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ABSENCE EPILEPTIC SEIZURES AND COGNITIVE DEVELOPMENT

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Abstract: Absence epilepsy (EA) is the most common type of epilepsy in children. It is characterized by a brief loss of consciousness lasting seconds or a few minutes, with up to 200 attacks per day. Despite its benign character due to the low incidence of tonic-clonic seizures and being self-limiting, it is a disease that can generate short- and long-term cognitive and psychosocial impairments. This literature review aims to understand the effects of EE on children's cognitive development. For this, articles published in *the Virtual Health Library (BVS)* and*PubMed* in the years 2010 to 2021. A high rate of psychomotor deficits was demonstrated and an important relationship between these and school, social and family problems, both in children and in adults after remission of the disease. To prevent these damages, the importance of a multidisciplinary care for children was highlighted as an attempt to improve their quality of life and minimize cognitive and psychosocial losses.
Keywords: Absence-type epilepsy; cognition; learning.

INTRODUCTION

Epileptic seizures have been reported since ancient history and were commonly associated with spiritual problems or divine punishment. Thus, the therapeutic approach to the sick varied from prayers, physical punishment or any other religious practice. In 1857, Charles Locock proposed that the causes of the crises would be excess of female sexuality and instituted a treatment based on potassium bromide, an anti aphrodisiac. Such thinking and treatment was used until the commercialization of the first antiepileptic in 1912, Phenobarbital. (LIBERALESSO, 2018).

In general, an epileptic seizure can be defined by a sensory, motor and autonomic syndrome with or without loss of consciousness triggered by brain electrical discharges, being a transient and involuntary event lasting a few minutes. (BARONE; PUTTEN; VISSER, 2020).

The prevalence of epilepsy in Brazil is between ten and fifteen inhabitants per thousand. Among these are those with Absence Epilepsy (AS), formerly called "petit mal", the most common type of epilepsy in children. (LIBERALESSO, 2018).

AS is an autosomal dominant genetic disorder and has its onset around 6-8 years of age or adolescence, depending on the specific type of absence. It is characterized by a brief loss of consciousness in which the child presents himself with a fixed and distant look for a few seconds and then returns to his normal activity without having the perception of what happened (LIBERALESSO, 2018).

This type of epilepsy has a benign characteristic as it is generally not accompanied by tonic- clonic seizures and has a high incidence of remission in early adulthood. However, most children with AS are affected by other psychiatric pathologies and impairments in cognition as a result of the effects of the crisis. For example, attention deficit, depression, family and social problems, which may persist even after the pathology has completely resolved (CRUNELLI *et al,* 2020).

The diagnosis of the disease is usually made when children enter school, where they often start to have low performance and poor interaction with peers, thus showing the first signs of psychosocial damage in children's lives (GOMES *et al,* 2013).

Within this context, the importance of studying the consequences of absence crises in child development is shown, whether neuropsychomotor, school, family or social (CRUNELLI *et al,* 2020). In view of the above: the objectives of this work were:

GENERAL PURPOSE:

To discuss, through a literature review, the effects of absence epilepsy on the cognitive development of children who attended school.

SPECIFIC PURPOSE:

- Knowing Absence Epilepsy: classification, clinical picture and treatment of the target population of this study.
- List the main cognitive deficits presented by children with AS.

LITERATURE REVIEW

According to Gomes *et al.* (2013) epilepsy is an ancient disease and is named after the Greek word *epilambaneima.*which means surprise. In the past, epileptic seizures were believed to come from divine or magical forces. They are reported for more than 5,000 years, before Christian eras, but there are also reports in biblical gospels. In this sense, for a long time epilepsies were treated as religious problems and did not receive the due attention of scholars (LIBERALESSO, 2018).

Hippocrates was the first researcher to disregard the supernatural factor as an influencer of epilepsies and thus the first correlations of epilepsy with neurological defects were established. Later, Charles Lokock, in 1857, proposed that the crises were a consequence of the excess of female sexuality and instituted one of the first drug treatments for the disease, which was based on inhibiting this supposed stimulus with potassium bromide, an anti - aphrodisiac. In the 20th century, the first really effective drug was produced and marketed in 1912, phenobarbital (LIBERALESSO, 2018).

Epilepsy has a high degree of importance on the world stage as it is the most prevalent neurological disease, responsible for affecting 60 to 65 million people worldwide. It is estimated that, in Brazil, this prevalence is around 1 to 2% of the entire population. Prevalence rates vary according to the population involved, however, children always have higher numbers of cases. Among them, absence epilepsy is the most frequent. Responsible for 10 to 12% of epilepsies in children under 16 years of age (ZUBERI; SYMONDS, 2015); (BARONE; PUTTEN; VISSER, 2020, p. 1); (LIBERALESSO, 2018); (GOMES *et al,* 2013).

Conceptually, epilepsy is defined by a brain condition that characterizes a genetic predisposition to uncontrolled electrical synapses capable of generating different types of seizures (BARONE; PUTTEN; VISSER, 2020).

As one of the types of epilepsy, AS is characterized as generalized brain discharges with peak waves of 3 to 4 Hz, evidenced in the electroencephalogram (EEG), responsible for a brief loss of consciousness, usually from 3 to 30 seconds, which can occur up to 200 times daily (BARONE; PUTTEN; VISSER, 2020); (LIBERALESSO, 2018); (GOMES *et al,* 2013).

Even though, in the vast majority of seizures, there is no motor involvement, it is known that in some cases, mild signs of localized or generalized tremors may be present, and thus characterize specific types of absence seizures (BARONE; PUTTEN; VISSER, 2020)

There are several types of AE already reported, the main ones are infantile absence epilepsy (IAE) and juvenile absence epilepsy (EAJ), however the clinical separation is difficult and they differ in some details. (WALD *et al,* 2019).

AIS usually presents between 4 and 10 years of age, with an increased frequency of attacks per day, impairment of the most important level of consciousness and a higher incidence of case remission. In contrast, JAE starts around 10 and 17 years of age, has a lower number of seizures per day with milder

impairment of consciousness, associated tonic- clonic seizures and a lower chance of cure, despite treatment and neurological maturation. (WALD *et al,* 2019).

In the past, it was thought that there would be no cognitive deficits in the life of a child with AS, however, recent studies show such impairments in intelligence, motor functioning, language and especially attention and social interaction. (WALD *et al*, 2019).

It is difficult to accurately estimate the degree of cognitive impairment in these children, as there are several ways to assess them, and this way, change the result. However, most studies showed worse percentages for the population with AS. (WALD *et al*, 2019, p. 443).

A cognitive deficit is never something specific in child development, it is usually related to another impairment in the cognitive domain. The most important vulnerability observed was in intelligence, executive functions and especially attention, which directly influence the child's school performance, memory and social interaction. (WALD *et al,* 2019).

To assess intelligence, the Intelligence Quotient (IQ) was used. Although some studies show biases regarding this assessment, the mean values in this regard for children with AS dropped by 5.32 compared to the control group. (WALD *et al,* 2019).

Regarding executive cognition, the results for children with AS were also lower. The studies showed difficulties in planning and verbal fluency, in addition to low cognitive flexibility. (WALD *et al,* 2019).

Clear impairments in attention were observed from inferior results in sustained attention, selective attention, and divided attention. In addition, the diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) is commonly associated with AE, and even with remission of seizures, ADHD remains in adulthood. (WALD *et al,* 2019).

In numbers, children with absence epilepsy are 2.5 to 5 times that are more likely to develop ADHD, and in this population the prevalence of ADHD is 30 to 60%. (BARONE; PUTTEN; VISSER, 2020).

Attention is considered a basic mechanism for the functioning of several other skills, so it is one of the most studied cognitive domains and also one of the ones that generate the most damage, in the short and long term, if it is diminished (BARONE; PUTTEN; VISSER)., 2020).

Based on EEG assessments, specific patterns of electrical activation were observed in the frontal brain areas, which are related to impaired attention in AS patients. In addition, peak wave duration, amplitude, rhythmicity, and frontocentral distribution also correlate with severe impairment in alertness and memory. These EEG presentations, along with greater amplitude and generalization of seizure activity, were associated with significantly worse attention. (BARONE; PUTTEN; VISSER, 2020).

Concomitantly with impairments in attention, and because this deficit is multifactorial in nature, playing a role in several psychosocial aspects, low school performance is evidenced in most children with AS. Previous studies showed that 65% of them had mild to severe academic difficulties and 42% had other associated comorbidities. (WALD *et al,* 2019).

School difficulties are generally related to the occurrence of crises and the deficits in attention generated by them. In addition, it relates to age of onset, frequency, degree, seizure control, etiology, and type of medication used. (GOMES *et al,* 2013).

Knowledge of the disease by family members influences attitudes and important decision-making in the child's life. School absences, parents' ban on sports, low

expectations of parents and teachers regarding the child's performance, possibility of being rejected by peers and teachers, low self-esteem, are factors present in the life of the individual with AS. Thus, biopsychosocial impacts on learning are also relevant in children's school and social development and are characterized as inherent consequences of the epileptic condition. (GOMES *et al,* 2013).

The problems resulting from EA that arise in childhood that translate into ADHD, low school performance and social isolation are related to problems in adult life, such as high levels of unemployment and depression. Therefore, studies that assess the correlation of AE with cognitive disorders may be useful in the search for the well-being of patients with this pathology. (BARONE; PUTTEN; VISSER, 2020).

Many factors in AS are responsible for the evidenced cognitive impairment. Thus, an early diagnosis and drug intervention brings better prognosis regarding long-term cognitive losses. (GOMES *et al,* 2013).

It is not completely clear whether attention improves with time, but other cognitive dysfunctions can be prevented by instituting pharmacological treatment. (BARONE; PUTTEN; VISSER, 2020).

In addition, it is recommended that children with AS are always evaluated in the early search for cognitive deficits, with the intention of instituting new studies and correlations of the disease with cognitive impairments and in the prevention of other associated pathologies. (WALD *et al,* 2019).

METHODOLOGICAL PROCEDURE

LITERATURE REVIEW

This is a literature review study on the thematic effects of absence epilepsy (AS) on children's cognitive development.

When a literature review is presented, a synthesis, analysis and presentation of the scientific knowledge already produced on the subject in question is sought, based on previous studies.

PREPARATION OF THE LITERATURE REVIEW

For the elaboration of this literature review, the following steps were taken: establishment of the hypothesis and objectives of the review (formulation of the question to be answered with the study); establishment of inclusion and exclusion criteria for articles (sample selection); definition of the information to be extracted from the selected articles; elaboration of the literature review based on the main topics brought in the selected articles to the theme.

Through the question: **Can Absence Epilepsy bring cognitive impairment to children?** The following elements were used in the selection of studies: population/patient (children between 4 and 18 years old); interest (absence epilepsy patients); outcome (patients with cognitive impairment); time (studies between 2010 and 2021).

In view of the articles found in the literature, tables were prepared for the insertion of the collected data and subsequent analysis.

The databases of articles indexed in the health area Virtual Health Library (VHL) and PubMed (Public/editor MEDLINE) were established for data collection. Those published in Portuguese, Spanish and English were selected.

INCLUSION CRITERIA

Inclusion criteria were: articles from the last 10 years (January 2010 to March 2021) published and indexed in the aforementioned databases, with free and fully released texts, in Portuguese, English or Spanish. Children, aged for categorization from 04 to 18 years of age.

To search for scientific articles in the aforementioned databases, the descriptors " *AbsenceEplepsy* ", " *Childhood* ", *"Learning"*. Also," *freefulltext* ", " *randomizedcontrolltrials"*, *"review"*, *"systematic review"* and "*10 years* " were the filters chosen for the selection of texts.

To compose the search strategies, the descriptors were combined with each other, with the help of the Boolean operators, AND and OR.

EXCLUSION CRITERIA

The following criteria were used to exclude articles: year of publication of the article different from January 2010 to March 2021, duplicate articles, articles referring to other types of epilepsy, articles that did not mention pediatric patients.

CATEGORIZATION OF ARTICLES

In a second stage, after readings and re-readings, the thematic categorization of the articles was carried out in view of the diversity of the themes found. Subsequently, tables were prepared in which the themes were grouped according to each database consulted.

ETHICS COMMITTEE:

In the case of documentary research in the literature review modality, the study project was not submitted to the ethical procedures that involve approval by a research ethics committee. However, all studies mentioned were cited in order to be identified by authorship and published journal.

RESULTS

Initially, 18 articles were selected from the aforementioned bases, of which 13 were eligible for the work, as they fit the inclusion criteria.

Between March and April 2021, a complete bibliographic reading was carried out together with the highlighting of the key points of each article that encompass the objectives of this work. In addition, even at this stage, articles were excluded that, after a detailed reading, did not fit the interest of this review, leaving at the end, 9 selected articles, which contained the population involved (children from 4 to 18 years old), who had epilepsy of absence and cognitive impairment.

Finally, this document was prepared based on the articles selected in the previous stages.

FINAL CONSIDERATIONS

Despite the literature presenting AS as a benign self-limiting pathology, the analyzed data showed a high rate of cognitive losses, such as attention and social/family interaction, even after remission of epileptic seizures. Such losses are responsible for short-term and long-term problems.

These cognition problems have been shown to be multifactorial in nature and to be related to other impairments in child development that bring problems even into adulthood.

Reduced attention levels can result in ADHD and low school performance, which in the long term are associated with persistent ADHD, social isolation, depression and higher unemployment rates for this population. In addition, other cognitive losses related to seizures were observed, such as in intelligence, language and motor functioning.

Epilepsies make up the most prevalent group of neurological diseases in childhood, with AS being the most common. And its diagnosis is usually late, suspected from a low academic performance. (ZUBERI; SYMONDS, 2015); (GOMES, 2013).

Given the above, it is understood the importance of early diagnosis and treatment

in order to minimize future damage resulting from the symptoms of AS. Pharmacological treatment may consist of sodium valproate, divalproex sodium, ethosuximide or lamotrigine, (LIBERALESSO, 2018).

However, the management of children with AS must not be restricted to antiepileptic drugs. Due to the multifactorial nature of cognitive and psychosocial losses, an interdisciplinary approach to the patient is necessary. A team made up of a general pediatrician, a pediatric neurologist and a psychologist make a difference in the evolution of the disease and in the improvement of children's quality of life.

In addition, the study showed an important relationship between school and family in the psychomotor development of patients. This way, it is necessary that education professionals and family members are also aligned and aware of the possible deficits of students with AE.

REFERENCES

LIBERALESSO, Paulo Breno. Síndromes epilépticas na infância. Uma abordagem prática. **Residência Pediátrica,** Curitiba, v. 8, n. 1, p. (56-63), Maio, 2018. Disponível em: https://cdn.publisher.gn1.link/residenciapediatrica.com.br/pdf/v8s1a10.pdf. Acesso em: 10/03/21.

LIBERALESSO, Paulo Breno. Estado de mal epiléptico. Diagnóstico e tratamento. **Residência Pediátrica,** Curitiba, v. 8, n. 1, p. (35-39), Junho, 2018. Disponível em: http://residenciapediatrica.com.br/detalhes/339/estado%20de%20mal%20epileptico-%20diagnostico%20e. Acesso em: 10/03/21.

CRUNELLI, Vincenzo *et al*. Clinicaland experimental insight intopathophysiology, comorbidityandtherapy of absenceseizures. **Revista Brain,** Oxford, Inglaterra,v. 143, n. 8, p. (2341-2368), Maio, 2020. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7447525/pdf/awaa072.pdf. Acesso em: 10/03/21.

WALD, Eric L. A *et al.* Fonseca. Towards a BetterUnderstanding of CognitiveDeficits in AbsenceEpilepsy: a Systematic Review and Meta-Analysis. **Neuropsychology Review,** Maastricht, The Netherlands, v. 29, p. (421-449), Novembro, 2019. Disponível em: https://doi.org/10.1007/s11065-019-09419-2. Data de acesso: 10/03/21

PARISI, Pasquale *et al*. The relationshipbetweensleepandepilepsy: theeffect on cognitivefunctioning in children. **Developmental Medicine &ChildNeurology,** Londres, Inglaterra, v. 52, n. 9, p. (805-810), Agosto, 2010. Disponível em: https://doi.org/10.1111/j.1469-8749.2010.03662.x. Acesso em: 11/03/2021.

WALD, Eric L. A *et al*. Fonseca. Cognitivedevelopment in absenceepilepsyduringlong-term follow-up. **ChildNeuropsychology,** Holanda, v. 25, n. 8, p. (1003-1021), Maio, 2019. Disponível em: https://doi.org/10.1080/09297049.2019.1614156. Data de acesso: 11/03/2021.

ZUBERI, Summer M; SYMONDS, Joseph D. Update on diagnosisand management of childhoodepilepsies. **Jornal de Pediatria.** Rio de Janeiro, v. 91, n 1, p. (S67-S77), Julho, 2015. Disponível em: http://dx.doi.org/10.1016/j.jped.2015.07.003. Acesso em: 12/03/21.

GOMES, Roberta de Figueiredo *et al*. Epilepsia de Ausência na Infância e seu Impacto na Aprendizagem. **Revista Neurociências,** São Paulo, Brasil, v. 21, n. 4, p. (628-632), dezembro, 2013. Disponível em: https://doi.org/10.34024/rnc.2013.v21.8144. Acesso em: 12/03/21.

BARONE, Valentina; PUTTEN, Michel J. A. M. van; VISSER, Gerhard H. Absenceepilepsy: Characteristics, pathophysiology, attentionimpairments, andtherelatedrisk of accidents. A narrative review. **Epilepsy&Behavior,** Estados Unidos, v. 112, n. 10342, p. (1-9). Disponível em: https://doi.org/10.1016/j.yebeh.2020.107342. Acesso em: 12/03/2021.