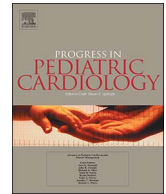




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Assessment of cognitive performance among Mexican children and adolescents afflicted by simple to complex congenital heart diseases. Preliminary study[☆]

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ABSTRACT

Among patients afflicted by congenital heart diseases (CHD) diverse, and complex neurological alterations are commonly observed. These have neither been completely identified nor understood. With the aim of identifying specific neurocognitive alterations among children and adolescents afflicted by CHD we investigated the possible presence of cognitive disorders related to the presence of cardiovascular disease with the aid of a sample of 20 patients (12 teenagers and 8 school-age children). Taken altogether, 9 of them were afflicted by simple and 11 by complex pathologies (respectively, CHDs/c). The Neuropsychological Test for Memory and Attention (Neuropsi), standardized for Mexico by Ostrosky et al. (2004), was individually applied to all participants. The information of cognitive performance was obtained in relation to the categories attention and memory, and the same areas allowed us to assess global performance. CHDc subjects performed significantly poorer compared to CHDs in i) attention and executive function, ii) memory and iii) attention and memory. Likewise, among CHDc subjects a significantly higher proportion of cases were diagnosed as abnormal in the same variables. Also a significant and negative correlation was determined between CHD severity and neuropsychological scoring. Children and adolescents afflicted by CHD are at high risk of developing cognitive function alterations including aspects of memory, attention and executive functions, alterations which are likely to be worst among those cases carrying CHDc conditions.

1. Introduction

The incidence of moderate to severe congenital heart disease (CHD) has been estimated at approximately 6–8 per 1000 children born alive, constituting in itself the second most frequent disease in infancy [1]. In México, Mendieta-Alcántara et al. [2] inform of an incidence of 7.4 per 1,000 children born alive. In the last decades, owing to progress in intervention strategies and surgical treatments the long-term survival among neonates suffering from CHD has substantially increased. Nowadays, due to the fact that the survival expectancy is high among a high percentage of cases, the condition is now considered as a life-long or chronic disease [3]. In parallel to this, the interest has now importantly progressed towards the identification of possible CHD-correlated afflictions. This is, to functional co-morbidities evolving from neonatal stages to adolescence, and adulthood. Of specific interest are

the possible alterations which might appear along brain development due to altered blood perfusion. Reduced tissue oxygenation throughout development may lead to considerable insufficiencies in terms of cognitive performance.

The biological circumstances, either biochemical or physiological, underlying the neurological injuries in CHD patients appear to be many, varied and not entirely clear. These frequently include hypoxia-ischemia events triggered by hypoperfusion, and this either due to the pathology itself or resulting from cardiac surgery. A multiplicity of other factors comprising genetic, prenatal, as well as pre- and post-operative influences may contribute to the alterations observed among these patients [4,5].

Some forms of CHDc lead to atypical brain development features, and these are observed as early as 25–30 weeks of intrauterine life [6]. Also, high ratios of microcephaly, and hypotonia, and other alterations

[☆] All authors declare hereby they have no conflict of interest.

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have been determined by neuroimaging [7]. Other specific lesions include periventricular leukomalacia, present in up to 59% of cases before surgery [8].

Lags in neurodevelopment constitute the most frequent co-morbidity conditions among school-age children carrying CHD alterations [9–11]. In general, IQ is well preserved as it has been determined among these children. Nevertheless, a significant proportion of cases show alterations in motor skills, and in the cognitive traits of attention, memory, and language. Low academic achievement and deficient social development are also typical manifestations [4,10,12–14].

Commonly, the studies carried among CHD children have centered focused their attention on early infancy or early school ages. Recently, Cassidy et al. [15] studied executive function performance among school-age children and adolescents (10–19 years old) exhibiting cyanotic CHD. They reached the conclusion that the condition constitutes in itself an important risk factor for the optimal development and acquisition of executive functions.

Taken altogether, children and teenagers CHD patients, are ostensibly at high risk of presenting diverse neurocognitive alterations. Among them minor skills are often intact although in parallel to the increased severity of the disease the patients progressively show increased difficulties in integrating and coordinating those skills so as to achieve higher order goals [16]. According to Bellinger et al. [16–18], among the most noticeable deficits observed are those related to non-verbal skills, together with alterations in social cognition, and executive performance. The severity of the condition, particularly amid complex cardiopathological cases, poses serious threats to brain development and the acquisition of optimal cognitive abilities.

Considering that the studies related to the outcome and development of CHD-associated afflictions among these patients are still limited, particularly in Mexico where the comorbidity aspects of CHD are insufficiently acknowledged, the present work was carried out with the aim of identifying some of the main cognitive alterations among Mexican children and adolescents afflicted by CHD (simple and complex) through the application of the neuropsychological test Neuropsi.

2. Materials and Methods

2.1. Ethical Considerations

The present research protocol was approved in advance by the Bioethics Committee of the School of Medicine, State of Mexico Autonomous University, in compliance with the Declaration of Helsinki [19]. In every instance, both parents and participating children were informed in advance in relation to the aims and procedures of this study as well as of possible risks and benefits. At the same time, it was clearly explained that all information was going to be kept confidential and the results delivered free of charge to the parents of participating minors. All considerations were included both in the oral explanation as in the informed written consent. After approval, this last one was signed by parents and participating children and teenagers.

2.2. Sample

This consisted of 20 patients (9 females and 11 males) of ages between 7 and 16 years, 12 teenagers and 8 under 13 years old. Of the whole sample 9 cases were afflicted by uncomplicated CHD conditions, this is, free of hemodynamic compromise and hereby named simple (CHDs) and 11 by complex (CHDc) pathologies involving either reduced blood flow, reduced blood oxygenation or both. All cases studied were patients gathered from the Child's Hospital, belonging to the Institute for the Mother and Children from the State of Mexico (IMIEM), Toluca City, Mexico. All cases were diagnosed and assessed by a medical doctor specializing in pediatric cardiology and of the total sample, 10 cases had not undergone surgical treatment at the moment of assessment. These data are summarized in Table 1.

Table 1

Types of congenital heart diseases diagnosed in the studied sample.

Cardiopathy	n	Type	Previous surgery
Coarctation of aorta	1	CHDc	Yes
Ventricular septal defect	1	CHDc	Yes
Atrial septal defect	3	CHDs	Yes
Patent ductus arteriosus	3	CHDs	No
Patent oval foramen	3	CHDs	No
Severe pulmonary stenosis	1	CHDc	Yes
Ebstein anomaly	1	CHDc	No
Tetralogy of Fallot	1	CHDc	Yes
Pulmonary atresia	1	CHDc	Yes
Common arterial trunk	1	CHDc	No
Atrial septal defect and Ebstein anomaly	1	CHDc	No
Tricuspid atresia	1	CHDc	No
Transposition of the great arteries and single ventricle	1	CHDc	Yes
Coarctation of aorta + secondary systemic arterial hypertension	1	CHDc	Yes

CHDs: simple congenital heart diseases; CHDc: complex congenital heart diseases.

2.2.1. Inclusion Criteria

Children and teenagers of ages between 7 and 16 years afflicted by simple or complex CHD.

2.2.2. Exclusion Criteria

Personal or family background of central nervous system (CNS)-related alterations including a background of CNS perinatal risk or damage; genetic conditions which might involve CNS risk or damage; any physical complaint not allowing them to take the tests; development or acquisition of new or correlated pathological alterations along the course of the study.

2.3. Procedures

Neuropsi (Neuropsychological Test for Memory and Attention) had been previously standardized for Mexico by Ostrosky et al. [20] was applied individually to all participants. The instrument includes a base of normative data for people between the ages of 6–85 years. Neuropsi was designed to assess in a detailed manner and independently of each other attention and memory processes as well as to complete a global estimate among psychiatric, geriatric, neurologic and other patients presenting diverse medical conditions. Specifically, in this study, the different areas examined covered various attention subcategories including orientation, selective attention, sustained attention and attentional control. Also, diverse subtypes of memory were evaluated. Among them working, verbal and visuospatial short and long-term memories. The test provided qualitative and quantitative estimates from both raw and normalized data. Separately, Neuropsi provided information of performance in the cognitive categories of attention and memory, and in this area of global performance too. The subdivision of the test in categories and subcategories allows the clinician or research worker to precisely identify the presence of attention or memory deficits in the patient under examination (see Table 2).

2.4. Statistical Analysis

To investigate the existence of differences between groups (CHDs vs. CHDc) and due to the size of the sample, a non-parametric and multivariate permutation test was applied [21,22]. This method does not require a normal distribution of data due to the construction of its own empiric distribution. Thus, the global test was calculated applying the permutation distribution of the Student's *t*-test maximum (tmax). After applying the permutation technique, the estimated distribution of tmax served to set the levels of significance, a procedure which at the same time controls and avoids increasing type I error. Using the Student's *t*-

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