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ORIGINAL ARTICLE

Electroencephalographic and neurodevelopmental alterations in severe congenital heart disease: A follow-up study

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Abstract

Congenital heart defects are the most common malformations at birth. Due to the fact that the developmental windows at early stages close rapidly, the aim of this study was to determine the impact of congenital heart defects on the central nervous system at short and medium terms after applying traditional and quantitative electroencephalography techniques and a test of neurodevelopment. Twenty-one patients (8-27 months, ˙x = 14.8) with severe congenital heart defects who had been studied previously, and a control group of 19 healthy children (8-29 months, ˙x = 14.6) were included. In all of them traditional electroencephalography, quantitative electroencephalography, and a test of neurodevelopment were performed. The results between groups (control vs. congenital heart defects) and between congenital heart defects (previous vs. present) were compared. In the second evaluation, congenital heart defect children maintained abnormal quantitative and traditional electroencephalography recordings. Comparing quantitative electroencephalography among congenital heart defects (previous vs. present) and between controls and congenital heart defects, significant differences of theta band activity in frontal, central, and temporal leads were found (p < 0.05). Upon assessing neurodevelopment, 86% of the previously studied congenital heart defect cases kept the same diagnosis of abnormality, of which mild-to-moderate hypotone was the most frequently observed. As hypothesized, congenital heart defect diseases have a very important impact on central nervous system function as determined by neurodevelopmental testing and traditional and quantitative electroencephalography recordings. The alterations observed persisted throughout the period studied. (Gac Med Mex. 2015;151:549-58)

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Introduction

The world-wide incidence of congenital heart disease (CHD) is estimated to be from 6 to 8 cases for every thousand live births[1] and, in Mexico, Bermúdez and Alarcón[2] have reported similar figures. Mendieta-Alcántara et al.[3], in a study conducted in 2 hospitals of Toluca City, Estado de México, found a CHD incidence of 7.4/1,000 live births, thus substantiating world- and national-wide data.

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Currently, survival of children with CHD is considerably high due to the accuracy and sofistication of diagnostic tools and the success of surgical techniques. For this reason, attention has focused now on the study of the probable impact of CHDs themselves as nosologic entities on other organs, especially the central nervous system (CNS)[4-6]. Additionally, it is of current interest for the impact of surgical techniques employed in the treatment of CHD on the CNS integrity to be studied[7-10]. Neuroimaging studies have demonstrated a high incidence of preoperative cerebral abnormalities[5,11-14], as well as developmental delay[15,16]. In a review of the subject, Owen et al.[17] conclude that a significant percentage of newborns with CHD show neurobehavioral and electrophysiological abnormalities.

Although electroencephalogram (EEG) and quantitative EEG (qEEG) are highly sensitive and reflect the sum of several factors affecting the cerebral function, there are few studies of this nature in children with CHD. EEG shows multiple positive features that make it an ideal tool to assess CNS integrity. It is a non-invasive, objective and readily available tool; it is sensitive to CNS hipoxic-ischemic damage; it constitutes the best tool to detect epileptic-like activity, even subclinical, and has been highly helpful to assess alterations present in the CNS in patients with conditions that might have a direct impact on neurodevelopment[18].

In the early 70's, Branthwaite[19] obtained EEG recordings during cardiac surgery in 140 patients with severe CHD (SCHD), and detected that a high rate of brain electrical activity alterations incidence occurred during the procedure. Similarly, Kritkou & Branthwaite[20] observed electroencephalographic abnormalities during the entire procedure in 100 patients with SCHD.

In a work recently conducted in our laboratory, Mendieta et al.[21] studied 30 children, between 15 days and 12 years of age, with SCHD with hemodynamical involvement and/or chronic hypoxia. They found 13 cases (43.3%) with abnormal EEGs, with most common abnormalities being background activity immaturity, focal and multifocal paroxysms of sharp waves and spike/slow wave complexes. Among the acyanogenic heart conditions, 9/21 (42.8%) showed abnormal EEGs, whereas among the cyanogenic ones, 4/9 (44.4%) did. In addition to its diagnostic value, the EEG started being used as a tool with prognostic value. In a follow-up study conducted in 117 patients with SCHD, EEG was recorded before and after the performance of surgical procedures. Patients with either generalized or asymmetric electroencelographic delta activity abnormalities, as well as paroxysmal activity, were found to be the ones with the worst prognosis. After surgical treatment, these patients had different neurological deficits and in some cases even death occurred. Conversely, in patients whose EEG recordings were normal or had minor disturbances, clinical evolution was more favorable[22].

Neurological and EEG alterations in patients with SCHD are not only observed perioperatively but also on the long term. In a 5-year follow-up work, Sotaniemi[23] examined the EEG in 55 patients with SCHD. Of them, 45% had an abnormal EEG prior to surgery and of these, 25% of the cases continued to exhibit anomalies 5 years later. Other follow-up studies conducted in children with SCHD have shown that there is statistical association between EEG abnormalities and neurological deficits. Limperopoulos et al.[24], in a cohort of 60 children with SCHD undergoing cardiac surgery, observed that the presence of epileptiform activity prior to surgery was associated in all cases with neurological alterations. Similarly, moderate and severe background activity abnormalities during the post-operative period showed a strong correlation with neurological disorders. In 100% of the cases, background activity severe abnormalities were predictive of death in those patients. The aforementioned works have demonstrated that the EEG is a highly useful tool in the assessment of cerebral functions and that this screening tool provides highly significant information on the severity of different cerebral dysfunctions, as well as on the effectiveness of different ongoing treatments[25]. In the past decades, the EEG quantitative analysis (qEEG) has provided important results in the evaluation of patients with cerebral lesions[26-28].

On the other hand, the presence of neurodevelopmental abnormalities in children with SCHD is an extensively studied phenomenon. Since surgical treatment is often applied early, most published works refer to CNS alterations that follow the surgical procedure or abnormalities detected during surgery[7-9,29,30]. An important percentage of infants with either cyanogenic or acyanogenic SCHD has neurological and developmental abnormalities that that persist at school-age and might affect the patient for the rest of his/her life. At the start of school life, compromised children have been determined to have a series of points of developmental delay, including fine and gross motor coordination, manual dexterity and behavioral disorders such as inattentiveness, shyness and cognitive difficulties[31]. Such deficiencies lead to the appearance of dificculties of varying degrees for the performance of daily

activities and for the acquisition of personal independence[32]. Donofrio and Massaro[33] determined that, in 5-year-old children with SCHD, dificculties are observed especially in social and self-care activities. In these children, socialization, daily-life skills, communication and adaptive behavior difficulties were also observed and, additionally, functional limitations were identified in 11 to 17% of the cases.

In Mexico, no follow-up studies have been carried out in children with SCHD aiming to track the course of SCHD abnormalities. Particularly, in the Child's Hospital of the DIFEM *(Sistema para el Desarrollo Integral de la Familia* – System for Comprehensive Development of the Family) and the "Mónica Pretelini" Hospital (Estado de Mexico's Health Institute), where this work was developed, frequently, and for different reasons – both economic and cultural –, children often have late access to healthcare services and to the necessary clinical and surgical treatments. Logically, when the children attend hospital facilities, care is immediately directed to the solution of the cardiac problems. However, it is a fact that in daily medical practice, care to collateral neurological damages that SCHD might cause is practically excluded. Since neurodevelopment at early ages is highly accelerated and its windows of opportunity are closed very rapidly, i.e., the stages where certain skills normally develop and therefore are periods when intervention with rehabilitation purposes has better probabilities of success, the present follow-up study aimed to determine the short-term impact of SCHD as a chronic condition on neurodevelopment and CNS function in chidren younger than 36 months. With this goal in mind, to assess the cerebral function, traditional and quantitative electroencephalogram was used as study technique. On the other hand, to assess the cerebral function, a neurodevelopment evaluation test, created by the National Institute of Pediatrics was applied (see Material and methods). This investigation pretends to draw attention on this subject and to demonstrate that a significant percentage of children who suffer from SCHD exhibit CNS disorders that are persisting and require attention and specific medical care.

Having in mind all the aforementioned antecedents and especially that, at younger ages, the stages where usually some skills are developed – and therefore represent the periods where intervention with rehabilitation purposes has better probabilities of success – are rapidly closed, assessment of the cerebral function and neurodevelopment is important in infant patients with SCHD, especially prior to surgical treatment.

Materials and methods

Twenty-one children younger than 21 months, born in the "Mónica Pretelini" Perinatal Maternal Hospital (ISEM) of the city of Tolca between February 2010 and January 2013, carriers of SCHD, whose follow-up was carried out at the Hospital for the Child (DIFEM), and who were part of a previously studied group of 41 patients, were included in the present study. This investigation was carried out in two parts: an initial study, and the follow-up study, here presented. In the first study, average age of the children with SCHD was 7 months with a range of 1 to 21 months[34]. The follow-up study was carried out 6 to 10 months after the initial study and the group with SCHD was comprised by 21 patients of the previously studied 41. Average age of these children was then 14.8 months, with a range of 8 to 27 months. At the moment of this study, none of the patients had undergone surgery, and the majority was only on drug treatment. The types of heart conditions diagnosed in the SCHD group are presented in table 1.

A control group (C) was also formed, with 19 children of 8 to 29 months of age (average: 14.6 months), who were under the care of the "healthy child" outpatient clinic of the Hospital for the Child. The C group was equally assessed by the pediatric cardiologist, who verified the absence of any heart condition or systemic disease.

Procedure

In both groups, conventional EEG was performed with a Medicid 5 digital electroencephalograph (Neuronic Mexicana) with a gain factor of 10,000x and band width between 0.3 and 30 Hz. Electrode impedance was maintained below 5,000 Ohm. The recording was carried out in a dimly-lit, sound-proof room and during spontaneous sleep. The children remained on their mothers' lap. For the EEG recording, the children wore a Lycra cap with surface electrodes, distributed according to the 10-20 International System, in 19 monopolar leads (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, FZ, CZ and PZ) and using as reference the earlobes in short-circuit. Minimum EEG recording time was 30 minutes. From the monopolar recording, the longitudinal, transverse, Laplacian and average reference montages were obtained.

The EEG was categorized as normal or abnormal, with those recordings with slow continuous or intermittent background activity and/or presence of paroxysmal activity being considered abnormal. The recordings were independently interpreted by two specialists

with no previous knowledge on the clinical diagnosis of each case. For the qEEG study (stage II of sleep), 24 segments of the EEG record of 2.56 seconds each, free of artifacts, sleep spindles and paroxysmal activity, were visually selected off-line. Then, broad band spectral measurements (absolute and relative potency, AP/RP) were calculated at the following frequency ranges: delta, 1.5 to 3.5 Hz; theta, 4.0 to 7.5 Hz; alpha, 8 to 12.5 Hz, and beta, 13 to 19.4 Hz.

A neurodevelopmental assessment instrument, created in the Neurodevelopment Follow-up Laboratory of the National Institute of Pediatrics, and standardized in the Mexican population, was also applied[35]. The instrument explores active and passive muscle tone, locomotion posture, ranges of motion by segments, reflexes and primitive reactions (automatisms), balance, motor coordination, exteroceptive and myotatic reflexes, as well as sensory and motor development characteristics in different positions (prone, supine, sitting, walking and standing). The instrument qualifies the delay or qualitative changes frequently occuring in association with neurological damage. These represent altered functional expression patterns, for example, asymmetries, persistence of primitive behaviors, deviations in the ontogenetic acquisition sequence, etc. The evaluation was individually performed with the child in optimal performance status or Precht's 4 status; i.e., awake and not crying and with the mother or main caregiver present. The exploration sequence that was followed was in the cephalocaudal sense, consisting in observing and manipulating the child at each position: dorsal decubitus, ventral decubitus, sitting, standing and walking. Each individual test had an approximate duration of 20 to 30 minutes, in the course of which, a video-recording was made for later analysis and qualification.

The explored developmental areas were: a) tonus type: eutonic, hypotonic or hypertonic; b) gross and fine motor areas; c) language area, and d) cognition area, by means of which the way the child perceives, learns and refers to its surrounding is assessed. These areas were scored according to the presence or absence of the age-expected behavior and were categorized as normal, slight delay and severe delay. Only 21 patients of all 41 in the preliminary study[34] completed the second stage.

Table 1. General description of the heart diseases sample

Sex	Diagnosis
F	Tricuspid atresia
F	VSD + ASD + PAH
M	Tricuspid atresia, ASD, VSD + pulmonary stenosis
M	VSD
M	ASD + septal hypertrophy
M	Ebstein syndrome
M	VSD
F	Perimembranous VSD
M	VSD + foramen ovale
F	PDA
F	VSD + PDA + PAH
M	CoA
M	VSD
F	CoA + tricuspid and mitral insuficiency
F	VSD + ASD + tricuspid atresia
F	PDA
F	VSD
F	VSD + PDA
F	VSD + PDA
F	VSD

VSD: ventricular septal defect; ASD: atrial septal defect; CoA: coarctation of the aorta; PDA: patent ductus arteriosus; PAH: pulmonary arterial hypertension.

Ethical considerations

This project was approved by the Bioethics Committees of the Faculty of Medicine from the Universidad Autónoma del Estado de México and of the "Mónica Pretelini" Perinatal Maternal Hospital and the Child's Hospital. Following the recommendations of the Declaration of Helsinki, in all cases, the parents who agreed for their children to participate in the study were previously informed on the purposes and procedures to be followed, on the possible risks and inconveniencies, as well as on the benefits the research would involve. Additionally, the right to withdraw from the study without this implying any penalty was explained. Only children whose parents accepted and signed the informed consent letter agreeing to it participated in the study.

Statistical analysis

The results of the traditional EEG and neurodevelopmental assessment of the first and second recordings

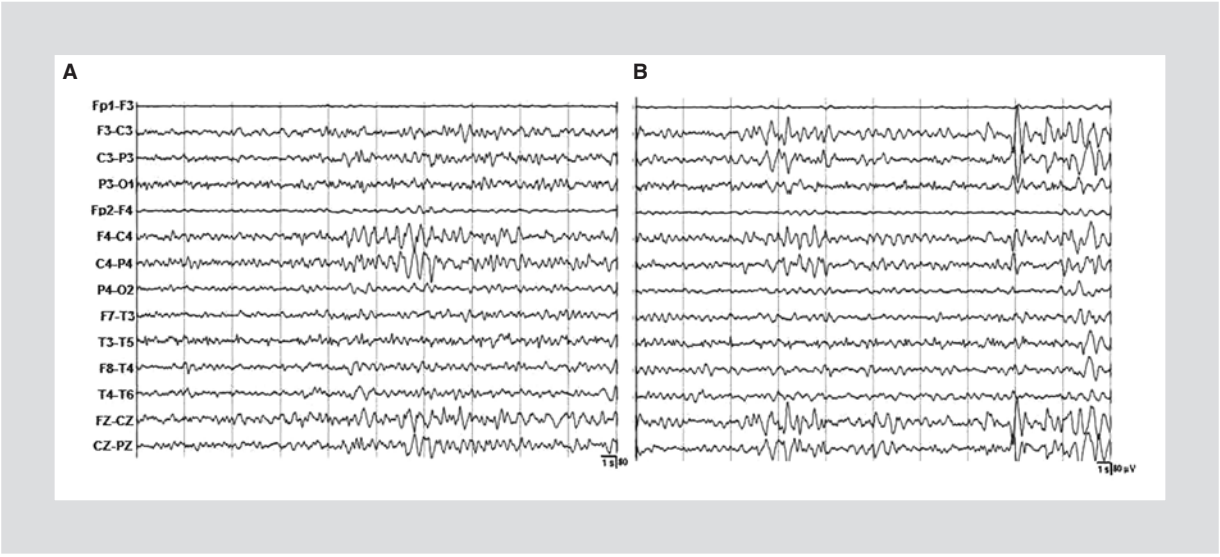

Figure 1. *Female patient. Diagnosis: Ventricular septal defect + atrial septal defect + tricuspid atresia. Longitudinal montage.* **A:** *first record at 4 months of age. Presence of 4.8 hz sharp wave type-paroxysms of 210 mV in right fronto-central and central-parietal regions.* **B:** *second record at 11 months of age. Paroxysms are appreciated in the same regions now in both hemispheres, with presence of widespread increased voltage discharges. Neurological diagnosis: Moderate hypotonia with predominance in lower trunk with mild delay in gross and fine motor area, persisting on both assessments.*

were compared in contingency tables using the McNemar test, with a p-value < 0.05 accepted as being significant. As for the qEEG, once the AP and RP values were obtained, the Wilcoxon test was applied in order to evaluate the differences in the four bands (alpha, beta, delta and theta) between the first and the second recordings. For the qEEG analyses, transformation of the obtained data into natural logarithm was used. Previously, all the obtained values were subtracted the global scale factor, a factor related to bone characteristics, skull geometry and skin conductance[26]. This factor is constant for each subject and all frequencies, leads and performance statuses and varies with age. AP is associated with a scale multiplicative factor that is responsible for 40% of intersubject variability[26]. For between-group comparison, the Mann-Whitney mean differences test was used, with a p-value < 0.05 accepted to be significant.

Results

EEG

In both assessments, 13 of the 21 cases (62%) showed an abnormal record (see example in fig. 1), consisting of paroxysms with sharp waves, spikes, spike-wave and slow waves. Other 3 patients (14%) maintained a normal EEG on both assessments (Fig. 2). In the first recording, 4 cases (19%) showed a normal trace, but not in the second study, where the EEG turned out to be abnormal. Only one child improved in the second recordings, since in the first recording the EEG was abnormal and in the second, normal (Table 2).

Neurodevelopmental Test

In the second assessments, 18 cases (86%) were qualified again as being abnormal, whereas 3 of them (14%) had a normal evaluation (Table 2). The most common neurological disturbance was hypotonia of the mild and moderate types, although on the second evaluation, the number of cases with abnormalities in the cognitive area was increased (2 out of 8 cases, respectively).

The McNemar test, used to compare EEG and neurodevelopment results between the first assessments and follow-up evaluations did not yield statistically significant results (p < 0.088).

qEEG

No statistically significant differences between the first and the second records were found when the Wilcoxon test was applied. In most cases, they remained unchanged, as the EEG did. When the AP was compared between controls and CHD carriers, significant differences were observed only in the theta band, especially in the frontal, central and temporal leads. The SCHD

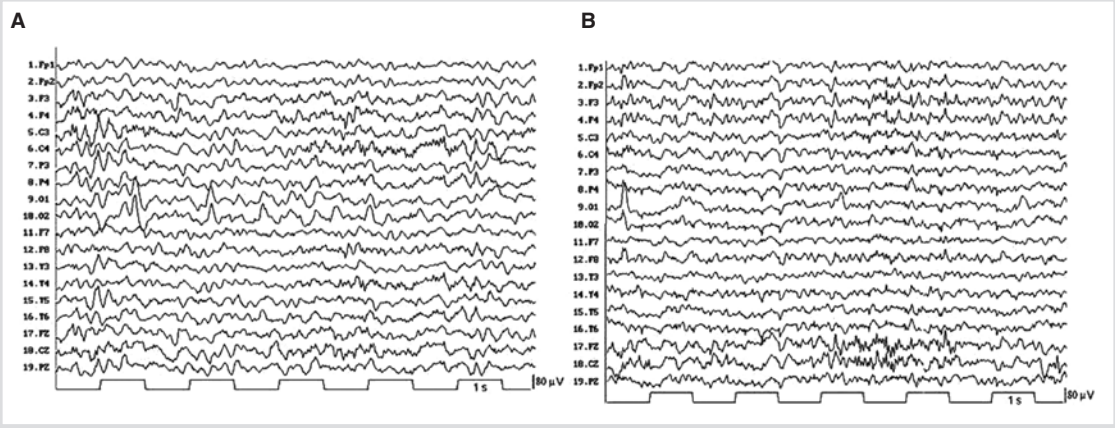

Figure 2. *Male patient. Diagnosis: Ventricular septal defect. Monopolar montage.* **A:** *first recording at 3 months of age. Normal EEG.* **B:** *second recording at 11 months of age. Normal EEG. Neurological diagnosis: 1st assessment: mild delay in fine motor area. 2nd assessment: normal.*

Table 2. EEG and neurodevelopment results: First and second assessment

	EEG assessment		Neurodevelopment assessment	
Cases	**1st**	**2nd**	**1st**	**2nd**
1	Abnormal	Abnormal	Abnormal	Abnormal
2	Abnormal	Abnormal	Abnormal	Abnormal
3	Normal	Abnormal	Abnormal	Abnormal
4	Abnormal	Abnormal	Abnormal	Abnormal
5	Normal	Abnormal	Abnormal	Abnormal
6	Abnormal	Normal	Abnormal	Abnormal
7	Normal	Normal	Abnormal	Normal
8	Abnormal	Abnormal	Abnormal	Abnormal
9	Abnormal	Abnormal	Abnormal	Abnormal
10	Abnormal	Abnormal	Abnormal	Abnormal
11	Abnormal	Abnormal	Abnormal	Abnormal
12	Abnormal	Abnormal	Abnormal	Abnormal
13	Normal	Abnormal	Abnormal	Abnormal
14	Abnormal	Abnormal	Abnormal	Abnormal
15	Normal	Normal	Abnormal	Normal
16	Abnormal	Abnormal	Abnormal	Abnormal
17	Normal	Abnormal	Abnormal	Abnormal
18	Abnormal	Abnormal	Abnormal	Abnormal
19	Abnormal	Abnormal	Abnormal	Abnormal
20	Abnormal	Abnormal	Abnormal	Abnormal
21	Normal	Normal	Abnormal	Abnormal

Table 3. qEEG. Mean differences between controls and SCHD carriers

	θ AP (μV)		
Leads	**Controls**	**SCHD carriers**	**p**
FP1	6329.39	10628.72	.010
FP2	6542.18	11155.76	.004
F3	9278.28	15362.95	.008
F4	9387.44	16457.89	.004
C3	10537.46	20323.31	.005
C4	9794.67	19329.79	.005
F7	6277.81	11085.51	.008
F8	6843.36	12319.91	.006
T3	6695.64	10331.83	.022
T4	6640.88	12812.30	.024
FZ	17252.41	39542.08	.009
CZ	27504.12	32983.89	.050

θ AP: theta absolute potency.

group had higher values than the C group, and no significant differences were found in the rest of the frequency bands (Table 3).

Discussion

Chidren with SCHD are at high risk for neurodevelopmental problems. Although serious neurological deterioration in these children is infrequent and most exhibit normal cognition, a significant number of them do show higher-order motor and linguistic disadvantages, as well as in attention capacity among other deficits[36]. Currently, cerebral development is accepted to be compromised in patients with SCHD. An increasing number of investigations indicate that neonates with SCHD often have abnormal brain development, maturation delay and brain damage before having undergone any surgical intervention[5,11,33,37], although this is an important point to be further investigated, since the association between CHD and cerebral abnormality is not yet clearly established.

Due to the accelerated developmental rate observed at early ages, the present work aimed to follow-up on the previous one[34]. The current study has attempted to determine the neurodevelopmental and EEG short-term evolution in children with SCHD who were previously studied. We found that the EEG remained essentially unchanged in most patients between the first and the second evaluation (non-significant McNemar test), with the trace being abnormal in most cases on both assessments (Table 2 and Fig. 1). EEG trace worsening was observed in 4 patients and only in one case there was normalization of it (Table 2 and Fig. 2).

This result is consistent with previous works. In 1985, Sotaniemi[23] conducted an EEG trial in 55 patients with SCHD prior to surgical treatment and 5 years later. An abnormal EEG was found in 45% of the cases prior to surgical intervention, and 5 years later, abnormal record persisted in 6 patients (25%). In the referred study, the percentage of cases where electroencephalographic abnormalities persisted was considerably lower than those reported in the present work. However, it should be noted that, in this work, none of the patients had received surgical treatment and that the follow-up recording by Sotaniemi was obtained many years after surgery was performed. Remarkably, Sotaniemi's study shows that, in spite of surgical treatment and time elapsed, an important number of cases maintain a pathological EEG. Limperopoulos et al.[24] analyzed the association between perioperative EEG and neurological status in a cohort of 60 infants. One year after surgery, the authors found a significant relationship between EEG abnormalities and neurological evolution. In a study in 150 infants to establish the relationship between the presence of perioperative epileptiform crises, with the background activity pattern using the amplitude-integrated EEG technique, and neurodevelopmental evolution 2 years after surgical treatment, the prolongation of time to background activity recovery was found to be associated with an increased risk for early mortality and worsened neurodevelopment[38].

In the present study, according to the qEEG analysis, no significant changes were observed between the first and second measurements, with slow activity predominating on both recordings. When the results of the qEEG analysis were compared between the C vs. SCHD groups, an increase in theta AP was obtained in the children with SCHD with regard to their healthy peers. This background activity slowing is probably directly related to a global delay in CNS maturation: neuronal migration, myelination, synaptic connections formation, dendritic arborisation, etc. Early organogenesis of both the brain and the heart occur simultaneously in the human fetus. In the brain, it involves both temporally and spatially specific developmental programs that as a result of cell proliferation, migration and differentiation determine final tissue cytoarchitecture and functions. SCHDs lead to disturbances in fetal

and/or postnatal blood flow and translate into altered cerebral growth and development. The presence of abnormal events can be determined by using different assessment tools, including magnetic resonance[39], psychomotor development tests, EEG and qEEG, etc.[21,33,34]. The formation and refinement of neuronal connections, including myelination and formation of synaptic connections, require the same brain activity, which leads to an increase in the basal metabolic rate; i.e., under rest or activity conditions, the minimal rate of energy output increases. Consequently, this leads to a higher dependence of brain tissue on the heart function for the delivery of oxygen and metabolic substrates[40-42]. If the latter process is altered, global cerebral development is directly affected. The delay in cerebral development is often accompanied by a particular vulnerability of the white matter in newborns with CHD. Therefore, both the delay in brain development and the presence of white matter lesions may underly the cognitive disorders that are frequently observed in children even after surgical and drug treatment[39].

This observation is important, since in spite of the short time elapsed between the first and the second assessment – 6 to 10 months –, the studied ages constitute a period of not only complex but also accelerated brain development. Even in some children with SCHD, the slowing of the EEG background tends to worsen.

While the qEEG enables an objective assessment of background brain electrical activity, the EEG revealed the presence and persistence of epileptiform-like. This type of electroencephalographic activity has been previously reported. Limperopoulos et al.[24] described the EEG of 60 infants with SCHD. In that study, prior to surgery, 19% of them showed epileptiform activity and 33% background activity alterations in addition to these irregularities being associated with neurological abnormalities. In a study of our own[24], a pathological EEG was found in 43.3% of children with SCHD, with most frequent irregularities being background activity immaturity, as well as focal and multifocal paroxysms with sharp waves and presence of spike/slow wave complexes. Knowing that the white matter sustains damage as a result of hemodynamical alterations[25], our hypothesis to explain our findings in the electroencephalographic records has been that the hemodynamical disturbance present since the fetal stage in the affected children might favor the development of ectopic grey matter zones in areas that under normal circumstances are predominantly regions of white matter. The presence of seizures both clinical and in the EEG trace after surgery in cases of Fallot tetralogy have been correlated with worse neurodevelopmental perspective at ages of 1 and 2.5 years[43]. Although some authors do not consider electroencephalographic findings to be conclusive, these shouldn't be dismissed[44] and instead be conferred due importance, since they constitute direct evidence of cortical electrical activity.

On the other hand, the qEEG demonstrated there is background activity that is slow for the age. In this regard, we have not found references of works on qEEG in SCHD cases; however, our results show that the follow-up study of children with SCHD by means of EEG and qEEG is important to obtain complete information of the morphofunctional status of the CNS in these patients.

With regard to the neurodevelopmental study, most of the studied cases (86%) were found to maintain the abnormal categorization of the first assessment, which was verified by using the McNemar test. According to Wernovsky[45], depending on the severity of the cardiac defect, the incidence of neurodevelopmental irregularities reaches as high as 70% of the cases. The present study is consistent with the previous one, although with a somewhat higher percentage, since all patients were SCHD carriers. By means of different imaging techniques, Miller et al.[11] examined 41 infants with SCHD before undergoing surgery. Brain damage evidence was found in 39% of the cases, a result that is similar to that found by Licht et al[5]. Another longitudinal trial was conducted in a cohort of 131 neonates and infants requiring open heart surgery. These were assessed prior and after surgery and 18 months after the procedure. Abnormalities were observed on neurological examination in 41% of the cases, with hypotonia as a distinctive feature[16]. This is consistent with the results obtained in our study.

With the purpose to summarize the neuropsychological sequels associated with different types of CHD, Miatton et al.[44] carried out a review on the subject including more than 20 empirical studies. With regard to the intelligence quotient (IQ), the majority of the reviewed works conclude that it falls within normal range. However, in terms of school performance, chldren affected by SCHDs, such as Fallot tetralogy, showed low results in arithmetic, learning and general knowledge tests. Furthermore, children with cyanogenic CHDs showed lower-than-normal arithmetic, reading and spelling skills for their age. In fact, although most children that are surgically intervened due to the presence of CHD subsequently have an acceptable school performance, about 20% of them show below-average performance.

With regard to language, the authors conclude that most studies find important problems in this area. Up to 42% of children with SCHD have deficiencies in both fine and gross motor domains as well. This, along with previous observations of ours, reinforce the results of the present study[44,46].

Porcayo et al.[46] determined the psychomotor development in 65 infants with ages ranging from 1 to 36 months, divided into 3 groups according to their medical condition: 1) simple heart conditions (n = 21); 2) severe heart conditions (n = 22), and 3) healthy controls (n = 22), with abnormalities being found mainly in the fine and gross motor areas, but also in cognition, self-care and social-emotional behavior. Importantly, the study highlights the existence of a strong correlation between the severity of the clinical condition and the delay in the acquisition of the explored skills.

It is important pointing out that although the most common neurological abnormality was hypotonia, in the second assessment, the number of cases with alterations in the cognitive area was increased (from 2 of 8 cases), which is consistent with other studies where cognitive performance has been also observed to be affected in the mid- and long-term[16,32,47].

Conclusions

Both our observations and those by other investigators point towards the fact that SCHDs have a highly important negative impact on CNS development. The study on CNS development and maturation performed in the present work by means of EEG records and qEEG analyses, strongly suggests that SCHDs are associated with background brain activity abnormalities and that, in most cases, the alterations persist in the observation period followed in this study. Although none of the patients had been surgically intervened, all were on drug treatment and, therefore, it is important to emphasize that medical management of the heart condition has not necessarily positive effects on brain electrical activity and, in general, on neurodevelopment. The neurodevelopmental assessment showed evidence that neurological irregularities detected in children with SCHD correspond mainly to changes in the muscle tone, persisting 6-10 months after the first determination. A relevant fact is that, between both assessments, deficiencies in the cognitive areas were increased, which should be regarded as a sign of alarm, since an important proportion of infants with SCHD have been reported to exhibit learning dificculties when they reach school-age[32,47].

Considering the results of the current work and reports in the literature, the authors of this work consider that, as a routine part of the treatment of children who are born with CHD, it is urgent to implement an early stimulation program that allows to palliate the motor and cognitive abnormalities that an important percentage of these children will inevitably develop on the short-, mid- and long-term.

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