where appropriate, were applied. P values <0.05 were considered statistically significant.

For statistical analysis it used the software STATISTICA (data analysis software system, version 6, StatSoft, Inc. (2001).

### Results

The two groups were comparable for age ( $p=0.117$ ) and sex distribution ( $p=0.251$ ). CAE children showed significantly higher score than controls for anxiety ( $p<0.001$ ) and depressive symptoms screening tests ( $p<0.001$ ) (Table 1).

	CAE	Controls	p
Age	9.36 ± 1.32	8.54 ± 2.01	0.117
Sex (F/M)	8-Oct	32/11	0.251
CDI total score	15 ± 7.513	8.667 ± 1.88	<0.001
SAFA-A total score	59.225 ± 7.341	48.857 ± 9.986	<0.001

**Table 1:** Shows differences between subjects affected by childhood epilepsy absence (CAE) and typical developing children (Controls) for age, sex, CDI total score and SAFA-A total score.

For comparison between the two groups (CAE and controls) t- Test and Chi-square test were applied, when appropriate.

P values <0.05 were considered statistically significant.

### Discussion

In general, internalizing symptoms may be relevant in neurological disorders of developmental age<sup>(7-13)</sup>, as reported in many studies as significantly influencing neurological disorders management and care and patients' quality of life<sup>(14-19)</sup>. In fact, internalizing symptoms (mainly depressive symptoms) could impact cognitive and behavioural functions in children affected by neurological and /or pediatric chronic diseases<sup>(20-34)</sup>.

Moreover, as reported in 2011 by Vega et al.<sup>(35)</sup>, CAE children tend to experience subclinical levels of affective problems relative to peers, thus placing them at risk for developmental issues such as poor academic achievement and social adjustment, thus impacting quality of life.

On the other hand, prefrontal circuits may be interested by epileptic activity and explaining the high prevalence of internalizing symptoms in CAE children, not only related to live with a chronic dis-

ease. In this perspective, fMRI data showed that spike and wave discharges are the result of epileptic activity generated within the cortico-thalamocortical circuit, supporting the hypothesis of a trigger zone within a specific area of the thalamic-cortical system genetically determined<sup>(2)</sup>.

In this light, our findings could be explained by the known key role of these regions in human mood and anxiety regulation<sup>(36-50)</sup>.

In conclusion, results of present study suggest the importance of screening for anxiety and depressive signs in CAE children, in order to optimize their management beyond the exclusive idea to control and stop epileptic seizure only.

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