Instituto Superior de Ciências da Saúde - Norte

Mestrado em Psicologia Clínica e da Saúde

Impacto do Desenvolvimento Fetal no Funcionamento neurocognitivo em Adolescentes com Cardiopatias Congénitas Cianóticas e Acianóticas

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Impact of fetal development on neurocognitive performance of adolescents with cyanotic and acyanotic congenital heart disease

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ABSTRACT

Background: Our aim was to evaluate the neurocognitive performance in adolescents with CHD and to determine whether parameters of fetal development evaluated in neonates, such as head circumference, length, weight and Apgar scores, are somehow related to their neurocognitive performance.

Methods: We evaluated 77 CHD patients (43 males) aged from 13 to 18 years old (mean=15.04 ± 1.86), 46 cyanotic (23 Tetralogy of Fallot, 23 Transposition of the Great Arteries) and 31 acyanotic (Ventricular Septal Defect) enrolled in this study. The control group included 16 healthy children (11 males) ages ranging from 13 and 18 (mean=15.69 ± 1.44). All assessment measures for CHD patients were once obtained in a tertiary hospital; the control group was evaluated in school. Neuropsychological assessment included Wechsler's Digit Test, direct and reverse (WDD, WDR) and Symbol Search (WSS), Rey's Complex Figure (RCF), BADS's Key Searching Test (BKS), Color-Word Stroop Test (CWS), Trail Making Test (TMT) and Logical Memory Task (LMT).

Results: CHD patients compared to control group showed lower scores on every test, except for a logical memory task. Patients with VSD when compared with patients with TF and TGA showed better results in all neuropsychological tests, although the only significant differences were in evidence RCF, copy (F=4,936; p=.010). Several correlations were apparent between fetal/ neonatal parameters and neuropsychological abilities in each type of CHD. However, head circumference at birth stands as a main correlation with cognitive development later on in all kinds of CHD (WDD: rho=.339, p=.011; RCF, copy: rho=.297, p=.027; CWS, interference: rho=.283, p=.036; TMT A: rho=-.321, p=.017).

Conclusions: Adolescents with CHD have worse neuropsychological performance than the control group, mainly the cyanotic patients. Fetal circulation seems to have impact

on cerebral and somatic growth, predicting cognitive impairment in adolescents with CHD.

Key words: Fetal Development, neurocognitive functioning, neonatal variables, congenital heart disease

INTRODUCTION

Congenital heart disease has been considered as the most common cause of child morbidity and mortality.[1]

In recent decades, the advances in surgical interventions and treatment in patients with CHD, have contributed to the increase of life expectancy of these children. However, over half of these children will develop some kind of neurological damage.[2,3,4]

In the literature, different studies refer to the existence of changes in cognitive development of young people with congenital heart disease. These consequences are related to perioperative factors (syndromes, extracorporeal circulation during surgery and post-surgical complications).[5]

Many children that were submitted to cardiac surgery in the neonatal period, show a pattern of neurological problems throughout their development, such as, cognitive deficits, attention problems and executive functioning, visual-motor e visual-spatial skills , delay in expressive language acquisition and learning difficulties.[6,7,8,9,10,11,12,13]

Until today, studies about neurological development in children with congenital heart disease have only been focused on factors related to surgeries, such as cerebral perfusion being compromised during extra corporal circulation[1] and these factors were considered precursors of potential complications neurocognitive.[14] Despite this, other studies have found a high percentage of neurological abnormalities, anatomical and

functional, before surgery in newborn babies with congenital heart disease[15,16,17] and also found a connection between these abnormalities and cognitive development throughout childhood.

According to some studies, neurobehavioral abnormalities, such as hypotonic, agitation, motor asymmetry, lethargy and autistic characteristics, were found prior to surgery in over 50% of newborns (less than a month old) and 38% of children (between one month old and 2 years old) with congenital heart disease. These abnormalities usually persist or get worse in the postoperative period, when cranial nerve damage may also occur.[18,19]

Still during the postoperative period, other complications may also occur, being the most common ones characterized as agenesis or dysgenesis of corpus callosum, holoprosencephaly, microcephaly, lissencephaly,[20] incomplete closure of the operculum, ischemic changes and white substance lesion characterized by periventricular leukomalacia (PVL).[21]

Newborns with congenital heart disease show higher risk of developing hypoxia, hypotension and acidosis.

The fetal hypoxia affects the normal development of the brain, namely in the hippocampus (a brain structure responsible for converting short-term memory into long term memory) and the cerebral cortex (the brain structure responsible for cognitive areas related to memory, attention , language, perception and thought).[22] This may due to the fact that congenital cardiac malformations and abnormalities in fetal growth are related.[23,17]

Other hypothesis suggest that abnormalities in cerebral development, inter-uterus hemodynamic alterations and congenital cerebral abnormalities and acquired cerebral lesions, linked to prolonged cyanosis and hypoperfusion after birth,[1] also contribute to the neurological development difficulties in children with congenital heart disease.[15]

Newborns with congenital heart disease show high levels of acquired cerebral lesions, proved by studies using postoperative magnetic resonance imaging scans. The high number of cases of newborns with lesions in the white substance suggests that there is a vulnerability that might be related with the delay in brain development. These abnormalities in newborns with congenital heart disease may reflect trouble in cerebral blood flow in the fetus.[24]

For many newborns, congenital heart disease seems to be an isolated anomaly, leading to the belief that the brain has potential for a normal development.[25] Although brain and heart development occur simultaneously in the fetus with congenital heart disease, being the first morphogenetic programs of each organs share the same genetic pathways.

In the seventh week of the gestation period the heart is considered to be morphologically mature, but brain development will continue on, as different morphological events occur throughout the first two trimesters,[24] such as neuronal migration and arborization, synaptogenesis, programmed cellular death, oligodendrocytes maturation and reorganization or synaptic connections.[15]

Following this period, there is a constant brain growth and it is directly linked with the formation and perfectioning of connections in the third trimester and neonatal period.[24] This development is associated with the increase in metabolic activity in which the brain relies on the heart for oxygen and nutrient supply.

The existence of congenital heart disease will increase the chances of blood flow abnormalities in the fetus, resulting in a compromised brain development due to the complex relations between common cells, genetic programming, physiological consequences of cerebral blood flow alterations and the dynamic of oxygen distribution during brain development.[24] This can be seen as good evidence that these factors take an important role in cerebral growth.[26]

In what is considered as normal fetal circulation, gas exchange occurs through the placenta. The deoxygenized blood coming from the vena cava goes directly in the right ventricle and through the arterial canal to the placenta. The Eustachian valve and the arterial septum move together to get the venous blood from the hepatic inferior vena cava to the right ventricle and the oxygenated blood from the venous canal over the oval foramen through the left ventricle to the aorta and cerebral circulation.

When the fetal oxygenation is compromised there is a blood redistribution to the cerebral circulation, this phenomenon is known as brain sparing,[1] resulting in a pattern of global distribution of the somatic growth, with preservation of the head growth.[24]

This hemodynamic growth is represented by the diastolic flow in the cerebral arteries and the decrease of diastolic flow in the descending and umbilical aorta.[1] It is believed that many brain areas may be better protected than others. According to Dubiel, Gunnarsson & Gunnarsson[27], a study with pregnant women with complications in their pregnancy due to maternal hypertension and placenta dysfunction, cerebral vasodilatation was found in 41% of women in the anterior cerebral artery, 30% in the posterior cerebral artery and 24% in the medium cerebral artery. In this way, anterior cerebral arteries show a better auto regulative response, were the redistribution of blood flow is favorable to the perfusion of the frontal lobes. Although, medium cerebral arteries are presented as less reactive.[1]

This mechanism has been found to be a contributor to an adverse neurological development, since the cerebral vasodilatation occurs when there is a compromise in the fetal oxygenation. This protection mechanism doesn't seem to be enough to keep a normal brain development and growth in prolonged stress situations in the uterus. In a normal fetal blood circulation, the oxygenated blood is taken to the brain and the deoxygenized blood goes to the placenta.[1]

As previously said, studies show abnormalities in blood flow, that occur in congenital heart disease, such as Hypoplasic Left Heart Syndrome, Transposition of the Great Arteries, Tetralogy of Fallot, may contribute to an abnormal brain development.[1,15, 24]

In fetus with Hypoplasic Left Heart Syndrome there may be an increase in the resistance to cerebral flow, where the blood flow returns through an istmo-aortic hypoplasic in order to get to the brain.

In fetus with Transposition of the Great Arteries, the venous blood from the cerebral circulation goes back directly to the brain.

When Tetralogy of Fallot and Hypoplasic Right Heart Syndrome, is found in fetus, the deoxygenized blood goes in the cerebral circulation due to the intracardiac mix.

This allows the statement that the type of injury does not only affect the cerebral blood flow but also the degree of deoxygenized blood distributed in the cerebral circulation. [1]

All alterations in the blood flow may be related to some sort of abnormal somatic growth in uterus, having an influence in the neonatal anthropometry. [23]

When comparing to newborns without congenital heart disease, newborns with Hypoplasic Left Heart Syndrome show lower weight, length and head circumference smaller than normal and the head volume is disproportionally low when compared to their weight. Newborns with Transposition of the Great Arteries show normal weight, but a lower head circumference when compared to their weight. These statements are corroborated by Rivkin and collaborators, who reported that adolescents with TGA undergoing surgery type "pressure switch" in the first months of life, have abnormalities of the white substance, namely the reduction of the same.[28] On the other hand, newborns with Tetralogy of Fallot have normal proportions, although their weight,

length and head circumference are smaller than expected. Children with Coarctation of the Aorta have higher head volume, when compared to their weight at birth.[1, 23, 24,29]

Many factors are believed to be related to the low weight at birth, including genetic syndromes, placenta insufficiency, and inter-uterine growth restriction. All these may increase the risk of neurodevelopment delays.

Recently, Gaynor, Jarvik, Bernbaum, Gerdes, Wernovsky et al[30] showed that, in general, factors inherent to the patient, such as weight at birth, head circumference at birth and the Apgar score in the first and fifth minute, better explain the vulnerability of mental and psychomotor growth than the intraoperative factors (weight in surgery, cooling time, deep hypothermic circulatory arrest time, cardiopulmonary bypass time, lowest nasopharyngeal temperature).

Patients and Methods

The sample consists of 93 participants, between 13 and 18 years of age, divided in two groups: a congenital heart disease group (CHD), composed of 77 patients recruited from the outpatient pediatric cardiology clinic at the Hospital de Sao Joao (Porto); and a group control (CG), made up of 16 adolescents from several schools in the Porto city area (Table 1). The CHD group is further divided in three groups corresponding to different types of congenital heart disease: Transposition of the Great Arteries (TGA) (n=23); Tetralogy of Fallot (TF) (n= 23); Ventricular Septal Defect (VSD) (n= 31). Tables 1 and 2 display the characteristics of the sample.

Control group and CHD group do not differ according to age (p=.197), gender (χ^2= .906; p=.412) and years of education (p=.055). The same is valid for the three

subgroups of CHD regarding age (H=.420; p=.811), gender (χ^2= 3,195; p=.202) and years of education (H=.531; p=.767).

Neuropsychological Assessment

In order to collect all necessary information for this study, all participants underwent a brief neuropsychological assessment, designed to evaluate a number of neurocognitive functions over a short period of time.

Different tests were used for this purpose such as, Wechsler's Digit Test, in direct and indirect form, focused on the assessment of immediate auditory-verbal attention and working memory, respectively; Wechsler's Symbol Search, used to evaluate psychomotor performance, speed of execution, perceptive organization and persistence. Rey's Complex figure, copy and reproduction from memory three minutes after image exposure, was used in order to assess visual constructional ability and visual constructional memory. The Key Search Test, from the Behavioral Assessment of the Dysexecutive Syndrome- children, focuses on the evaluation of the capability for efficient planning.

Color-word Stroop Test was used to assess attention efficiency. Trail Making Test, part A focuses on the evaluation of visual spatial orientation, psychomotor speed, while part B is to assess divided attention.

Finally, Wechsler's Logical Memory Task was used in order to evaluate verbal memory.

Statistical Analysis

Statistical analysis was carried out using the program IBM SPSS Statistics for Windows, version 21. A comparison of the obtained results on the neuropsychological tests between the control and CHD group and also between the CHD subgroups was made through the U of Mann-Whitney. The Spearman correlations were used in order to correlate neonatal variables (weight, length, cephalic perimeter and APGAR indexes) with the results obtained by the CHD group and subgroups. Finally, a regression analyse was conducted to determine the relationship between the independent variables (head circumference and cyanosis) and the indice of total cognitive performance. Significance was determined with $p \leq 0.05$.

Results

Relatively to the performance of the Control and CHD groups, in the neuropsychological tests, it can be verified through the Table 3 the significant differences in the neurocognitive performance between the groups, with better resulted in the performance of the CG, with exception of the task Logical Memory.

The table 4 represents the comparison of the results obtained in the neuropsychological tests by the subgroups of CHD (VSD, TF and TGA). Thus, we see that the VSD subgroup show better results compared to the cyanotic subgroups (TF and TGA), presenting only as statistically significant differences in RCFm ($p = .010$).

In order to verify the existence of a significant correlation between indices of fetal brain development and neonatal parameters and cognitive performance in neuropsychological tests administered in the total sample and in the group and subgroups of CHD, we used the Spearman correlation (rho), since the distribution of the sample is not homogeneous.

With regard to table 5 analysis verifies that, the CHD group, indices of fetal brain development correlates positively and significant statistically with the neuropsychological tasks: head circumference with WDD (rho=.339; p=.011), RCFc (rho=.297; p=.027) and StroopI (rho=.283; p=.036); weight with RCFc (rho=.254; p=.035) and BKS (rho=.340; p=.004). Even in this group, the head circumference variable correlates negative and significant statistically with the TMT A (rho=-.321; p=.017).

According to table 6, it turns out that in VSD group, the indices of fetal brain development correlates positive and significant statistically with neuropsychological tasks: head circumference with BKS (rho=.463; p=.017), length with StroopW (rho=.428; p=.023) and weight with BKS (rho=.518; p=.004).

In the table 7 it is possible to verify that, in TF subgroup, the neonatal variable Apgar indice (2) correlates positive and significant statistically with StroopW (rho=.523; p=.031) and StroopC (rho=.559; p=.020). The weight variable correlates positive and significant statistically with RCFc (rho=.458; p=.037).

Table 8 shows that, in TGA subgroup, the Apgar indice (1) correlates positive and significant statistically with TMT-B (rho=.565; p=.018) while the Apgar indice (2) correlates positive and significant statistically with TMT-B (rho=.584; p=.015).

Even in this group, the Apgar indice (2) correlates positive and significant statistically with WDI (rho=-.506; p=.038) and WSS (rho=-.502; p=.040).

Finally, as we conducted the regression analyses we could confirm some of these tendencies. The variables that could predict a worse cognitive performance were a presence of cyanosis (p=.042) and a low value of head circumference, which has a *p* value very close to .05 suggesting that is also a good predictor (p=.053) (table 9).

Discussion

According to the results, it is possible to confirm one of our hypothesis, saying that adolescents with congenital heart disease, when compared to the control group, have lower performance in neuropsychological tasks in almost every dimension studied, with the exception of Weschler`s logical memory. What it is commonly found in current publications is that children with congenital heart disease, in fact, show lower performance in neuropsychological evaluation, in several cognitive domains.[7]

Congenital heart disease children had more difficulties in auditory-verbal immediate attention tasks, selective attention (Stroop Test Word, Color and Interference) and divided attention (Trail Making Test – part B). This may be explained by previous studies where congenital heart disease patients had lower scores on tasks related with attention domains[7,8,9,10,31,32] and by results of behavioral assessment evaluation, by the parents of children with congenital heart disease, having described attention problems.[33]

As for Key Search Test, we came to the conclusion that congenital heart disease children have poorer performance. This may suggest some difficulties in executive functions, such as planning ability. Our results go along other studies that state the existence of alterations on executive functioning, planning ability, organization and problem resolution.[7,8,13,34] Alterations on executive functioning are also consistent with low results in Trail Making Test – part B.

In this study, we were able to verify that congenital heart disease patients show deficits in visual-constructive ability Rey's Complex Figure – copy and visual-spatial (Rey's Complex Figure - Memory e Trail Making Test – part A). According to Miatton et al[7], Brosig et al[9]; Bellinger et al[2]; Bellinger et al[34] , children with different types of congenital heart disease reveal difficulties in tasks involving visual-spatial abilities. Visual-spatial deficits may be implicated in perceptive organization.[2]

We also found that congenital heart disease patients have worse performance in visual memory tasks (Rey's Complex Figure - memory) and working memory (Inverse Digits).

Other studies also show that these children have memory deficits (Bellinger et al[2]; Miatton et al[7]; Majnemer et al[13]), more specifically in working memory[2] and visual memory.[35] In the mean time, other studies claim that congenital heart disease children do not have any memory deficits, when compared to healthy children.[35]

In this investigation were also made comparisons relating to performance in neuropsychological tests between the subgroups of congenital heart disease, particularly cyanotic cardiopathies (TF and TGA) and acyanotic cardiopathies (VSD). When comparing the 3 subgroups (cyanotic and acyanotic), as to performance on neuropsychological tests, we found that teens with cyanotic cardiopathy have worst results compared with the acyanotic group. However, the significant differences are only in RCFc, RCFm and StroopI. These results suggest that, in this way the cyanotic subgroup possible presents deficits in the visual construction ability, visual memory and selective attention. As Hovels-Gurich and collaborators[12], in studies with children with cyanotic and acyanotic cardiopathies, there is a higher risk of attention dysfunction in children with cyanotic heart disease compared to acyanotic, corroborating this way part of the results of the present study, since although not significant, it is clear that on average, adolescents with TF and TGA show lower results than the adolescents with VSD.

Nevertheless, there are several studies not consistent with our results, which point in equality of neuropsychological performance between cyanotic and acyanotic subgroups [12,36,37,38, 39, 40].

Concerning indices of fetal brain development (head circumference, weight and length) and neonatal parameters (Apgar 1 and 2) we know that these can indicate some

vulnerability in mental and psychomotor development.[30] So, since apparently there is a correlation between the fetal/neonatal parameters and neuropsychological abilities, it becomes important to study the correlations between these variables and cognitive performance in neuropsychological activities in adolescents with congenital heart disease.

Relatively though the results of the present investigation, it is concluded that the main correlation between indices of fetal brain development and cognitive development in long-term is notoriously in head circumference. This variable correlates positively with the immediate auditory-verbal attention, visual constructive ability, executive functioning (planning and problem-solving), selective attention and verbal immediate memory. Still in the head circumference it is denoted a negative correlation with visual-spatial orientation and psychomotor speed.

Being this fetal variable a likely indicator of a poor performance on cognitive activities, which involve the operation of the frontal lobe, and once, in the presence of congenital cardiopathies is often the compromise fetal oxygenation is, consequently harmed the self-regulation mechanism of blood flow of brain areas, particularly the frontal lobes.[1]

With regard to weight variable, there was a positive correlation with the ability to visual constructing and executive functioning, especially with the planning ability and problem solving. In the literature, there are several studies that corroborate our findings, once that indicate a strong relationship between low birth weights with changes in cognitive abilities.[41, 42]

As mentioned earlier, in the case of oxygenation problems, there is a global constraint of somatic growth, due to redistribution of brain circulation.[22, 43, 44] This way there is a delay in fetal growth may have influence later in neurocognitive performance.

According to the results mentioned above, in which the head circumference correlates with much of neuropsychological tasks, this seems that fetal variable has a strong influence on neuropsychological performance of adolescents with congenital cardiopathies.

With regard to the different groups of congenital heart diseases (VSD, TF and TGA), can be verified the positive correlations that exist in VSD subgroup between the head circumference and planning ability and problems solving. These results suggest that children with congenital cardiopathies and low head circumference can have neurodevelopment consequences later[1, 45], particularly in executive functions.

Even in this group, there is positive correlation between length variable and selective attention, a negative correlation between head circumference with visuo-spatial orientation and psychomotor speed, and a positive correlation between weight and planning ability and problems solving.

In the subgroup TF, there were positive correlations between the Apgar indice (2) and the selective attention, these results are supported by the commitment of fetal oxygenation manifest in congenital heart diseases. Even in this subgroup, were perceptible positive correlations between the weight and visual constructive ability.

As for the TGA subgroup, there were positive correlations between Apgar scores, 1 and 2, with the visuospatial orientation ability, psychomotor speed and divided attention. According to Massaro and collaborators[46] the presence of congenital heart diseases in newborns is accompanied by hypoxic-ischemic lesions, detected by magnetic resonance[47], being likely their relationship with low Apgar scores (1 and 2) which will later translate into difficulties on the cognitive performance of children. [22, 44] Even in the TGA subgroup, there was a negative correlation between the Apgar score (2) and work memory (WDI) and the psychomotor performance (WSS), which points towards a

relationship between psychomotor performance in children with TGA and Apgar score (2).

Analyzing the predictors of a worse cognitive performance, we conclude that the presence of cyanosis in these patients and a low head circumference reveal themselves a strong predictors of a worse cognitive performance in adolescents with congenital heart disease.

As such, according to our results it can be concluded that adolescents with congenital heart diseases exhibit a worse neurocognitive performance compared to healthy adolescents. It is also notorious the implications of fetal and neonatal parameters on neurocognitive performance of these adolescents, later.

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Tables

Table 1. Characteristics of the sample

	C	CHD
Age (M/SD)	15,69/ 1,44	15,09/ 1,71
Gender (Male/Female)	11/5	43/34
Education (M/SD)	10,13/1,36	9,13/1,95

Table 2. Characteristics of the CHD subgroups with reference to the parameters of fetal development

	TGA	TF	VSD
Age (M/SD)	14,91/1,95	15,17/1,8	15,16/1,43
Gender (Male/Female)	16/7	13/10	14/17
Education (M/SD)	8,91/2,03	9,3/ 2,12	9,16/1,79
Head circumference (M/SD)	33,87/1,51	32,96/2,93	34,4/ 2,38
APGAR 1 (M/SD)	8,06/ 1,2	7,82/ 2,01	7,5/ 2,39
APGAR 2 (M/SD)	9,29/ 0,99	9,53/0,87	9,86/0,36
Weight (M/SD)	3,17/0,44	2,87/ 0,76	3,21/0,66
Length (M/SD)	48,05/2,55	46,79/5,25	48,11/3,11

Table 3. Comparison of results obtained by the groups (CG and CHDG) in different neuropsychological tasks

	Control Group	CHD Group		
	N=16	N=77		
	Mean Rank	Mean Rank	u	*p*
WDD	**69,09**	**42,41**	**262.5**	**<.001**
WDR	**75,09**	**41,16**	**166.5**	**<.001**
RCFc	**75,97**	**40,98**	**152.5**	**<.001**
RCFm	**76,19**	**40,94**	**149.0**	**<.001**
WSS	**32,25**	**50,06**	**380.0**	**.016**
BKS	**75,47**	**41,08**	**160.5**	**<.001**
StroopW	**76,31**	**40,91**	**147.0**	**<.001**
StroopC	**71,44**	**41,92**	**225.0**	**<.001**
StroopI	**77,16**	**40,73**	**133.5**	**<.001**
TMT - A	**14,22**	**53,81**	**91.5**	**<.001**
TMT - B	**16,66**	**53,31**	**130.5**	**<.001**
MLT	52,50	45,86	528.0	.368
Total Performance	**82,31**	**39,66**	**51.0**	**<.001****

* $p \leq 0.05$ ** $p \leq 0.01$

Table 4. Comparison between the cyanotic groups (TF and TGA) and the acyanotic group (VSD)

	IVC N=31		FT N=23		TGA N=23			
	M	SD	M	SD	M	SD	F	*p*
WDD	10,52	2,67	9,57	3,07	9,09	3,03	1,713	.187
WDR	5,58	2,31	4,26	2,20	4.96	2,44	2,150	.124
RCFc	31,45	7,09	29,11	7,89	28,46	6,39	1,341	.268
RCFm	**19,65**	**6,58**	**15,54**	**8,19**	**13,61**	**7,13**	**4,936**	**.010***
WSS	53,42	18,65	49,30	16,45	51,52	12,52	0,418	.660
BKS	7,10	3,76	6,04	2,95	5,91	2,94	1,073	.347
StroopW	78,69	17,16	74,74	18,46	72,17	13,77	1,025	.364
StroopC	63,35	12,91	58,96	12,32	59,39	11,03	1,095	.340
StroopI	39,97	9,73	37,52	9,13	34,52	9,09	2,235	.114
TMT-A	46,10	28.44	52,13	27,85	46,96	13,70	0,430	.652
TMT-B	78,06	43,07	94,09	48,64	84,91	35,73	0,924	.402
MLT	13,10	5,18	11,52	4,43	11,35	4,04	1,194	.309
Total Performance	0,46	7,91	-3,53	8,12	-3,64	6,68	2,609	.080

* $p \leq 0.05$ ** $p \leq 0.01$

Table 5. Spearman's correlation between indices of fetal brain development and neonatal parameters and the results of neuropsychological tests in CHD group.

	Índex Apgar(1) N=62		Índex Apgar(2) N=62		Head circumference N=55		Length N=66		Weight N=69	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
WDD	-.044	.735	.216	.092	**.339***	**.011**	.064	.610	.078	.523
WDR	-.179	.163	-.037	.772	.260	.055	-.044	.729	.067	.583
RCFc	-.172	.182	.147	.253	**.297***	**.027**	.207	.095	**.254***	**.035**
RCFm	-.228	.075	.166	.197	.091	.507	.040	.752	.100	.414
WSS	-.196	.126	-.066	.611	-.017	.901	.095	.448	.060	.626
BKS	-.182	.157	-.059	.648	.264	.051	.128	.306	**.340****	**.004**
StroopW	.052	.688	.245	.055	.231	.089	.185	.136	.089	.467
StroopC	-.015	.906	.158	.220	.256	.059	.115	.356	.144	.239
StroopI	.164	.203	.207	.107	**.283***	**.036**	.122	.329	.076	.535
TMT-A	.062	.631	-.014	.915	**-.321***	**.017**	-.015	.908	-.147	.227
TMT-B	.081	.531	.024	.853	-.127	.355	-.012	.926	-.148	.224
MLT	-.211	.099	.035	.789	.263	.052	.197	.114	.177	.146
Total Performance	-.181	.160	.121	.351	**.361****	**.007**	.130	.298	.232	.055

* $p \leq 0.05$ ** $p \leq 0.01$

Table 6. Spearman's correlation between indices of fetal brain development and neonatal parameters and the results of neuropsychological tests in VSD group.

	Índex Apgar (1) N=28		Índex Apgar (2) N=28		Head circumference N=26		Length N=28		Weight N=29	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
WDD	-.110	.578	.204	.298	.154	.454	.012	.952	.038	.846
WDR	-.214	.274	-.108	.583	.149	.467	-.134	.498	-.172	.373
RCFc	-.092	.642	.077	.698	.145	.479	.309	.110	.236	.217
RCFm	-.260	.292	.177	.367	.178	.384	.056	.776	.126	.516
WSS	-.296	.127	-.013	.949	-.078	.704	.200	.307	.170	.378
BKS	-.035	.860	.204	.297	**.463***	**.017**	.082	.677	**.518****	**.004**
StroopW	-.041	.835	.278	.152	.108	.601	**.428***	**.023**	-.289	.128
StroopC	-.046	.815	.139	.480	.221	.277	.269	.166	.232	.226
StroopI	.282	.146	.209	.285	.186	.363	.249	.201	.178	.355
TMT - A	-.038	.849	-.165	.403	**-.397***	**.045**	-.335	.082	-.333	.077
TMT - B	-.003	.987	-.051	.798	.020	.923	.008	.968	-.197	.305
MLT	-.120	.543	.013	.949	.305	.130	.115	.560	.333	.078

* $p \leq 0.05$ ** $p \leq 0.01$

Table 7. Spearman's correlation between fetal brain development indices and neonatal parameters and the results of neuropsychological tests in TF group.

	Índex Apgar (1) N=17		Índex Apgar (2) N=17		Head circumference N=14		Length N=19		Weight N=21	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
WDD	.127	.627	.406	.106	.506	.065	.141	.564	.317	.162
WDR	.012	.963	.221	.393	.478	.084	.166	.496	.366	.102
RCFc	-.297	.247	.210	.418	.358	.209	.371	.118	**.458***	**.037**
RCFm	-.343	.177	.073	.782	.067	.820	-.024	.922	.160	.490
WSS	-.003	.992	.101	.700	.245	.399	.015	.952	.077	.741
BKS	-.270	.295	-.223	.389	.300	.298	.143	.559	.149	.519
StroopW	.323	.206	**.523***	**.031**	.316	.272	.184	.450	.016	.946
StroopC	.267	.301	**.559***	**.020**	.357	.211	.212	.384	.256	.263
StroopI	.178	.495	.378	.134	.507	.064	.087	.724	.150	.516
TMT - A	.023	.929	-.103	.694	-.129	.659	.216	.374	-.030	.899
TMT - B	-.102	.696	-.171	.512	-.374	.187	.007	.977	-.120	.604
MLT	-.280	.276	.030	.909	.286	.321	.096	.694	.004	.985

* $p \leq 0.05$ ** $p \leq 0.01$

Table 8. Spearman's correlation between fetal brain development indices and neonatal parameters and the results of neuropsychological tests in TGA group.

	Índex Apgar (1) N=17		Índex Apgar (2) N=17		Head circumference N=15		Length N=19		Weight N=19	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
WDD	-.130	.618	-.204	.432	.366	.180	.059	.812	-.239	.324
WDR	-.430	.085	**-.506***	**.038**	.208	.457	-.079	.748	-.016	.948
RCFc	-.181	.487	-.164	.529	.290	.294	-.322	.179	-.144	.556
RCFm	-226	.383	-.329	.197	-.261	.347	-.169	.490	-.293	.223
WSS	-.448	.072	**-.502***	**.040**	-.241	.387	-.023	.924	-.141	.564
BKS	-.261	.312	-.103	.693	-.146	.604	.017	.944	.229	.346
StroopW	-.182	.485	-.223	.389	.432	.108	-.252	.298	-.203	.405
StroopC	-.298	.246	-.339	.184	.184	.511	-.379	.110	-.310	.197
StroopI	-.082	.755	-.265	.304	.145	.605	-.243	.317	-.395	.094
TMT - A	.273	.290	.446	.073	-.273	.326	.291	.226	.242	.318
TMT - B	**.565***	**.018**	**.584***	**.014**	-.002	.995	.210	.389	.120	.624
MLT	-.206	.424	-.133	.610	-.085	.764	.423	.071	.094	.701

* $p \leq 0.05$ ** $p \leq 0.01$

Table 9. Linear Regression: Cyanosis and head circumference are the main predictors of neuropsychological performance in CHD patients in adolescence.

Model	R	R^2	F	p	β	t	p
1	.408	.167	5,203	**.009**			
					.256	1,979	.053
Head Circumference							
					-.270	-2,086	**.042**
Cyanosis							

Apêndice

Apêndice I

Artigo em Português

Impacto do Desenvolvimento Fetal no Funcionamento neurocognitivo em Adolescentes com Cardiopatias Congénitas Cianóticas e Acianóticas

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Resumo

Objetivos: O objetivo deste estudo foi avaliar a performance neurocognitiva em adolescentes com cardiopatia congénita e determinar se os parâmetros de desenvolvimento fetal avaliados em recém-nascidos, tais como o perímetro cefálico, comprimento, peso e índices de Apgar, estão de alguma forma relacionados com o seu desempenho neurocognitivo.

Método: Foram avaliados 77 pacientes com Cardiopatia Congénita (43 homens) com idades compreendidas entre os 13 e 18 anos de idade (x= 15,04 ± 1,86), sendo que 46 são cianóticos. O grupo controle incluiu 16 crianças saudáveis (11 homens) com idades entre 13 e 18 anos (x= 15,69 ± 1,44). Os testes neuropsicológicos selecionados foram

administrados a ambos os grupos, envolvendo uma ampla gama de funções neurocognitivas, como a memória a curto prazo (verbal e visuo-construtiva), memória de trabalho, velocidade de processamento, atenção (dividida e seletiva) e planeamento.

Resultados: Pacientes coronários em comparação ao grupo controlo apresentaram resultados inferiores na totalidade das provas, exceto na prova Memória Lógica. Os pacientes com CIV quando comparados com os pacientes com TF e TGA, apresentaram melhores resultados em todas as provas neuropsicológicas, embora as únicas diferenças significativas foram na prova FCRc (F=4,936; p=.010). Diversas correlações eram aparentes entre os parâmetros fetais/neonatais e as capacidades neuropsicológicas nos diferentes subgrupos de cardiopatias. No entanto, a principal correlação verifica-se entre o perímetro cefálico e as provas Dígitos Diretos (rho=.339; p=.011), Figura Complexa de Rey (rho=.297; p=.027), Stroop Interferências (rho=.283; p=.036) e Trail Making Test (rho=-.321; p=.017).

Conclusão: Adolescentes com cardiopatia congénita apresentam um pior desempenho neuropsicológico comparativamente ao grupo controlo, principalmente os pacientes cianóticos (TF e TGA). A circulação fetal parece ter um forte impacto sobre o crescimento cerebral e somático, prevendo um comprometimento cognitivo em adolescentes com cardiopatias congénitas.

Palavras Chave: Desenvolvimento Fetal, Funcionamento Neurocognitivo, Variáveis Neonatais, Cardiopatia Congénita

Introdução

A doença cardíaca congênita tem sido considerada a causa mais comum de morbilidade e mortalidade infantil.[1]

Nas últimas décadas, os avanços nas intervenções cirúrgicas e tratamento em pacientes com doença cardíaca congénita, têm contribuído para o aumento da expectativa de vida dessas crianças. No entanto, mais de metade dessas crianças irão apresentar algum tipo de dano neurológico.[2,3,4]

Na literatura, diferentes estudos apontam para a existência de alterações no desenvolvimento cognitivo de jovens com cardiopatias congénitas, consequências estas relacionadas com fatores peri operatórios (síndromes, circulação extra corporal durante a cirurgia e complicações pós-cirúrgicas).[5]

Um grande número de crianças que foram submetidas a cirurgia cardíaca no período neonatal, demonstraram um padrão de desenvolvimento de problemas neurológicos, caracterizados por défices cognitivos, de atenção e funcionamento executivo, de capacidades visuo-motoras e visuo-espaciais, de atraso na aquisição da linguagem expressiva e de dificuldades de aprendizagem.[6,7,8,9,10,11,12,13] A maioria dos estudos que focam os resultados neurológicos em crianças com cardiopatias congénitas, salientam os fatores relacionados com a cirurgia, especificamente quando a perfusão cerebral pode estar comprometida durante a circulação extra corporal [1]sendo que estes fatores, foram considerados percursores de possíveis complicações neurocognitivas.[14] No entanto, outros estudos demostram uma alta prevalência de anormalidades neurológicas anatómicas e funcionais antes da cirurgia em recém-nascidos com cardiopatia congénita[15,16,17], focando a relação entre estas anormalidades e o desenvolvimento cognitivo durante a infância.

Conforme alguns estudos, foram encontradas anormalidades neurocomportamentais como hipotonia, agitação/inquietação, assimetria motora, letargia e características autistas, anteriores à cirurgia em mais de 50% dos recém-nascidos (menos de um mês) e 38% de crianças (entre 1 mês e 2 anos de idade) com cardiopatias congénitas. [18,19] São ainda diagnosticadas no período pré operatório, a presença de agenesia ou disgenesia do corpo caloso, holoprosencefalia, microcefalia, lisencefalia[20], abertura do opérculo, enfartes isquémicos e lesão da substancia branca caracterizada por leucomalácia periventricular.[21] Estes estudos concluíram ainda que essas anormalidades persistiam ou pioravam no período pós-operatório, incluindo o aparecimento de anormalidades nos nervos cranianos.[18,19]

Os recém-nascidos com cardiopatia congénita apresentam potenciais riscos de apresentarem hipoxia, hipotensão e acidose. A presença de hipoxia-isquémica num período pré-natal (desenvolvimento fetal) pode causar complicações no desenvolvimento neurológico a longo prazo.

A hipoxia fetal afeta o desenvolvimento normal do cérebro, nomeadamente ao nível do hipocampo (estrutura cerebral responsável pela conversão da memória a curto-prazo em memória a longo prazo) e do córtex cerebral (estrutura cerebral responsável pelas áreas cognitivas relacionadas com a memória, atenção, linguagem, perceção e pensamento).[22] Este facto revela a possibilidade de as malformações cardíacas congénitas e as anomalias no crescimento fetal estejam causalmente relacionadas.[23,17] Com isto, mantem-se ainda a hipótese de que as anormalidades do desenvolvimento cerebral, as alterações hemodinâmicas intrauterinas, as anormalidades cerebrais congénitas e lesões cerebrais adquiridas, relacionadas com cianose prolongada e hipoperfusão após o nascimento[1], contribuem para efeitos adversos no desenvolvimento neurológico em crianças com cardiopatia congénita.[15]

Vários estudos de ressonância magnética realizados num período peri-operatório, corroboram que os recém-nascidos com cardiopatias congénitas apresentam uma alta frequência de lesão cerebral adquirida e lesão da substância branca. Estas anormalidades no desenvolvimento cerebral em recém-nascidos com cardiopatias congénitas podem refletir anormalidades no fluxo sanguíneo cerebral do feto e consequentemente um atraso no desenvolvimento do cérebro.[24]

Uma vez que muitos recém-nascidos apresentam a cardiopatia congénita como patologia isolada, supõe-se que o cérebro apresenta um potencial de desenvolvimento normal.[25] Contudo, é de realçar que o cérebro e o coração compartilham vias genéticas comuns, ocorrendo o seu desenvolvimento em simultâneo no feto com cardiopatia congénita.

Por volta da sétima semana de gestação, o coração torna-se morfologicamente maduro enquanto que o desenvolvimento cerebral prolonga-se ao longo de um período de tempo mais alargado. É durante este período que decorrem diversos eventos morfológicos durante os primeiros dois trimestres[24], nomeadamente a migração e arborização neuronal, sinaptogénese, morte celular programada, maturação dos oligodendrócitos e extensa reorganização das conexões sinápticas.[15] Após este período ocorre um crescimento cerebral marcante e dependente da formação e aperfeiçoamento de conexões no terceiro trimestre e período pós-natal.[24] Esta fase de desenvolvimento caracterizada por um visível aumento da atividade metabólica, torna o cérebro dependente do coração para o fornecimento de oxigénio e de nutrientes.

A presença de cardiopatias congénitas leva a anormalidades no fluxo sanguíneo fetal, nomeadamente alterações na dinâmica de distribuição de oxigénio no cérebro em desenvolvimento.[24] Com isto, torna-se evidente a importância destes fatores no crescimento e maturação cerebral.[26]

Na circulação sanguínea normal do feto, as trocas gasosas ocorrem através da placenta. Enquanto que o sangue venoso desloca-se da veia cava inferior hepática para o ventrículo direito, o sangue oxigenado dirige-se do canal venoso sobre o forâmen oval através do ventrículo esquerdo para a aorta e circulação cerebral. Porém, quando a oxigenação fetal se encontra comprometida, há uma redistribuição sanguínea para a circulação cerebral, fenómeno este designado de "brain sparing".[1] Este fenómeno conhecido pela restrição global do crescimento somático, com relativa preservação do crescimento da cabeça[24], é caracterizado pelo aumento do fluxo diastólico nas artérias cerebrais e pela diminuição do fluxo diastólico nas artérias aorta descendente e umbilical.[1] No entanto, supõe-se que existem regiões específicas do cérebro, que se encontram mais protegidas do que outras. Conforme Dubiel, Gunnarsson & Gunnarsson[27], num estudo realizado com grávidas com hipertensão materna e disfunção da placenta, verificou-se vasodilatação cerebral em 41% na artéria cerebral anterior, em 30% na artéria cerebral posterior e em 24% na artéria cerebral média. Com os resultados deste estudo, concluiu-se que as artérias cerebrais anteriores apresentam uma melhor resposta autorreguladora, na qual a redistribuição do fluxo sanguíneo favorece a perfusão dos lobos frontais, ao contrário das artérias cerebrais médias que apresentam-se menos reativas.[1] Uma vez que a vasodilatação cerebral ocorre quando a oxigenação fetal está comprometida, este mecanismo de proteção pode ser insuficiente para manter o crescimento e desenvolvimento cerebral normal em situações de stress prolongado *in útero.*

Na circulação sanguínea fetal normal, o sangue oxigenado é conduzido para o cérebro e o sangue desoxigenado para a placenta.[1] No entanto, e como referido anteriormente, estudos demonstram que a existência de anormalidades na circulação sanguínea, consequentes de cardiopatias complexas, nomeadamente no Síndrome

Hipoplásico do Coração Esquerdo, Transposição Das Grandes Artérias, Tetralogia de Fallot, podem contribuir para um desenvolvimento cerebral anormal.[1,15, 24]

Segundo Donofrio & Massaro[1] o tipo de lesão não só afeta a origem do fluxo sanguíneo cerebral, mas também o grau de sangue desoxigenado distribuído através da circulação cerebral. Considera-se que em fetos com Síndrome Hipoplásico do Coração Esquerdo é provável um aumento da resistência ao fluxo cerebral, no qual a circulação sanguínea retrocede através de uma hipoplasia istmo-aórtica para chegar ao cérebro; na presença de Transposição de Grandes Artérias, o sangue venoso da circulação cerebral volta diretamente para o cérebro do feto, ao passo que em fetos diagnosticados com Tetralogia de Fallot e Síndrome Hipoplásico do Coração Direito, o sangue relativamente desoxigenado entra na circulação cerebral devido à mistura intracardíaca. Assim, todas estas alterações na circulação sanguínea poderão ser percursores de um crescimento somático anormal in útero, influenciando a antropometria neonatal.[23]

Comparando recém-nascidos sem patologia congénita cardíaca e recém-nascidos com Síndrome Hipoplásico do Coração Esquerdo, os últimos apresentam peso, comprimento e perímetro cefálico inferiores aos parâmetros normais e o volume da cabeça é desproporcionalmente pequena comparativamente ao peso. No que diz respeito aos recém-nascidos com Transposição das Grandes Artérias, estes apresentam peso dentro dos parâmetros normais, ao contrário do perímetro cefálico que se apresenta inferior relativamente ao peso, uma vez que Rivkin e colaboradores mencionam que adolescentes com TGA sujeitos a cirurgia do tipo "arterial switch", nos primeiros meses de vida, apresentam anormalidades da substancia branca, nomeadamente a redução da mesma.[28] Contudo, os recém-nascidos com Tetralogia de Fallot têm proporções normais, apresentando no entanto, peso, comprimento e perímetro cefálico inferiores aos parâmetros normais. Em crianças com diagnóstico de Coartação da Aorta, observa-

se um maior volume da cabeça comparativamente ao peso logo após o nascimento.[1, 23, 24,29]

Deste modo, considera-se que são vários os fatores que contribuem para um baixo peso ao nascimento, nomeadamente os síndromes genéticos, insuficiência placentária e restrição do crescimento intra-uterino, e que possivelmente poderão aumentar o risco de atrasos no neurodesenvolvimento.

Conforme Gaynor, Jarvik, Bernbaum, Gerdes, Wernovsky et al[30], em estudos recentes, os fatores inerentes ao paciente, nomeadamente peso à nascença, perímetro cefálico ao nascer e índices de Apgar no 1º e no 5º minuto, revelam-se melhores preditores da vulnerabilidade do índice de desenvolvimento mental e psicomotor, comparativamente aos fatores intraoperatórios (peso na cirurgia, tempo de resfriamento, paragem circulatória por hipotermia profunda, duração da circulação extracorporal e baixa temperatura nasofaríngea).

Amostra e Método

A amostra é composta por 93 participantes, entre 13 e 18 anos de idade, divididos em dois grupos: um grupo de adolescentes com cardiopatia congênita (CC), composto por 77 pacientes recrutados no serviço de cardiologia pediátrica do ambulatório do Hospital de São João (Porto); e um grupo controle (GC), composto por 16 adolescentes de várias escolas na área da cidade do Porto (Tabela 1). O grupo CC é dividido em três grupos, correspondentes a diferentes tipos de doença cardíaca congênita: Transposição das Grandes Artérias (TGA) (n = 23), Tetralogia de Fallot (TF) (n = 23) e Comunicação Interventricular (CIV) (n = 31). As Tabelas 1 e 2 mostram as características da amostra.

O grupo controle e o grupo CC não diferem relativamente à idade (p = .197), género ($\chi 2$ = .906, p = .412) e anos de escolaridade (p = .055). O mesmo é válido para os três

subgrupos de CC relativamente à idade (H = .420, p = .811), género ($\chi 2$ = 3,195, p = .202) e anos de escolaridade (H = .531, p = .767).

Avaliação Neuropsicológica

A fim de recolher todas as informações necessárias para este estudo, todos os participantes foram submetidos a uma breve avaliação neuropsicológica, desenhada para avaliar uma série de funções neurocognitivas durante um curto período de tempo. Diferentes testes foram utilizados para este fim, tais como, a subprova Memória de Dígitos Diretos (DD) e Inversos (DI), com foco na avaliação da atenção auditivo-verbal imediata e memória de trabalho, respetivamente; a subprova Código (Cd) parte B usada para avaliar o desempenho psicomotor, velocidade de execução, organização perceptiva. Figura Complexa de Rey, cópia (FCRc) e reprodução (FCRm) por memória três minutos após a exposição da imagem, teste utilizado para avaliar a capacidade de construção visual e memória visual. O teste Procura da Chave (PC), da bateria *Behavioural Assessment of the Dysexecutive Syndrome* (BADS), centra-se na avaliação da capacidade para o planeamento e resolução de problemas.

O teste Stroop - Cor (StroopC), Palavra (StroopP) e Interferência (StroopI) foi utilizado para avaliar a capacidade de atenção seletiva. O Trail Making Test - parte A (TMT-A) e B (TMT-B), centra-se na avaliação da orientação visuo-espacial e velocidade psicomotora (TMT A), enquanto que o TMT B avalia a atenção dividida.

Finalmente, a Memória Lógica da Wechsler (ML) foi utilizada para avaliar a memória imediata verbal.

Análise Estatística

A análise estatística foi realizada através do programa IBM SPSS Statistics para o Windows, versão 21.0. Inicialmente no sentido de caracterizar a amostra e estabelecer a comparação entre os resultados obtidos nos testes neuropsicológicos pelos quatro grupos foi realizada uma análise descritiva. No sentido de comparar os resultados nas provas neuropsicológicas, entre o Grupo Controlo e Grupo de Cardiopatias Congénitas e ainda entre os subgrupos de CC, foi utilizado a teste não paramétrico U de *Mann-Whitney*.

Posteriormente, as correlações de Spearman foram utilizadas para correlacionar variáveis fetais (peso, comprimento e perímetro cefálico) e as variáveis neonatais (Apgar 1 e 2) com os resultados obtidos pelo o grupo e subgrupos de CC.

Finalmente, foi realizada uma análise de regressão no sentido de determinar a relação entre as variáveis independentes (perímetro cefálico e presença/ausência de cianose) e o índice total de performance cognitiva. O nível de significância foi determinado com $p \leq 0,05$.

Resultados

Relativamente à performance dos grupos Controlo e CC, nas provas neuropsicológicas, verificamos através da *Tabela 3* as diferenças significativas no desempenho neurocognitivo entre os grupos, com melhores resultados na performance do GC, com exceção da subprova Memória Lógica da Wechsler.

Na *tabela 4* é apresentada a comparação dos resultados obtidos nas provas neuropsicológicas pelos subgrupos de CC (CIV, TF e TGA). Assim, verificamos que o subgrupo CIV apresenta resultados superiores aos adolescentes com cardiopatias

cianóticas (TF e TGA), apresentando-se apenas como diferença significativa no que concerne ao desempenho neuropsicológico na prova FCRm (*p*=.010).

Com o objetivo de verificar a existência de uma correlação significativa entre índices de desenvolvimento cerebral fetal e parâmetros neonatais e o desempenho cognitivo nas provas neuropsicológicas administradas, no grupo e subgrupos de CC, utilizou-se a correlação ordinal de Spearman (rho), uma vez que a distribuição da amostra não é homogénea.

Face à análise da *tabela 5* observa-se que, no grupo CC os índices de desenvolvimento cerebral fetal correlacionam-se positiva e estatisticamente significativa com as seguintes provas neuropsicológicas: perímetro cefálico com DD (rho=.339; *p*=.011), FCRc (rho=.297; *p*=.027) e StroopI (rho=.283; *p*=.036); peso com FCRc (rho=.254; *p*=.035) e PC (rho=.340; p=.004). Ainda neste grupo, a variável perímetro cefálico correlaciona-se negativa e estatisticamente significativa com a prova TMT-A (rho=-.321; *p*=.017).

De acordo com a *tabela 6*, verifica-se que no subgrupo CIV, as variáveis fetais correlacionam-se de forma positiva e estatisticamente significativa com as seguintes provas neuropsicológicas: perímetro cefálico com PC (rho=.463; *p*=.017), comprimento com StroopP (rho=.428; *p*=.023) e peso com PC (rho=.518; p=.004). Ainda neste grupo, a variável perímetro cefálico correlaciona-se negativa e estatisticamente significativa com a prova TMT-A (rho=-.397; *p*=.045).

Pela análise da *tabela 7* é possível verificar que, no subgrupo TF, a variável neonatal Índice Apgar (2) correlaciona-se de forma positiva e estatisticamente significativa com a prova StroopP (rho=.523; *p*=.031) e StroopC (rho=.559; p=.020). A variável peso correlaciona-se positiva e estatisticamente significativa com a prova FCRc (rho=.458; *p*=.037).

Pela análise da *tabela 8* verifica-se que, no subgrupo TGA, a variável neonatal, Índice Apgar (1) correlaciona-se positiva e estatisticamente significativa com a prova TMT-B (rho=.565; p=.018) enquanto o Índice Apgar (2) correlaciona-se de forma positiva e estatisticamente significativa com a prova TMT-B (rho=.584; *p*=.015). Ainda neste grupo, o Índice Apgar (2) correlaciona-se negativa e estatisticamente significativa com a prova DI (rho=-.506; p=.038) e Cd (rho=-.502; p=.040).

Finalmente, realizada a análise de regressão pudemos confirmar algumas dessas tendências. Assim, as variáveis que poderiam prever uma pior performance cognitiva foram a presença de cianose (p=.042) e um valor abaixo para o perímetro cefálico, que apesar de não ser estatisticamente significativo, encontra-se muito próximo de ser significativo (p=.053) (tabela 9).

Discussão

De acordo com a análise dos resultados obtidos, quando comparamos a performance nas provas neuropsicológicas do grupo de adolescentes com CC com o grupo de adolescentes saudáveis, verificamos que o primeiro apresenta um desempenho inferior em quase todas as dimensões neuropsicológicas estudadas, exceto na subprova Memória Lógica da Wechsler. São vários os estudos que corroboram a ideia que, de facto as crianças com cardiopatias congénitas, demonstram um baixo desempenho na avaliação neuropsicológica, em vários domínios cognitivos.[7]

É de facto notório no desempenho do grupo de CC a existência de dificuldades ao nível da atenção auditivo-verbal imediata (Dígitos Diretos), atenção seletiva (Stroop) e atenção dividida (prova TMT B). Estes resultados foram confirmados por estudos prévios, em que os pacientes com cardiopatias congénitas obtiveram desempenhos inferiores em tarefas que requerem domínios atencionais[7,8,9,10,31,32] e pelos produtos

obtidos na avaliação comportamental efetuada pelos pais de crianças com cardiopatias congénitas, onde descrevem problemas atencionais por parte dos filhos.[33]

Quanto à prova PC, verificamos que os adolescentes com cardiopatias congénitas apresentam uma pior performance. Este dado sugere dificuldades ao nível do funcionamento executivo, nomeadamente na capacidade de planeamento. Os resultados são corroborados por estudos que referem a existência de alterações no funcionamento executivo, principalmente na capacidade de planeamento, organização e resolução de problemas[7,8,13,34] As alterações no funcionamento executivo também são consistentes com os baixos resultados na prova TMT B.

Relativamente à prova Cd, observamos um pior desempenho dos adolescentes com cardiopatias congénitas, o que indica dificuldades mais uma vez, ao nível do desempenho psicomotor, mas ainda da velocidade de execução e organização percetiva.

Assim, de acordo com os resultados obtidos, verificamos que os adolescentes com cardiopatias congénitas apresentam défices ao nível da capacidade visuo-construtiva (Figura Complexa de Rey - Cópia) e visuo-espacial (Figura Complexa de Rey - Memória e TMT A). Segundo Miatton et al[7], Brosig et al[9]; Bellinger et al[2]; Bellinger et al[34] crianças com diferentes tipos de CC revelam dificuldades em tarefas que envolvem a capacidade visuo-espacial. Os défices visuo espaciais, parecem estar implicados em alterações ao nível da organização percetiva[2]

Os nossos resultados, demostraram também que o grupo de cardiopatias congénitas apresenta um pior desempenho nas provas que avaliam a memória visual (Figura Complexa de Rey - Memória) e a memória de trabalho (Dígitos Inversos). Existe uma consistência destes resultados com alguns estudos existentes na literatura, onde mencionam que crianças com cardiopatias congénitas apresentam défices de memória (Bellinger et al[2]; Miatton et al[7]; Majnemer et al[13]), sobretudo ao nível da memória de trabalho[2] e memória visual.[35] No entanto, outros estudos mencionam que crianças com

cardiopatias não apresentam défices de memória, quando comparados com crianças saudáveis.[35]

Nesta investigação foram também efetuadas comparações relativas ao desempenho nas provas neuropsicológicas entre os subgrupos de cardiopatias congénitas, nomeadamente cardiopatia cianótica (grupo TF e TGA) e cardiopatia acianótica (grupo CIV). Quando comparados os 3 subgrupos (cianótico e acianótico), quanto à performance nas provas neuropsicológicas, verificamos que os adolescentes com cardiopatia cianótica apresentam piores resultados comparativamente com os acianóticos. No entanto, as diferenças significativas apresentam-se apenas na prova FCRm. Estes resultados sugerem deste modo que, os subgrupos cianóticos apresentam possíveis défices ao nível da capacidade de construção visual e memória visual. Conforme Hovels-Gurich e colaboradores[12], em estudos efetuados com crianças com cardiopatia cianótica e acianótica, existe um maior risco de disfunção atencional em crianças com cardiopatia cianótica comparativamente às acianóticas, corroborando deste modo parte dos resultados do presente estudo, uma vez que apesar de não serem significativos, é notório que em média, os adolescentes com TF e TGA apresentam resultados inferiores aos adolescentes com CIV.

No entanto, existem diversos estudos não consistentes com os nossos resultados, que apontam na igualdade da performance neuropsicológica entre os subgrupos cianótico e acianótico. [12,36,37,38, 39, 40]

No que diz respeito aos índices de desenvolvimento cerebral fetal (perímetro cefálico, peso e comprimento) e parâmetros neonatais (Apgar 1 e 2) sabemos que estes podem indicar alguma vulnerabilidade no desenvolvimento mental e psicomotor.[30] Assim, uma vez que aparentemente existe uma correlação entre os parâmetros fetais/neonatais e as capacidades neuropsicológicas, torna-se importante estudar as

correlações existentes entre essas variáveis e o desempenho cognitivo em atividades neuropsicológicas em adolescentes com doença cardíaca congênita.

Relativamente aos resultados da presente investigação, conclui-se que a principal correlação entre os índices de desenvolvimento fetal cerebral e o desenvolvimento cognitivo a longo prazo verifica-se notoriamente no perímetro cefálico. Esta variável correlaciona-se positivamente com a atenção auditivo-verbal imediata, capacidade construtiva visual, funcionamento executivo (planeamento e resolução de problemas), atenção seletiva e memória imediata verbal. Ainda na variável perímetro cefálico denotou-se uma correlação negativa com orientação visuo-espacial e velocidade psicomotora.

Sendo esta variável fetal um provável indicador de um baixo desempenho em atividades cognitivas, que implicam o funcionamento do lobo frontal, e uma vez que, na presença de cardiopatica congénita é frequente o comprometimento da oxigenação fetal, fica assim prejudicado o mecanismo de autorregulação da circulação sanguínea de áreas cerebrais, nomeadamente dos lobos frontais. [1]

No que diz respeito à variável fetal peso, verificou-se uma correlação positiva com a capacidade de construção visual e com o funcionamento executivo, nomeadamente com a capacidade de planeamento e resolução de problemas. Na literatura, são vários os estudos que corroboram os nossos resultados, uma vez que indicam uma forte relação entre o baixo peso à nascença com alterações das capacidades cognitivas.[41, 42]

Como mencionado anteriormente, no caso de problemas de oxigenação, há uma restrição global de crescimento somático, devido à redistribuição da circulação cerebral.[22, 43, 44] Deste modo, um atraso no crescimento fetal pode ter influência no desempenho neurocognitivo a longo prazo.

De acordo com os resultados mencionados anteriormente, em que a variável fetal perímetro cefálico se correlaciona com grande parte das provas neuropsicológicas,

indicia-se que esta variável fetal tem uma forte influência no desempenho neuropsicológico dos adolescentes com cardiopatias congénitas.

No que diz respeito aos diferentes grupos de cardiopatias congênitas (CIV, TF e TGA), verificou-se quanto ao subgrupo CIV que existem correlações positivas entre a variável fetal perímetro cefálico e a capacidade de planeamento e resolução de problemas. Estes resultados indiciam que crianças com cardiopatias congénitas e com baixo perímetro cefálico, podem ter consequências neurodesenvolvimentais a longo prazo [1, 45], nomeadamente nas funções executivas.

Ainda neste grupo, verifica-se correlação positiva entre a variável fetal comprimento e a atenção seletiva, uma correlação negativa entre a variável perímetro cefálico com a orientação visuo-espacial e a velocidade psicomotora e uma correlação positiva entre a variável peso e a capacidade de planeamento e resolução de problemas.

No subgrupo TF, verificaram-se correlações positivas entre o índice de Apgar(2) e a atenção seletiva, resultados estes suportados pelo comprometimento de oxigenação fetal manifesto nas cardiopatias congénitas. Ainda neste subgrupo, foram percetíveis correlações positivas entre a variável peso e a capacidade construção visuo-espacial.

Quanto ao subgrupo TGA, verificaram-se correlações positivas entre as variáveis neonatais Apgar 1 e 2, com a capacidade de orientação visuo-espacial, velocidade psicomotora e atenção dividida. Segundo Massaro e colaboradores[46] a presença de cardiopatias congénitas em recém-nascidos é acompanhada de lesões hipoxico-isquémicas detetadas por ressonância magnética[47], sendo provável a sua relação com os baixos índices de Apgar (1 e 2) que, mais tarde se traduzem em dificuldades no desempenho cognitivo dessas crianças.[22, 44] Ainda no subgrupo TGA, verificou-se uma correlação negativa entre o índice de Apgar(2) e a memória de trabalho (DI) e desempenho psicomotor (Cd), o que aponta no sentido de uma relação entre o desempenho psicomotor em crianças com TGA e o índice de Apgar(2).

Analisando os preditores de uma pior performance cognitiva, concluímos que a presença de cianose nestes pacientes e um baixo perímetro cefálico revelam-se fortes preditores de uma pior performance cognitiva em adolescentes com cardiopatia congénita.

Assim, de acordo com os nossos resultados é possível concluir que adolescentes com cardiopatias congénitas apresentam um pior desempenho neurocognitivo comparativamente com adolescentes saudáveis. É ainda notório as implicações dos parâmetros fetais e neonatais no desempenho neurocognitivo destes adolescentes a longo prazo.

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Tabelas

Tabela 1. Características da amostra

	GC	**GCC**
Idade (M/DP)	15,69/ 1,44	15,09/ 1,71
Género (Masculino/Feminino)	11/5	43/34
Educação (M/DP)	10,13/1,36	9,13/1,95

Tabela 2. Características dos subgrupos CC referentes aos parâmetros de desenvolvimento fetal

	TGA	TF	CIV
Idade (M/DP)	14,91/1,95	15,17/1,8	15,16/1,43
Género (Masculino/Feminino)	16/7	13/10	14/17
Educação (M/DP)	8,91/2,03	9,3/ 2,12	9,16/1,79
Perímetro Cefálico (M/DP)	33,87/1,51	32,96/2,93	34,4/ 2,38
APGAR 1 (M/DP)	8,06/ 1,2	7,82/ 2,01	7,5/ 2,39
APGAR 2 (M/DP)	9,29/ 0,99	9,53/0,87	9,86/0,36
Peso (M/DP)	3,17/0,44	2,87/ 0,76	3,21/0,66
Comprimento (M/DP)	48,05/2,55	46,79/5,25	48,11/3,11

Tabela 3. Comparação dos resultados obtidos pelos grupos (GC e GCC) nas diferentes provas neuropsicológicas.

	Grupo Controlo	Grupo CC		
	N=16	N=77		
	Mean Rank	Mean Rank	u	*p*
DD	**69,09**	**42,41**	**262.5**	**<.001****
DI	**75,09**	**41,16**	**166.5**	**<.001****
FCRc	**75,97**	**40,98**	**152.5**	**<.001****
FCRm	**76,19**	**40,94**	**149.0**	**<.001****
Cd	**32,25**	**50,06**	**380.0**	**.016***
PC	**75,47**	**41,08**	**160.5**	**<.001****
StroopP	**76,31**	**40,91**	**147.0**	**<.001****
StroopC	**71,44**	**41,92**	**225.0**	**<.001****
StroopI	**77,16**	**40,73**	**133.5**	**<.001****
TMT - A	**14,22**	**53,81**	**91.5**	**<.001****
TMT - B	**16,66**	**53,31**	**130.5**	**<.001****
ML	52,50	45,86	528.0	.368
Performance Total	**82,31**	**39,66**	**51.0**	**<.001****

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 4. Comparação entre os subgrupos de CC (CIV, TF e TGA) nas diferentes provas neuropsicológicas

	CIV N=31		TF N=23		TGA N=23			
	M	SD	M	SD	M	SD	F	*p*
DD	10,52	2,67	9,57	3,07	9,09	3,03	1,713	.187
DI	5,58	2,31	4,26	2,20	4.96	2,44	2,150	.124
FCRc	31,45	7,09	29,11	7,89	28,46	6,39	1,341	.268
FCRm	**19,65**	**6,58**	**15,54**	**8,19**	**13,61**	**7,13**	**4,936**	**.010***
Cd	53,42	18,65	49,30	16,45	51,52	12,52	0,418	.660
PC	7,10	3,76	6,04	2,95	5,91	2,94	1,073	.347
StroopP	78,69	17,16	74,74	18,46	72,17	13,77	1,025	.364
StroopC	63,35	12,91	58,96	12,32	59,39	11,03	1,095	.340
StroopI	39,97	9,73	37,52	9,13	34,52	9,09	2,235	.114
TMT-A	46,10	28.44	52,13	27,85	46,96	13,70	0,430	.652
TMT-B	78,06	43,07	94,09	48,64	84,91	35,73	0,924	.402
ML	13,10	5,18	11,52	4,43	11,35	4,04	1,194	.309
Performance Total	0,46	7,91	-3,53	8,12	-3,64	6,68	2,609	.080

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 5. Correlação de Spearman entre os índices de desenvolvimento cerebral fetal e parâmetros neonatais e os resultados do grupo CC nas diferentes provas neuropsicológicas.

	Índice Apgar(1) N=62		Índice Apgar(2) N=62		Perímetro Cefálico N=55		Comprimento N=66		Peso N=69	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
DD	-.044	.735	.216	.092	**.339***	**.011**	.064	.610	.078	.523
DI	-.179	.163	-.037	.772	.260	.055	-.044	.729	.067	.583
FCRc	-.172	.182	.147	.253	**.297***	**.027**	.207	.095	**.254***	**.035**
FCRm	-.228	.075	.166	.197	.091	.507	.040	.752	.100	.414
Cd	-.196	.126	-.066	.611	-.017	.901	.095	.448	.060	.626
PC	-.182	.157	-.059	.648	.264	.051	.128	.306	**.340****	**.004**
StroopP	.052	.688	.245	.055	.231	.089	.185	.136	.089	.467
StroopC	-.015	.906	.158	.220	.256	.059	.115	.356	.144	.239
StroopI	.164	.203	.207	.107	**.283***	**.036**	.122	.329	.076	.535
TMT-A	.062	.631	-.014	.915	**-.321***	**.017**	-.015	.908	-.147	.227
TMT-B	.081	.531	.024	.853	-.127	.355	-.012	.926	-.148	.224
ML	-.211	.099	.035	.789	.263	.052	.197	.114	.177	.146
Performance Total	-.181	.160	.121	.351	**.361****	**.007**	.130	.298	.232	.055

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 6. Correlação de Spearman entre os índices de desenvolvimento cerebral fetal e parâmetros neonatais e os resultados do subgrupo CIV nas diferentes provas neuropsicológicas.

	Índice Apgar (1) N=28		Índice Apgar (2) N=28		Perímetro Cefálico N=26		Comprimento N=28		Peso N=29	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
DD	-.110	.578	.204	.298	.154	.454	.012	.952	.038	.846
DI	-.214	.274	-.108	.583	.149	.467	-.134	.498	-.172	.373
FCRc	-.092	.642	.077	.698	.145	.479	.309	.110	.236	.217
FCRm	-.260	.292	.177	.367	.178	.384	.056	.776	.126	.516
Cd	-.296	.127	-.013	.949	-.078	.704	.200	.307	.170	.378
PC	-.035	.860	.204	.297	**.463***	**.017**	.082	.677	**.518****	**.004**
StroopP	-.041	.835	.278	.152	.108	.601	**.428***	**.023**	-.289	.128
StroopC	-.046	.815	.139	.480	.221	.277	.269	.166	.232	.226
StroopI	.282	.146	.209	.285	.186	.363	.249	.201	.178	.355
TMT - A	-.038	.849	-.165	.403	**-.397***	**.045**	-.335	.082	-.333	.077
TMT - B	-.003	.987	-.051	.798	.020	.923	.008	.968	-.197	.305
ML	-.120	.543	.013	.949	.305	.130	.115	.560	.333	.078

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 7. Correlação de Spearman entre os índices de desenvolvimento cerebral fetal e parâmetros neonatais e os resultados do subgrupo TF nas diferentes provas neuropsicológicas.

	Índice Apgar (1) N=17		Índice Apgar (2) N=17		Perímetro Cefálico N=14		Comprimento N=19		Peso N=21	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
DD	.127	.627	.406	.106	.506	.065	.141	.564	.317	.162
DI	.012	.963	.221	.393	.478	.084	.166	.496	.366	.102
FCRc	-.297	.247	.210	.418	.358	.209	.371	.118	**.458***	**.037**
FCRm	-.343	.177	.073	.782	.067	.820	-.024	.922	.160	.490
Cd	-.003	.992	.101	.700	.245	.399	.015	.952	.077	.741
PC	-.270	.295	-.223	.389	.300	.298	.143	.559	.149	.519
StroopP	.323	.206	**.523***	**.031**	.316	.272	.184	.450	.016	.946
StroopC	.267	.301	**.559***	**.020**	.357	.211	.212	.384	.256	.263
StroopI	.178	.495	.378	.134	.507	.064	.087	.724	.150	.516
TMT - A	.023	.929	-.103	.694	-.129	.659	.216	.374	-.030	.899
TMT - B	-.102	.696	-.171	.512	-.374	.187	.007	.977	-.120	.604
ML	-.280	.276	.030	.909	.286	.321	.096	.694	.004	.985

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 8. Correlação de Spearman entre os índices de desenvolvimento cerebral fetal e parâmetros neonatais e os resultados do subgrupo TGA nas diferentes provas neuropsicológicas.

	Índice Apgar (1) N=17		Índice Apgar (2) N=17		Perímetro Cefálico N=15		Comprimento N=19		Peso N=19	
	rho	*p*	rho	*p*	rho	*p*	rho	*p*	rho	*p*
DD	-.130	.618	-.204	.432	.366	.180	.059	.812	-.239	.324
DI	-.430	.085	**-.506***	**.038**	.208	.457	-.079	.748	-.016	.948
FCRc	-.181	.487	-.164	.529	.290	.294	-.322	.179	-.144	.556
FCRm	-226	.383	-.329	.197	-.261	.347	-.169	.490	-.293	.223
Cd	-.448	.072	**-.502***	**.040**	-.241	.387	-.023	.924	-.141	.564
PC	-.261	.312	-.103	.693	-.146	.604	.017	.944	.229	.346
StroopP	-.182	.485	-.223	.389	.432	.108	-.252	.298	-.203	.405
StroopC	-.298	.246	-.339	.184	.184	.511	-.379	.110	-.310	.197
StroopI	-.082	.755	-.265	.304	.145	.605	-.243	.317	-.395	.094
TMT - A	.273	.290	.446	.073	-.273	.326	.291	.226	.242	.318
TMT - B	**.565***	**.018**	**.584***	**.014**	-.002	.995	.210	.389	.120	.624
ML	-.206	.424	-.133	.610	-.085	.764	.423	.071	.094	.701

* $p \leq 0.05$ ** $p \leq 0.01$

Tabela 9. Regressão linear: cianose e perímetro cefálico são os principais preditores do desempenho cognitivo em adolescentes com cardiopatias congénitas.

Modelo	R	R^2	F	p	β	t	p
1	.408	.167	5,203	**.009**			
Perímetro Cefálico					.256	1,979	.053
Cianose					-.270	-2,086	**.042**

Apêndice II

Consentimento Informado

Termo de Consentimento Informado

Eu, _____, depois de ter sido integralmente informado dos objetivos e âmbito do Projeto de Investigação intitulado " Impacto do Desenvolvimento Fetal no Funcionamento neurocognitivo em Adolescentes com Cardiopatias Congénitas Cianóticas e Acianóticas", declaro que aceito participar neste estudo.

Além de ter sido garantida a confidencialidade dos dados recolhidos, fui também informado de que, em caso de não aceitar participar neste projeto, não ocorrerão quaisquer consequências na minha assistência médica habitual.

Porto, _____de _____ de 201 _

Assinatura: _____

Apêndice III

Ficha de Identificação

Ficha de Identificação

Código: ____ Data: ____

Nome: _____

Morada: _____

Localidade: _____ Telefone: _____ Telemóvel: _____

Nome da mãe: _____

Nome do pai: _____

Idade: _____ Data de Nascimento: ___/___/___ Nacionalidade: _____

Estado Civil: _____ Agregado Familiar: _____

Fratria: _____ Sexos: __ Masculino __ Feminino Idades: _____

Nível Escolar: _____ Profissão: _____

<u>Diagnóstico</u>

Cardiopatia: _____

Idade de Diagnóstico: _____

Terapêutica Médica: _____

Intervenção Cirúrgica: __ Sim __ Não Tipo de intervenção: _____

Perímetro Cefálico: _____

Comprimento: _____

Peso: _____

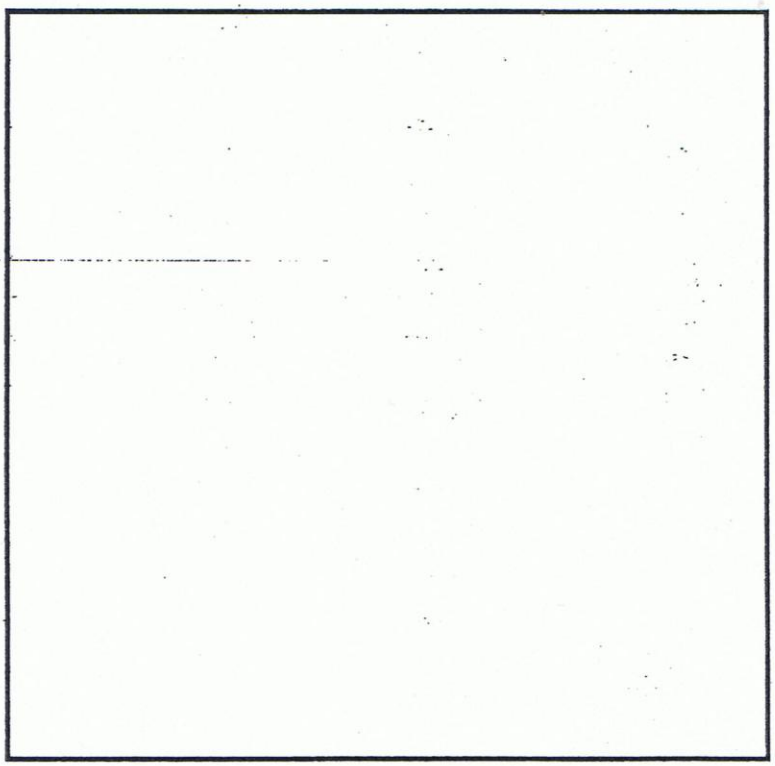
Apgar: (1) ____ Apgar (2) ____

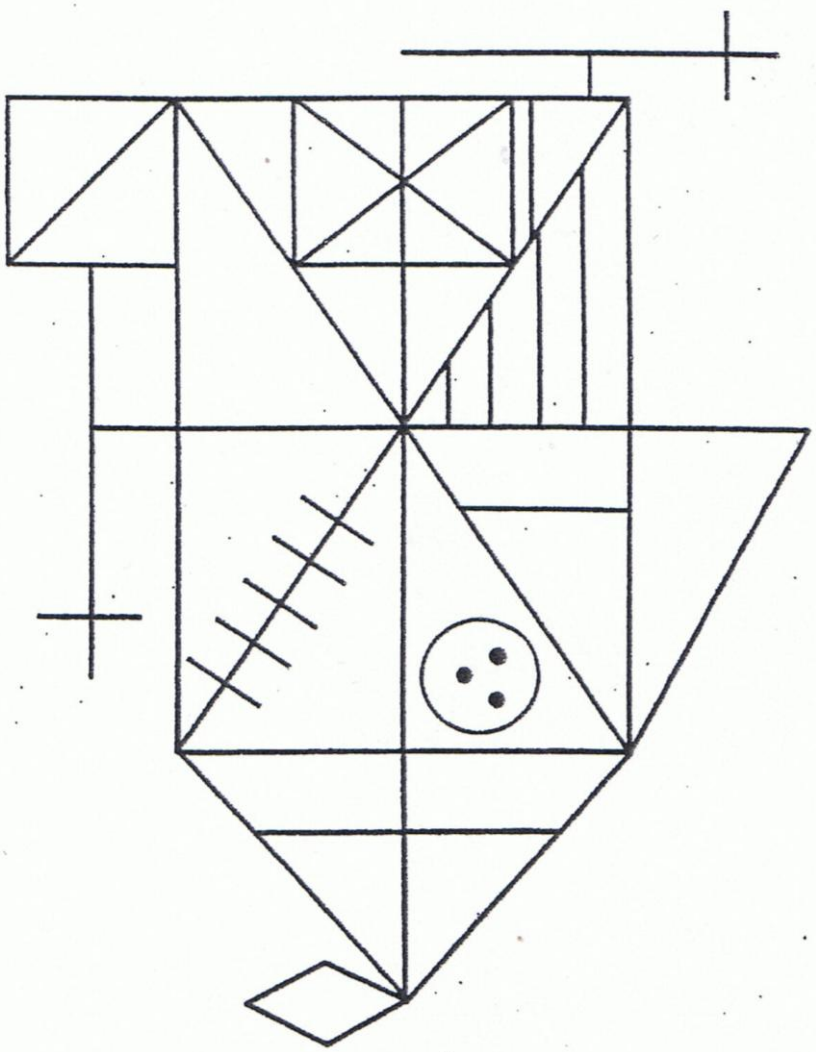
Apêndice IV

Instrumentos de Avaliação

Key Search Test

Subject's name





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VERMELHO	VERDE	VERDE	AZUL	AZUL
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VERMELHO	VERDE	AZUL	VERMELHO	VERDE
VERDE	VERMELHO	VERDE	AZUL	AZUL
VERMELHO	AZUL	VERMELHO	VERDE	VERMELHO
VERDE	VERMELHO	VERDE	AZUL	VERDE

B

Exemplo

2	1	4	6	3	5	2	1	3	4	2	1	3	1	2	3	1	4	2	6	3

1	2	5	1	3	1	5	4	2	7	4	6	9	2	5	8	4	7	6	1	8

7	5	4	8	6	9	4	3	1	8	2	9	7	6	2	5	8	7	3	6	4

5	9	4	1	6	8	9	3	7	5	1	4	9	1	5	8	7	6	9	7	8

2	4	8	3	5	6	7	1	9	4	3	6	2	7	9	3	5	6	7	4	5

2	7	8	1	3	9	2	6	8	4	1	3	2	6	4	9	3	8	5	1	8

11. Pesquisa de Símbolos

Interromper após 120 segundos

	6-7 Parte A	8-16 Parte B
Tempo limite	120"	120"
Tempo Despendido		
Nº de itens correctos		
Nº de itens incorrectos		
Pontuação Total Obtida (máximo = 45)		

12. Memória de Dígitos

Administrar ambos os ensaios de cada item, inclusive quando o Ensaio 1 é bem sucedido
Interromper após 2 insucessos consecutivos
Administrar os Dígitos em Sentido Inverso inclusive quando o sujeito obteve uma pontuação de 0 nos Dígitos em Sentido Directo

Dígitos em Sentido Directo — Tentativa de Início	Ensaio 1 / Resposta	Cotação	Ensaio 2 / Resposta	Cotação	Pontuação final 0, 1
1	2 - 9		4 - 6		
2	3 - 8 - 6		6 - 1 - 2		
3	3 - 4 - 1 - 7		6 - 1 - 5 - 8		
4	8 - 4 - 2 - 3 - 9		5 - 2 - 1 - 8 - 6		
5	3 - 8 - 9 - 1 - 7 - 4		7 - 9 - 6 - 4 - 8 - 3		
6	5 - 1 - 7 - 4 - 2 - 3 - 8		9 - 8 - 5 - 2 - 1 - 6 - 3		
7	1 - 6 - 4 - 5 - 9 - 7 - 6 - 3		2 - 9 - 7 - 6 - 3 - 1 - 5 - 4		
8	5 - 3 - 8 - 7 - 1 - 2 - 4 - 6 - 9		4 - 2 - 6 - 9 - 1 - 7 - 8 - 3 - 5		
				Total Dígitos em Sentido Directo (máximo = 16)	

Dígitos em Sentido Inverso — Tentativa de Início	Ensaio 1 / Resposta	Cotação	Ensaio 2 / Resposta	Cotação	Pontuação final 0, 1
Exemplo.	5 - 2		Exemplo: 5 - 6		
1	2 - 5		6 - 3		
2	5 - 7 - 4		2 - 5 - 9		
3	7 - 2 - 9 - 6		8 - 4 - 9 - 3		
4	4 - 1 - 3 - 5 - 7		9 7 - 8 - 5 - 2		
5	1 - 6 - 5 - 2 - 9 - 8		3 6 - 7 - 1 - 9 - 4		
6	8 - 5 - 9 - 2 - 3 - 4 - 2		4 - 5 - 7 - 9 - 2 - 8 - 1		
7	6 - 9 - 1 - 6 3 - 2 - 5 - 8		3 - 1 - 7 9 - 5 - 4 - 8 - 2		
				Total Dígitos em Sentido Inverso (máximo = 14)	

Pontuação Total Obtida (máximo = 30)

13. Labirintos

Interromper após 2 insucessos consecutivos, excluindo o Labirinto 1. Aos sujeitos com idades entre 8 anos administrar os Labirintos 1 a 3 em caso de insucesso ou sucesso parcial no Labirinto 4. Caso o su obtenha 0 pontos no Labirinto 4, fazer a demonstração do Labirinto Exemplo e administrar os Labir 1 a 3.

	Labirintos	Tempo Limite	Tempo Despendido	Número de erros	Cotação Rodear com um círculo a pontuação obtida.	Pontu
6-7	Exemplo					
	1	30"			2+ erros 0 / 1 erro 1 / 0 erros 2	
	2	30"			2+ erros 0 / 1 erro 1 / 0 erros 2	
	3	30"			2+ erros 0 / 1 erro 1 / 0 erros 2	
8-16	4	30"			2+ erros 0 / 1 erro 1 / 0 erros 2	
	5	45"			2+ erros 0 / 1 erro 1 / 0 erros 2	
	6	60"			2+ erros 0 / 1 erro 1 / 0 erros 2	
	7	120"			3+ erros 0 / 2 erros 1 / 1 erro 2 / 0 erros 3	
	8	120"			4+ erros 0 / 3 erros 1 / 2 erros 2 / 1 erro 3 / 0 erros 4	
	9	150"			4+ erros 0 / 3 erros 1 / 2 erros 2 / 1 erro 3 / 0 erros 4	
	10	150"			5+ erros 0 / 4 erros 1 / 3 erros 2 / 2 erros 3 / 1 erro 4 / 0 erros 5	

Pontuação Total Obtida

Recomendações para o subteste Labirintos (ver Capítulo 6 do Manual) (máximo = 28)

As seguintes recomendações podem ser fornecidas, caso sejam necessárias, mas cada uma delas só poderá ser feita uma vez no decurso da administração do subteste

1 "*Deves começar aqui.*" (apontar para o centro do quadrado)
2 "*Não podes passar através de uma parede.*"
3 "*Não pares. Continua até encontrares a saída. Podes voltar para trás*
4 "*Não começes outra vez. Continua a partir daqui* (apontar para o ponto atingido) *e tenta encontrar o caminho certo para saires.*"

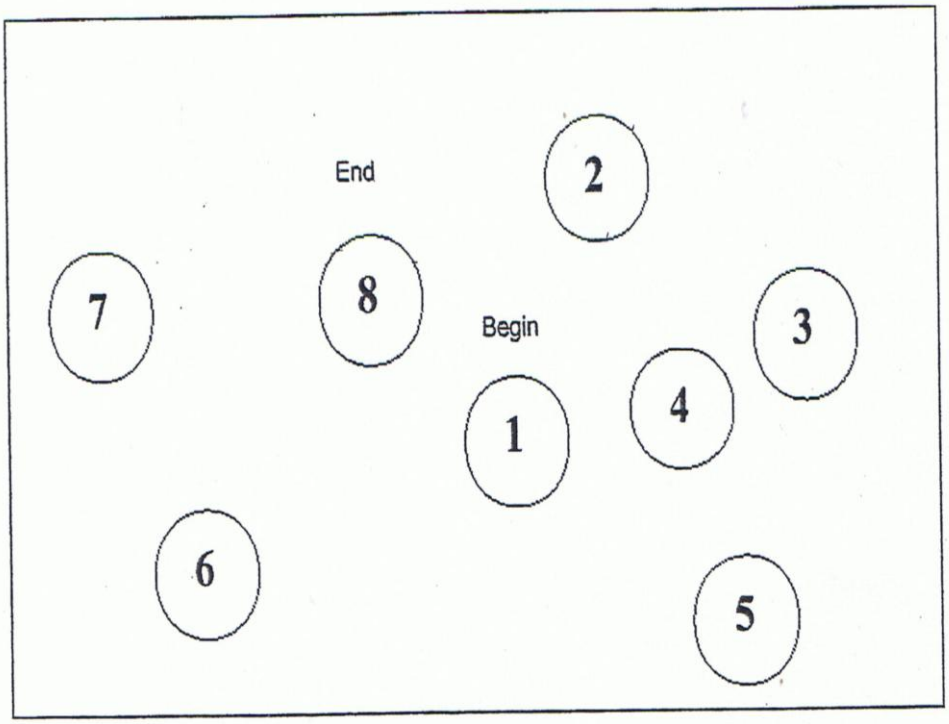
Nome ..... *Data* .....

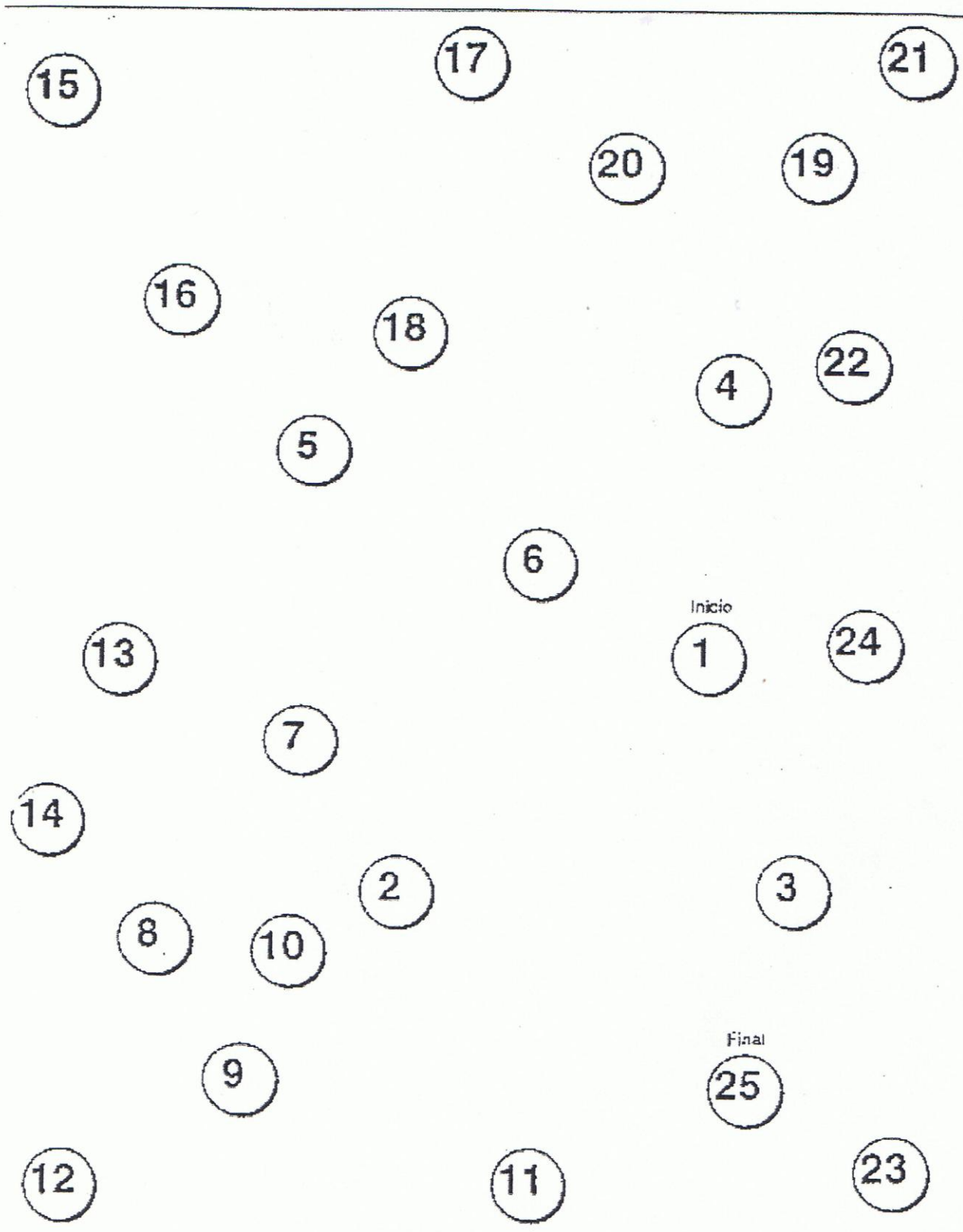
WISC-III PT

Escala de Inteligência de Wechsler para Crianças - Terceira Edição

ISBN: 972-8817-01-0

Trail Making Test Part A – *SAMPLE*

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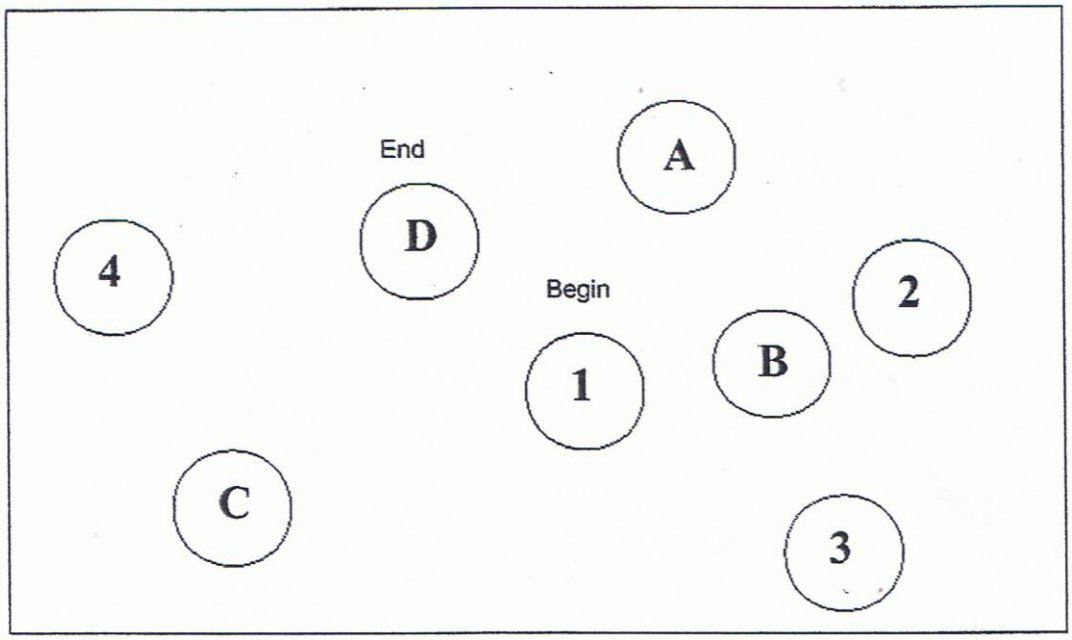
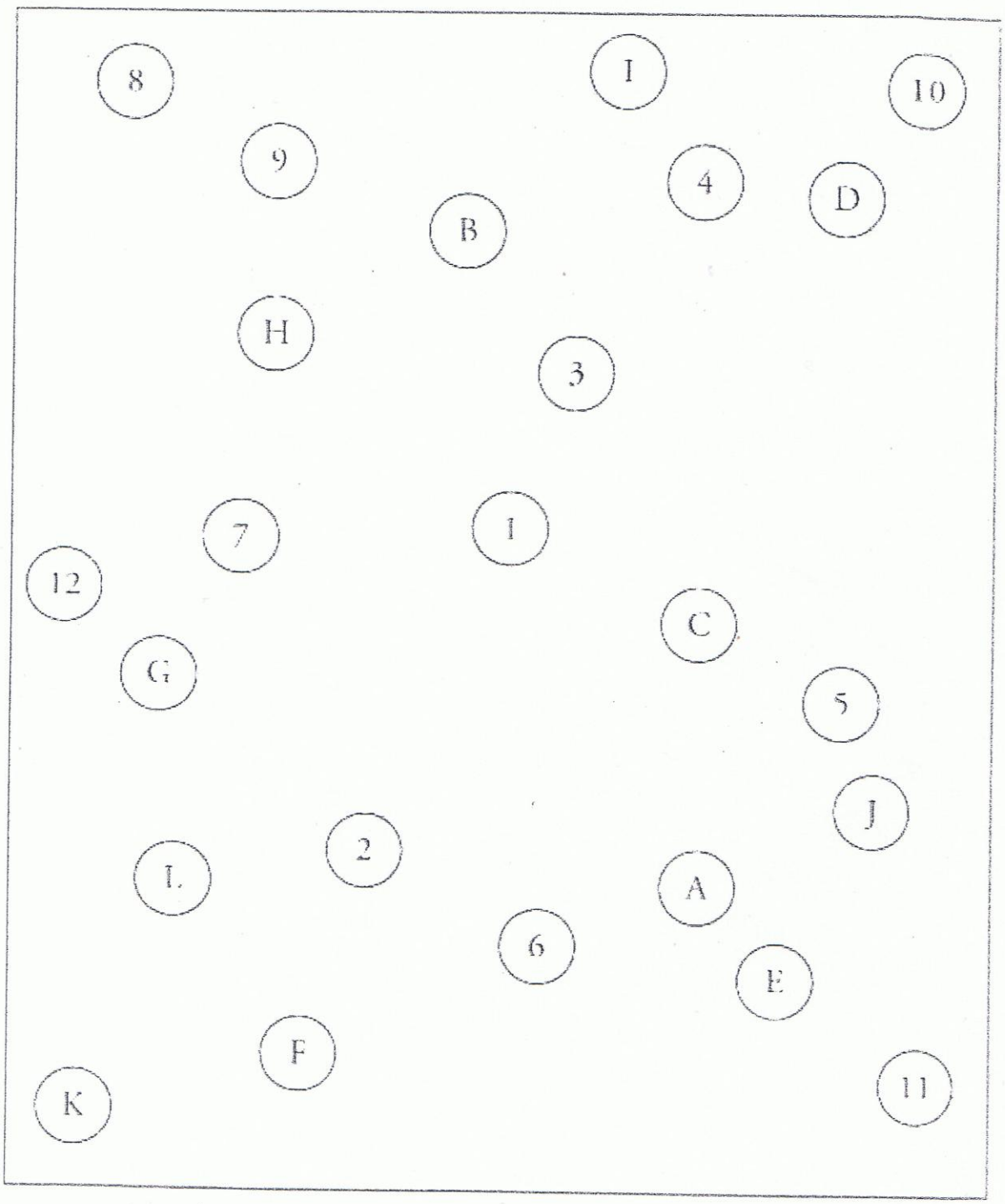
Trail Making Test Part B – *SAMPLE*

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2 Memória Lógica I

Registo:
Assinalar (✓) cada Unidade de História literalmente evocada. Em cada Unidade de História, registar as respostas não literais.

Cotação:
0 ou 1 ponto por cada unidade, de História ou Temática. Consultar os critérios de cotação descritos no Manual de Administração e Cotação (Capítulo 4 e Anexo A).

História A

Maria Lopes, que vive no Lumiar em Lisboa e que trabalha como cozinheira no refeitório de uma escola, queixou-se na esquadra da polícia de ter sido assaltada na Avenida da Liberdade, na noite anterior, e de lhe terem roubado cinquenta e seis euros. Tinha quatro filhos pequenos, a renda por pagar e não comiam há dois dias. A polícia, comovida com a história desta mulher, organizou um peditório em seu favor.

História A	Cotação: Unidade de História		Cotação: Unidade Temática		Critério de Cotação
Maria	0	1			É necessário referir *Maria*.
Lopes,	0	1			É necessário referir *Lopes*.
que vive no Lumiar	0	1			*Lumiar* (em qualquer contexto).
em Lisboa	0	1			*Lisboa* (em qualquer contexto).
			0	1	Indicação de que a protagonista é do sexo feminino.
e que trabalha	0	1			Indicação de que tem um trabalho.
como cozinheira	0	1			É necessário referir *cozinheira*, ou outra forma da palavra.
no refeitório	0	1			É necessário referir *refeitório* ou sinónimo.
de uma escola,	0	1			É necessário referir *escola* ou sinónimo.
			0	1	Indicação de que a protagonista está empregada ou a trabalhar.
queixou-se	0	1			Indicação de que foi feita uma queixa formal à autoridade (em qualquer contexto).
na esquadra	0	1			*Esquadra* (em qualquer contexto) ou uma palavra ou frase que indique que é uma esquadra da polícia.
da polícia	0	1			*Polícia* (em qualquer contexto).
de ter sido assaltada	0	1			Indicação de que foi assaltada.
na Avenida da Liberdade,	0	1			Na *Avenida da Liberdade* (em qualquer contexto).
na noite anterior,	0	1			Indicação de que o assalto ocorreu na noite anterior.
e de lhe terem roubado	0	1			Indicação de que foi roubada.
cinquenta e seis euros.	0	1			Indicação de um valor em dinheiro superior a 49 e inferior a 60 euros.
			0	1	Indicação de que a protagonista queixou-se de ter sido roubada.
Tinha quatro	0	1			É necessário referir o número *quatro*, juntamente com a indicação de que as crianças eram suas.
filhos pequenos,	0	1			É necessário referir *filhos pequenos* ou sinónimos.
			0	1	Indicação de que a protagonista tem filhos.
a renda por pagar	0	1			Uma frase indicando que tem a renda de casa por pagar.
e não comiam	0	1			Indicação de que as crianças ou família estavam sem comer (sem comida).
há dois dias.	0	1			É necessário referir *dois dias*, ou uma frase que indique cerca de dois dias.
			0	1	Indicação de que as personagens encontram-se necessitadas e precisam de ajuda.
A polícia,	0	1			Uma palavra ou frase indicando um ou mais elementos da polícia (em qualquer contexto).
comovida com a história desta mulher,	0	1			Indicação de que a sua história provocou empatia nos outros.
			0	1	Indicação de que a polícia se comoveu com a história da mulher.
organizou um peditório	0	1			Uma frase indicando que houve recolha de dinheiro.
em seu favor.	0	1			Indicação de que o dinheiro era para a mulher e/ou para os seus filhos.
			0	1	Indicação de que a polícia respondeu de imediato/directamente às necessidades da protagonista.

História A
Pont. Evocação Unid. História
Mínimo = 0 Máximo = 25

História A
Pont. Evocação Unid. Temáticas
Mínimo = 0 Máximo = 7

Apêndice V

Normas para submissão do Artigo à revista

"Journal of Congenital Heart Disease"

Journal of Congenital Heart Disease

Manuscript format

Manuscripts must be submitted in .doc or .rtf file format. Make sure all text is double-spaced with a ragged right margin. All textual elements should begin flush left with no paragraph indents. Please use one space between each paragraph and two spaces between sections of text. Be sure to keep a back up copy of the file for reference, as accepted manuscripts are not returned.

There are no restrictions on the length of any article type. If the article is of interest to the editors but is deemed to be too long, cuts will be requested in a revision.

Please arrange your text and other elements in the following order:

Title Page

The title page should be the first page of the manuscript text document and contain all the following:

- Title and short title
- Full names and affiliations for all authors, including the highest academic degree
- Full postal address, telephone number, fax number, and e-mail address for the corresponding author, to whom the proofs will be sent
- Conflict of Interest statement
- Disclosure of grants or other funding

*Authors***:** Names department(s) and institution(s) of all authors. Credit for authorship should be based on: [1] substantial contributions to research design, or the acquisition, analysis or interpretation of data; [2] drafting the paper or revising it critically; [3] approval of the submitted and final versions. Authors should meet all three criteria.

*Corresponding author***:** Name, address, email address, telephone and fax numbers. (Corresponding author should take responsibility for communicating with all other authors and getting their approval for the final version to be published. During online submission corresponding authors can nominate an individual, who may or may not be an author, to assist them with administration of the publication process.)

Abstracts and Keywords

The abstract, on the *page following the title page*, is required for all papers except a Letter to the Editor and must be 300 words or less. The abstracts for Case Reports, Reviews, and Commentaries should be unstructured. All other articles requiring an abstract should submit a structured abstract using the following headings, as appropriate: Objective, Design, Setting, Patients, Interventions, Outcome Measures, Results, and Conclusions (JAMA 1992;267:42–44). Up to six key words suitable for indexing must be provided with the abstract.

Body Text

Research papers should be structured as follows: Title page, as above; Abstract and keywords; Introduction; Methods; Results; Discussion; Acknowledgments (optional); Author Contributions; References; Tables; Figure legends (double-spaced); Figures.

Case Reports should be structured as follows: Title page, as above; Abstract and keywords; Introduction; Case presentation; Discussion; Acknowledgments (optional); Author Contributions; References; Tables; Figure legends (double-spaced); Figures.

Other articles: The above formats may be varied between the Introduction and Acknowledgments sections for other articles.

Details of Style: Follow guidelines set by *American Medical Association Manual of Style*, Ninth Edition, Lippincott Williams and Wilkins, 1998. Double-spaced throughout, including title page, abstract, text, acknowledgments, author contributions, references, legends for illustrations, and tables. Start each of these sections on a new page, numbered consecutively in the upper right-hand corner, beginning with the title page.

Drug names: Use generic names only in referring to drugs. If the trade name is necessary, e.g., in bio-availability studies, indicate it in parentheses.

Abbreviations: Keep abbreviations to the minimum, and define each at its first use. Do not use abbreviations in the abstract.

Author Contributions: All manuscripts must include a short description of each authors' contribution immediately before the References. (Examples of categories for authors' contributions: Concept/Design, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article, Statistics, Funding secured by, Data collection, Other.)

References: References for Congenital Heart Disease should follow the Vancouver (or numerical) system. Identify with Arabic numerals inside parentheses. A full list of references should be provided in numerical order, sequentially as they appear in the text. Do not alphabetize.

Use the *Index Medicus* reference style (see Uniform Requirements for Manuscripts Submitted to Biomedical Journals. *Ann Intern Med* 1988;108:258-65). For abbreviations of journal names, refer to *List of Journals Indexed in Index Medicus*. Provide names of all authors, full article titles and inclusive pages. Accuracy of reference data is the responsibility of the author.

Journal article:
1. Author AB, author CD. Title of paper. *J Title Abbrev* 1994;00:000–00.

Article in edited book:
2. Author AB, Author CD, Author EF. Chapter title. In: Editor AB, Editor CD, eds. Title of Book. Place: Publisher, 1994:000–00.

Book:
3. Author AB. *Book Title*, 5th edn. Place: Publisher, 1994.

Tables
Tables may appear at the end of the main manuscript document, or as a separate .doc or .rtf file. Each table must start on a new page. All tables should be double-spaced. Title all tables at the top, and number them in order of their citation in the text. Any notes should appear at the bottom of the table.

Apêndice VI

Co-Autora de um artigo submetido ao

American Heart Journal

Living with Congenital Heart Disease (CHD): Quality of life (QOL) in early adult life

Running Title: QOL of CHD patients in early adult life

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4 UNIPSA, Unidade de Investigação de Psicologia e Saúde, Gandra, Portugal
5 Unidade de Investigação Cardiovascular, Porto, Portugal
6 Faculty of Nutrittion, University of Porto, Portugal

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Key words: psychosocial adjustment; psychiatric morbidity; congenital heart diseases; quality of life; social support;

Ackowledgements:
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Abstract:

Aims: to assess the quality of life (QOL), psychiatric morbidity and the psychosocial adjustment (PSA) of adolescents and young adults with Congenital Heart Disease (CHD) and determine which variables play a role in buffering stress and promoting resilience and which ones have a detrimental effect; to investigate the situation on school performance and failures, social and family support, physical limitations and body image of these patients. **Methods:** The study enrolled 137 CHD patients (79 males), 12 to 26 years (M: 17.60 ± 3.450 years). The participants were interviewed regarding social support, family educational style, self-image, demographic information and physical limitations. They responded to questions in a standardized psychiatric interview (SADS-L) and completed self-reports questionnaires for assessment of QOL (WHOQOL-BREF) and PSA (YSR/ASR). **Results:** We found a 19.7% lifetime prevalence of psychopathology in our participants (27.6% in females and 13.9% in males). 48% had retentions in school (M=1.61 year $\pm$ 0.82). The perception of QOL of CHD patients is better compared to the Portuguese Population in the Social Relationships and Environmental Dimensions. However, is worse in complex forms of CHD than in moderate to mild ones, in cyanotic versus acyanotic patients, in moderate-to-severe versus mild residual lesions, in patients submitted versus those not submitted to surgery, in patients with versus without physical limitations, and patients who have versus those who haven't need for medication. Social Support is very important in improving QOL of patients in all dimensions as well as academic performance. **Conclusions:** Female patients and patients with poor academic performance and poor social support refer worse psychosocial adjustment and quality of life.

Introduction

Congenital heart disease (CHD) is defined as a malformation of the heart or the large blood vessels that develops during the fetal period. Clinically, it is classified as cyanotic or acyanotic based on the gradient of oxygen saturation in the blood [1,2].

Recent progress in early diagnosis and treatment has increased the life expectancy of patients with CHD. Today, 90% of newborns diagnosed with CHD live to adulthood, and this population is increasing at the rate of approximately 5% per year [3-6]. Advances in pediatric cardiac care have resulted in an increasing number of adults with CHD being followed up in tertiary care centers, fact that is generating interest in adult CHD on the standpoint of a new subspecialty of cardiology. The prevalence of CHD is changing all over the world and nowadays there are more adults affected with CHD than children[7].

As survival rates improve, psychosocial issues have emerged as a critical research area.

A prominent clinical concern is patient perception of quality of life (QOL)[8], psychosocial adjustment and psychiatric morbidity.

Evaluation of health-related quality of life is becoming increasingly important for patients with CHD in view of the increase of patients who survive. Quality of life is defined as a multi-dimensional construct integrating physical, emotional, and social well-being and functioning as perceived by the individual. [9,10]

To date, studies of QOL in CHD patients have reported contradictory findings. Some studies reported that poorer QOL is related to cardiac instability [11], disease severity [12,13], motor functioning and autonomy[14], although no differences were found for the variables of gender, age or marital status [11]. Some studies found poorer psychological well-being and QOL in CHD patients compared to healthy controls [15,16], while others claimed there was no difference between the two groups. Some researchers have reported that the

congenital nature of the disease leads CHD patients to have better QOL than healthy people [17,18].

Studies indicate that patients with CHD have persistent cardiac defects, a poor quality of life and psychosocial adjustment problems [19]. Moreover other studies indicate that individuals with CHD have a good psychosocial adaptation [20].

In the case of psychosocial adjustment, parents and partners tend to report more behavior and emotional problems than the patient himself.[20-22] Patients with CHD are considered to be at increased risk of psychological and emotional difficulties.[17,23] Thus, is very important to understand which variables have a detrimental effect in psychosocial adjustment and well-being of patients and which ones increase resilience and ability to adapt. The importance of our research was that it systematically addressed the question of which demographic or clinical variables have an impact over quality of life, psychosocial adjustment, or psychiatric morbidity.

Materials and methods

Participants

The study enrolled 137 CHD patients (79 males and 58 females) with a mean age: 17.60 ± 3.450 years (range:12-26 years old) who are followed in consultation in the Pediatric Cardiology or Adult Cardiology Departments of a tertiary hospital in Portugal. We excluded patients that had not achieved a basic educational level that enables to understand and complete the written questionnaires; we only included participants who had complete medical records.

At the time of the study, two participants were married, one was divorced, and two were living in a marital union. All the other participants were single (132). Of the all

participants, 20 were employed full- or part-time, 7 were unemployed, and all the others were students.

With regard to educational level, one completed the 4 first years in school, twenty the 6 first years, fifty-five the 9 first years, fifty-five completed the whole secondary education and six an university degree.

Patients' clinical files were provided by the department of Cardiology or Pediatric Cardiology. For 71 individuals, the congenital cardiac malformation was cyanotic, and for 66 patients, it was acyanotic. According to clinical files, at the time of diagnosis, 38 participants exhibited a severe form of CHD, 25 had a moderate form, and 74 had a mild form. As far as the residual lesions are concerned, 4 participants had severe residual lesions, 27 had moderate residual lesions, and 105 had mild residual lesions. The study also included the participation of 128 relatives.

The diagnosis was determined during the neonatal period for 73 of the participants, before the first birthday for 31, between the ages of 1 and 3 years for 5, between the ages of 3 and 6 years for 8 of the participants, between the ages of 6 and 12 years for 11 of the participants, and between the ages of 12 and 18 years for 9 of the participants. In several participants, the main CHD was combined with other heart diseases. Individuals with associated extra cardiac malformations or chromosomopathies were excluded from the study. Participants exhibited the following distribution of pathologies: Transposition of the Great Arteries (20 individuals; 4 also had Ventricular Septal Defect, 1 had Aortic Stenosis, 1 had Pulmonary Stenosis, and 2 had Coarctation of the Aorta), Tetralogy of Fallot (30), Coarctation of the Aorta (13, besides those 2 referred above), Ventricular Septal Defect (19, 1 also had Interrupted Aortic Arch, and another also had Mitral Insufficiency), Atrial Septal Defect (16 individuals; 1 had also Mitral Atresia and Pulmonary Hypertension), Atrioventricular Septal Defect (5), Aortic

Stenosis (8), Pulmonary Stenosis (13), Single Ventricle (2 individuals; 1 of these individuals also had Pulmonary Atresia, and 1 had Pulmonary Stenosis), Patent Ductus Arteriosus (2), Double Outlet Right Ventricle (1), Ebstein Anomaly (3), and Pulmonary Atresia (5). For participants who underwent surgery (103), the first surgery was performed during the neonatal period for 6, before the first birthday for 35, between the ages of 1 and 3 years for 19, between the ages of 3 and 6 years for 21, between the ages of 6 and 12 years for 11 of the participants, between the ages of 12 and 18 years for 10 of the participants, and after of 18 years for 1 of the participants.

One or more of the following psychiatric disorders had been diagnosed for 27 of the participants (19, 7%) before the interview: minor or major depressive syndrome (n=14), panic disorder (n=3), anxiety disorder (n=6), or manic syndrome (n=3), and cyclothymic personality (n=1).

Assessment Instruments

The subjects were interviewed on only one occasion. A complete clinical history and demographic information were collected in a questionnaire (e.g., diagnosis, severity and category of CHD, course of illness, surgeries, presence of residual lesions, and treatment with medication) and demographic information (e.g., marital status, educational level, and occupation).

The participants also responded to a semi structured interview covering topics such as social support, family educational style, environment, self-image, functional limitations, educational background, and emotional adjustment.

A standardized psychiatric interview (SADS-L) was administered to obtain a clinical diagnosis of any psychopathologic disorders that may have existed prior to the interview. The participants completed self-report questionnaires like WHOQOL-BREF

for assessment of their QOL, and YSR or ASR for assessment of psychosocial adjustment (PSA). One of their caregivers completed an observational version of the same questionnaires (CBCL or ABCL, according to the age of patients).

The WHOQOL-BREF is a self-report questionnaire that assesses subjective QOL in both healthy individuals and those with wide range of psychological and physical disorders. It is a 26-item Likert-type scale with ratings from 1 to 5. For almost all the scale items, higher scores reflect a higher QOL. However, for three items (questions 3, 4, and 26), higher scores reflect a lower QOL. The first two questions of the instrument assess general QOL. The WHOQOL-BREF also assesses four dimensions of QOL: physical (questions 3, 4, 10, 15, 16, 17, and 18), psychological (questions 5, 6, 7, 11, 19, and 26), social (questions 20, 21, and 22), and environmental (questions 8, 9, 12, 13, 14, 23, 24, and 25).

YSR or ASR are self-report questionnaires that assess behavior problems of youth or adults in the last 6 months. It is 112-item Likert-type scale for youth (YSR) and 123–item for adults (ASR) with ratings from 0 to 2. Items on the scale of youth are grouped into eight syndromes: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. Items on the scale of adults are grouped into eight syndromes: Anxious/Depressed, Withdrawn, Somatic Complaints Thought Problems, Attention Problems, Aggressive Behavior, Rule-Breaking Behavior and Intrusive.

Procedure

Prospective participants were contacted before or after scheduled hospital appointments. The subjects were asked to participate after being fully informed of the objectives and procedures of the investigation. Those who agreed completed an informed consent form

approved by the hospital's ethical committee, which followed international conventions guaranteeing the rights of the patients.

Design

All the assessment measures were obtained on a single occasion. Clinical data were collected retrospectively using each patient's clinical record, with assistance from hospital medical staff.

Methods of Statistical Analysis

Statistical analyses of the data were performed using the IBM Social Package for the Social Sciences (SPSS), version 20.0 (SPSS, Chicago, IL, USA). The distribution of all the variables was tested. Differences for parametric variables were established using Student's t-tests, and differences for nonparametric variables were established using Mann–Whitney U tests and Chi-square tests of association.

Results

We found a 19.7% lifetime prevalence of psychopathology (27.6% in females and 13.9% in males).

48% of our participants had retentions in school (M=1.61 year $\pm$ 0.82).

There were no significant differences in QOL for presence/ absence of psychiatric diagnosis. However, QOL (Physical dimension: t= -2.926; p= 0.004) is worse in complex than in moderate-to-mild forms of the CHD as well as PSA, with patients exhibiting more internalization problems (u= 1310.000; p= 0.019) and more delinquent behavior (u= 1435.000, p= 0.042). Cyanotic patients, compared to acyanotic, have

worse QOL on Physical (t= -2.575; p= 0.011) and Environmental (t= -3.149; p= 0.002) dimensions.

Patients with moderate-to-severe residual lesions had worse perception on QOL than those with mild lesions, in the Physical dimension (t= -2.379; p= 0.019). These patients also show worse psychosocial adjustment, with more somatic complaints (u=525.500; p=0.039) and internalization problems (u=1217.000; p=0.035).

Female patients refer more somatic complaints (u= 590.500; p= 0.007), more feelings of anxiety/ depression (u= 1566.000; p= 0.002), thought problems (u= 1578.500; p= 0.001), aggressive behaviors (u= 1552.500; p= 0.001), internalization (u= 1296.000; p= 0.000), and externalization (u= 1724.500; p= 0.049) problems in PSA scales. They also show worse QOL on Environmental dimension (t= 2.856; p= 0.05).

The perception of QOL of CHD patients is better than in the Portuguese population as a whole in the Social Relationships and Environmental Dimensions, but not in the Physical Dimension. (Table 1)

Table 1. Comparison between reference values and the values presented by the participants in quality of life.

Dimensions	**Reference Values ***	**Participants of our study**	**t**	**p**
Physical	M = 77.49 DP = 12.27	M = 66.69 DP = 13.72	-15.053	**0.000**
Psychological	M = 72.38 DP = 13.50	M = 70.72 DP = 12.06	-2.562	0.100
Social relationships	M = 70.42 DP =14.54	M = 75.20 SD = 15.33	3.540	**0.001**
Environmental	M = 64.89 DP = 12.24	M = 73.16 SD = 13.14	5.768	**0.000**
General QOL	M = 71.51 DP = 13.30	M = 73.83 DP = 14.14	1.234	0.107

* For the Portuguese population as a whole

Patients submitted to surgery (N=103) have worse perception of QOL, on the Physical (t= -3.202; p= 0.002), Psychological (t= -2.949; p= 0.004) Social Relationships (t= -1.982; p= 0.049) and General Dimensions (u= 1269.000; p= 0.011) than those who were not operated (N=34). Those submitted to more than two surgeries have also worse QOL, on Physical (t= -3.541; p= 0.024) Psychological (t= -2.145; p= 0.014) and general dimensions (u= 1659.500; p=0.004). In the assessment of Psychosocial Adjustment, they also show higher scores in withdrawn behaviors (u=1335.000; p=0.036), attention problems (u= 1262.000; p= 0.014) and externalization problems (u=1209.500; p= 0.032).

Patients with physical limitations (N= 44) showed a worse perception in Physical (t= -3.123; p= 0.002), Psychological (t= -2.902; p= 0.004) and General QOL (u= 1532.000; p= 0.012) than those without PL (N= 93). They also have more withdrawn behavior (u=1454.000; p=0.006), anxiety/ depression (u=1499.500; p=0.011), delinquent behavior (u=1586.500; p=0.032) and internalization problems (u=1435.000; p=0.016).

Patients with need for medication show worse QOL only in Physical dimension (t= -2.252; p= 0.026) than those who are not medicated.

Participants with better academic performance showed better QOL on Psychological (t= 2.454; p= 0.015), Environmental (t= 2.577; p= 0.011) and General dimensions (u= 1351.000; p= 0.015). Those with poor academic performance show worse psychosocial adjustment, with more feelings of anxiety and depression (u=1312.500; p=0.013), more attention problems (u=1171.500; p=0.001) and more externalization problems (u=1190.500; p= 0.005).

Social Support is very important in improving QOL of patients in all dimensions. (Table 2) Participants with poorer Social Support show also more withdrawn behavior (u= 781.000; p= 0.000) and more social problems (u= 1011.000; p= 0.010) in PSA scales.

Table 2. Comparison of the perception of social support (more or less social support) in the various dimensions of quality of life.

	More SS (N = 109)		Less SS (N = 28)			
Dimensions	**M**	**SD**	**M**	**SD**	**t**	**p**
Physical	26.08	3.818	24.07	3.558	2.520	**0.013**
Psychological	23.28	2.815	21.79	2.948	2.474	**0.015**
Social relationships	12.28	1.689	11.00	2.073	3.420	**0.001**
Environmental	31.89	4.038	29.54	4.293	2.703	**0.008**
	M	**SD**	**M**	**SD**	**U**	**p**
General QOL	8.07	1.100	7.12	1.236	949.000	**0.001**

Discussion

Individuals with CHD has been increasing in adult population all over the world due to advances in early diagnosis and medical and surgical treatment [7]. Thus, the contribution of our research is important because we tested the effects of different demographic, clinical, and psychosocial variables on the perception of QOL, on psychosocial adjustment and psychiatric morbidity of CHD patients. To our knowledge, no other published study before studied so many variables as we had.

To determine the extent to which these factors enhanced resilience or had a detrimental effect on individuals with CHD, we analyzed factors such as severity of illness, number of surgeries, presence of residual lesions, presence of cyanosis, occurrence of

psychopathologic disorders, education and academic achievement, size and functioning of the social support network, and physical abilities and limitations.

An intriguing finding of our study, however confirming data from other authors, is that CHD patients in the whole perceive in a better way their quality of life than the healthy population. [17, 18] That fact may be explained by the presence of some buffer variables, like family environment and cohesion, and social support.

However, when we look the different subgroups, we find that patients submitted to surgery show a worse perception on their quality of life than the whole group. These facts, more expected, may be explained by the daily life restrictions and residual side effects that limit physical performance and activity, and by the feeling of life threat and fragility, occurring in surgeries.

The comparison between cyanotic and acyanotic patients and those with moderate-to-severe or those with mild residual injuries show also a worse perception on quality of life. Complex CHD show a worse psychosocial adjustment and quality of life than moderate-to-mild forms of disease, as well.

In the literature the predictors of behavioral and emotional problems pointed are being female, having low exercise capacity, having restrictions imposed by physicians, the type of heart lesion, underwent surgery in early infancy, and a greater number of heart operations.[25-26] In this study for Psychosocial Adjustment, we found that being female, have poor academic performance, have a complex form of CHD, have moderate-to-severe residual lesions, are submitted to surgery and have physical limitations are a predictors.

The results of this study suggest that was 19.7% lifetime prevalence of psychopathology. In the others studies, the younger patients showed more psychopathology than the older patients.[23,24] On the other hand, studies on the level of

psychopathology in congenital heart disease adults show conflicting results, varying from elevated levels of psychopathology to levels similar to those of peers.[28, 29]

In Portugal, there are no final data on psychiatric morbidity nationwide, although some estimation on the prevalence of psychiatric disorders in the general population could be made on the basis of partial studies.[30] Referring to those findings, we may say that CHD patients seem to show a slightly increased proneness to psychopathology.

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Apêndice VII

Resumo submetido e aceite para poster no 46th Annual Meeting of the "*Association for European Paediatric and Congenital Cardiology (AEPC)*"

Impact of fetal development on neurocognitive performance of adolescents with cyanotic and acyanotic congenital heart disease (CHD)

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Purpose: Our aim was to evaluate the neurocognitive performance in adolescents with CHD and to determine whether parameters of fetal development evaluated in neonates, such as head circumference, length, weight and Apgar scores, are somehow related to their neurocognitive performance.

Methods: 77 CHD patients (43 males) aged from 13 to 18 years old (mean=15.04 ± 1.86), 46 cyanotic (23 Tetralogy of Fallot, 23 Transposition of the Great Arteries) and 31 acyanotic (Ventricular Septal Defect) enrolled in this study. The control group included 16 healthy children (11 males) ages ranging from 13 and 18 (mean=15.69 ± 1.44). All assessment measures for CHD patients were once obtained in a tertiary hospital; the control group was evaluated in school. Demographic information and clinical history were collected. Neuropsychological assessment included Wechsler's

Digit Test, direct and reverse (WDD, WDR) and Symbol Search (WSS), Rey's Complex Figure (RCF), BADS`s Key Searching Test (BKS), Color-Word Stroop Test (CWS), Trail Making Test (TMT) and Logical Memory Task (LMT).

Results: CHD patients compared to control group showed lower scores in WDD (u=262.500; p<0,001) and WDR (u=166.500; p<0.001) versions, in RCF, copy (u=152.500; p<0,001) and memory (u=149.000; p<0.001), in WSS (u= 380.000; p=0.042), in BADS`s Key Searching Test (u= 160.500; p<0.001) in CWS, words (u=147.000; p<0.001), colors (u=225.000; p<0.001) and interference (u=133,500; p<0.001) in TMT, A (u=91.500; p<0.001) and B (u=130.500; p<0.001) and in Total Performance (u=51,000; p<0.001). Cyanotic patients, when compared to acyanotic, showed lower scores in all neuropsychological tasks, although the only differences that were significant were in RCF, copy (u=935.500; p=0.020), memory (u=989.000; p=0.004) in CWS, interference (u=903,000; p=0.048). Several correlations were apparent between fetal/ neonatal parameters and neuropsychological abilities in each type of CHD. However, head circumference at birth stands as a main correlation with cognitive development later on in all kinds of CHD (WDD: rho=0.339, p=0.011; RCF, copy: rho=0.297, p=0.027; CWS, interference: rho=0.283, p=0.036; TMT A: rho=-0.321, p=0.017; LMT: rho=-0.263, p=0.052).

Conclusion: Adolescents with CHD have worse neuropsychological performance than the control group, mainly the cyanotic patients. Fetal circulation seems to have impact on cerebral and somatic growth, predicting cognitive impairment in adolescents with CHD.