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CASE REPORT

Cannabidiol use in a pediatric patient with autism spectrum disorder and epilepsy: case report.

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Abstract

Introduction: Autism spectrum disorder (ASDs) are made up of neuropsychiatric disorders characterized by difficulties in social interaction and communication associated with restrictive and stereotyped activities and interests. Conventional psychopharmacological medications are usually directed to the treatment of associated behaviors but do not treat the core deficits of ASD.

Clinical case: A 3-year-old boy was treated for delayed language acquisition and age-inappropriate behaviors compatible with manifestations of ASD. In addition, an electroencephalogram showed paroxysmal discharges coinciding with episodes of disconnection from the environment. The parents decided to use cannabidiol and to start a psychomotor, behavioral, and speech therapy intervention program.

Evolution: After one year of intervention and follow-up, there were significant advances in seizure control and improvement in empathic, adaptive, and relational skills. The child tolerates closed spaces better and follows orders and simple routines. The therapist indicates great progress, and the child has finished his first year of schooling with significant achievements. EEG study showed better conditions than previous results with better-structured baseline activity and decreased frontal epileptogenic activity.

Conclusion: This case report reinforces the idea that early therapeutic intervention and the use of cannabidiol as an add-on therapy may be able to aid in seizure control in epilepsy and decrease behavioral symptoms related to ASD. Further research is needed to elucidate the effectiveness of cannabidiol in ASD.

Key words: Autistic Disorder; Cannabidiol; Cannabinoid Receptor Agonists; Aggression, Epilepsy.

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Introduction

Autism spectrum disorders (ASDs) constitute a set of heterogeneous manifestations of neurodevelopment, [1] of early onset that present independently of race, ethnicity, or socioeconomic group [2]. ASD is characterized by persistent deficits in communication and social interaction associated with repetitive and restricted patterns of behavior, activities, and interests [3]. Other neuropsychiatric signs and symptoms are usually associated with the central manifestations of ASD, with the most common being intellectual disability, hyperactivity, epilepsy, aggressive behaviors [4], and sleep disturbances [3].

Despite being one of the chronic disorders with the greatest impact on child development, there is still no specific treatment for the manifestations of ASD [5]. Therefore, in most cases, pharmacological interventions tend to be oriented to the control of hyperactivity and aggressive behaviors that could coexist, in addition to behavioral, psychomotor, and educational therapies that help minimize the symptoms of ASD [6]. It is suggested that autism has a genetic basis, and it presents a complex inheritance pattern that involves multiple genes [7]. We must also consider environmental risk factors, especially in the pre- and perinatal period, which could promote the appearance of the disorder [5].

ASD results from altered early-brain development with abnormal neuronal reorganization [2] that affects cognitive functioning and emotional processing. Furthermore, it has been suggested that social deficits could have a direct connection with changes in the endocannabinoid system responsible for reward responses, control of emotional responses, behavioral reactivity, and social interaction [8]. Treatment with cannabidiol (CBD) is a new and interesting therapeutic proposal for not only its effectiveness in controlling seizures in refractive epilepsies [9], but also for the positive effects reported for alertness, behavior, the receptive and expressive capacity of language, mood, and quality of sleep [10].

Case report

The patient was a preschool Hispanic male aged 2 years and 6 months from the city of Quito. The patient was taken for neuropaediatric consultation by his parents due to poor language development and behavior. His parents reported that he occasionally pronounced single syllables with little or no understanding of commands and a lack of interest in games, as well as greater preference for playing alone. Regarding behavior, his peers describe him as restless, impatient, and impulsive, showing anguish in closed spaces, not responding to his name, not interacting with other people (including other children) or his environment, and persisting in carrying out one activity.

He sleeps with his father out of habit and finds it difficult to fall asleep, so he takes a 30-minute night walk. He was struck by brief periods of disconnection with cessation of activities associated with constant blinking and occasional shaking during sleep. The patient went to preschool education for children under 3 years of age, in which there were episodes of irritability and uncontrollable crying, so it was decided to withdraw him.

Pathological antecedents

The patient presented a prenatal pathological history of threatened abortion. His birth was carried out by cesarean section at 32 weeks prior to lung maturation with a low birth weight (1800 g), and he was admitted to the neonatology service for 10 days. Regarding the evaluation of his development, the patient did not breastfeed and had only formula through a bottle. Apparently, there were no difficulties in sleep, with a history of head support and sitting according to age, a short period of crawling, and beginning of ambulation at 12 months. He had partial sphincter control. The neurological examination did not show cranial nerve lesions or neurological focality. Among the family pathological antecedents, it was reported that one brother and two cousins had language delay, and the mother was diagnosed with epilepsy.

Diagnostic workshop

In the interview, the child was restless, he did not fix his gaze, there was no response to simple instructions, and he also presented an absence of symbolic play with stereotyped and repetitive attitudes. The parents were asked to leave the examination room, and the absence of search was reported to parents; the child did not seem to miss them. The M-CHAT scale (Modified Questionnaire for Early Detection of Autism) was

applied, which scores three critical items (does not indicate, does not imitate, there is no eye contact). The results gave a high suspicion of ASD. Neurophysiological evaluation (electroencephalogram) revealed frontal paroxysmal abnormalities (see Figure 1).

With the previously described antecedents, the following diagnoses were established: ASD (according to DSM V criteria) and associated epilepsy with frequent frontal paroxysmal activity in the electroencephalographic record. Parents accepted the start of treatment with 15% cannabidiol (1500 mg/10 ml) with 0.02% THC, for which follow-up was given. It was started with a dose of 0.4 mg/kg/day of CBD by sublingual administration divided into two doses. In addition, he received speech therapy, psychomotor, and family psychotherapy support.

Evolution

During follow-up, a registry of seizures and neurodevelopmental changes was made. Parents reported a decrease in critical episodes (disconnection from the environment associated with movements in the eyelids with cessation of activity and sporadic shaking during sleep), in addition to improved behavior, interaction with others, better eye contact and communicative intention, and responding to simple verbal commands. Also, no adverse effects were observed with the use of CBD. A dose increase to 0.9 mg/kg/day was proposed.

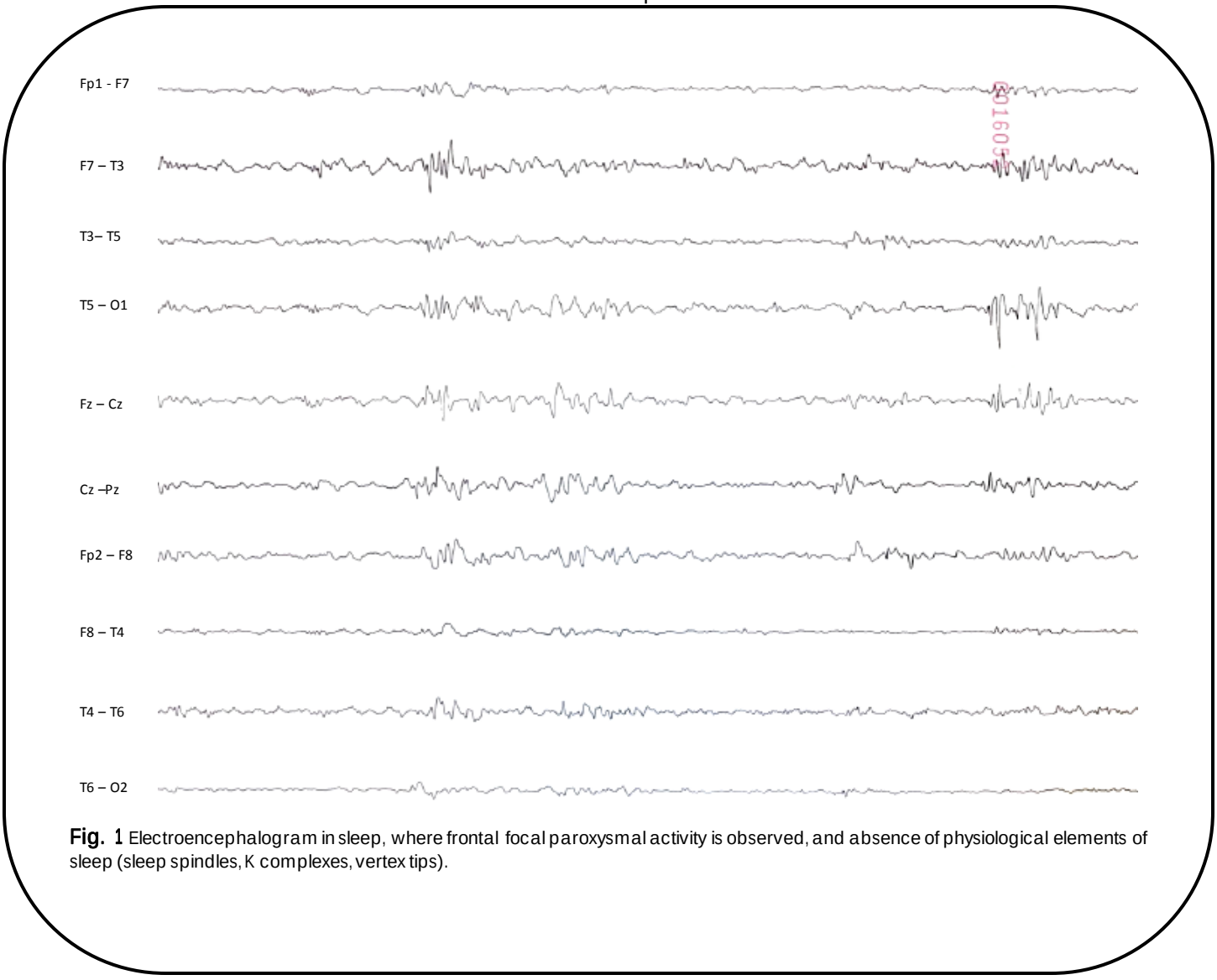

Fig. 1 Electroencephalogram in sleep, where frontal focal paroxysmal activity is observed, and absence of physiological elements of sleep (sleep spindles, K complexes, vertex tips).

During the evaluations at 3 and 6 months of treatment, a progressive and sustained improvement was observed. His parents reported that he is progressing in therapy, and there is good communicative intention, in addition to improved handling of emotions and language through the pronunciation of vowels. He repeats sounds and imitates gestures. He is still aggressive, but it is in response or reaction to something. The child began schooling in this period.

After 9 months of treatment, the evolution has been satisfactory. The disconnection episodes decreased, and the jerks in sleep disappeared. In this period, the child fixes his gaze and explores the environment, and there is imitation. Parents report that he has progressed in learning, is well integrated into the school environment, is affectionate, and relates better. He feeds himself and maintains a continuous sleep rhythm throughout the night. However, he still exhibits rigid behaviors and irritability. The dose adjustment of CBD to 1.15 mg/kg/day is continued due to his clinical and neurophysiological condition.

At the end of the first year of follow-up, significant progress has been reported, with a decrease in disconnection or blinking episodes, better functional adaptation, improvement in language acquisition, and better interrelation. The patient's parents report that at times, he laughs at play, interacts with his brother, and

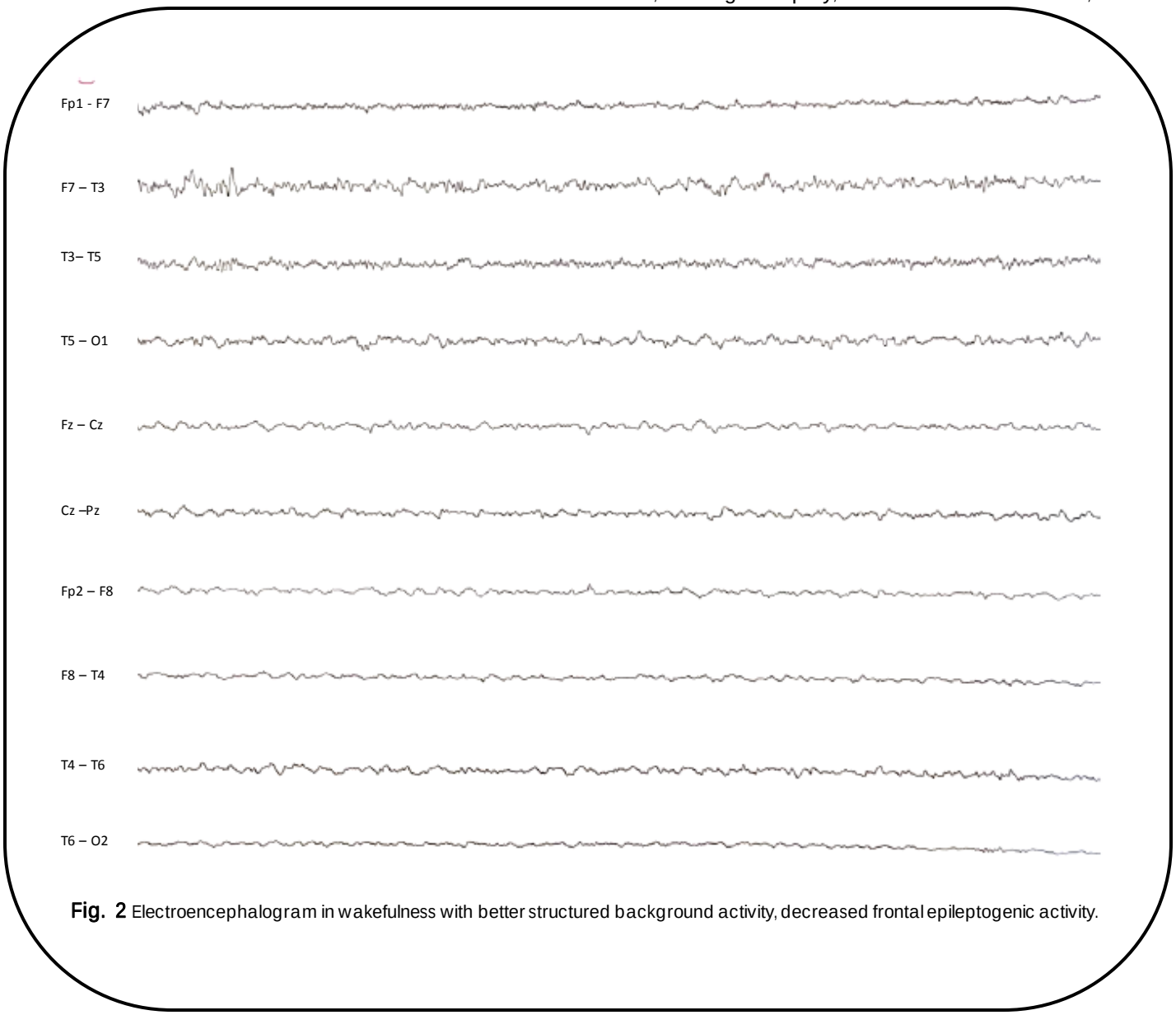

Fig. 2 Electroencephalogram in wakefulness with better structured background activity, decreased frontal epileptogenic activity.

integrates with other children. He better tolerates closed spaces and follows simple commands and routines. He is affectionate with parents, and his therapist and teacher indicate important advances in global psychomotor development. He finished his first year of school well adapted. The EEG result is better structured compared to the previous ones, with a slightly slowed baseline activity according to age and a decrease in frontal epileptogenic activity. (see Figure 2).

Discussion

There is currently strong evidence for pure CBD in the treatment of refractory epilepsy, irritability associated with ASD, Tourette syndrome, and spasticity [11]. It must be considered that epilepsy is one of the most frequent comorbidities in ASD, affecting 10-30% of children [12]. Despite receiving medical treatment, 40% present maladaptive behavior, severely impacting their quality of life [11].

Preclinical studies and case series report the success of the use of CBD-rich artisanal cannabis strains in children with ASD and severe irritability [13]. These studies were conducted because some parents prefer to try medical cannabis for irritability as a first-line treatment, as it is perceived as natural and therefore safer compared to FDA-approved antipsychotics [11]. In 2018, Suraev reported an average reduction of seizures in 75-100% of cases. Other beneficial health effects included improvements in cognition (35%), emotional well-being (31%), language skills (24%), social activity (14%), sleep (18%), preexisting gastrointestinal symptoms (10%), behavior (4%), and dystonia (2%) [14].

As in the present report, a decrease in epileptic seizures and improvements in functional adaptation, language acquisition, and interrelation of the individual are found. Reith-Meier pointed out that after treatment with CBD, the recording of EEG activity in the participants was better compared to the initial one, allowing an objective measurement of the efficacy of the treatment [15]. This is compatible with what was found in this case report.

Additionally, it has been described that CBD also has antipsychotic activity [16], being useful for some children with ASD with anxiety, which increases the risk of psychosis. However, the assessment of psychiatric disorders in people with ASD is challenging as negative symptoms and functional impairment can mask positive psychotic symptoms [6]. In the experience of the staff of the National Epilepsy Center-Quito in treating patients with refractory epilepsies, CBD is a safe and well-tolerated drug with which better control of seizures has been achieved. It also has positive side effects on communication, behavior, sleep, and learning. For an individualized intervention program, it is essential to allow comprehensive care for neurodevelopment and improve the quality of life of the patient and their family.

Thus, there is evidence at the basic science level that relates the use of CBD with a decrease in seizures, improvement in behavior, and management of irritability in ASD. But in relation to clinical experience and human evidence, only small studies and case reports are available, which demonstrate a beneficial effect of CBD as a treatment [16]. The lives of many children with ASD and epilepsy have improved today compared to previous years. They can talk, read, drive, graduate from school, and live in the community.

Conclusions

ASD has a great impact on child development, and a specific treatment is not yet available, so early detection and intervention turn out to be the key to prognosis. CBD may be an interesting therapeutic proposal to treat the behavioral symptoms related to ASD. More research is required to help understand the potential benefit of CBD in ASDs.

Abbreviations

ASDs: Autism spectrum disorder.
CBD: cannabidiol.
EEG: Electroencephalogram.
FDA: Food and Drug Administration.

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Authors' contributions

MXPR: Conceptualization, Data Conservation, Fund Acquisition, Research, Monitoring, Visualization, Writing - Original Draft, Writing: Review and Editing.
AMPM: Methodology, Project Management, Resources, software.
MGPR: Acquisition of funds, Research, Writing - original draft.
CPG: Formal analysis, Validation, Writing: revision and edition.
All authors read and approved the final version of the manuscript.

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Availability of data and materials
The data sets generated and / or analyzed during the current study are not publicly available due to the confidentiality of the participants, but are available through the corresponding author upon reasonable academic request.

Ethical statements
Protection of people
The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Singapore Declaration.

Data confidentiality
The authors declare that they have followed the protocols of their work center on the publication of patient data without identification.

Publication consent
Written informed consent was obtained from the patient's legal guardian for the publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of interest
The authors declare not to have any interest conflicts

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