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ORIGINAL ARTICLE

Comparative study of neupsychological functions in preterm and term childrens at eight years old

Estudio comparativo de funciones neuropsicológicas a los 8 años de niños prematuros y nacidos de término

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Abstract

Introduction: Monitoring of extremely preterm infants of school age reveals poor development of neuropsychological functions, compared to their full term peers. **Objective**: To compare the neuropsychological functions of schoolchildren with history of extreme prematurity and full term children of the same age. **Patients and Method**: Non-experimental, cross-sectional research. Forty-three preterm children who born weighting less than 1,500 g and/or less than 32 weeks of gestational age and a control group made up of forty full-term children, classmates of the sample group were included. Both groups had no diagnosis of neurological, sensory or cognitive disability. Parents signed informed consent forms and data were collected through the Child Neuropsychological Assessment-ENI2, which considers 14 items: construction skills, memory, Perceptual skills, language, metalinguistic skills, reading, writing, arithmetic, skills spatial, attention, conceptual skills, fluency, cognitive flexibility and planning. Data obtained were analyzed with Kruskal-Wallis test, establishing significance level at $p < 05$. **Results:** Research findings partially agree with problems reported in the literature. In general, a lower standard score was observed at lower gestational age. There were significant differences in subtests of graphical skills, auditory perception, auditory attention, and cognitive flexibility. **Conclusions**: Children with history of extreme prematurity who participated in this research showed a variety of deficits in neuropsychological functions, although their performance, as well as that of the control group, is disharmonic, with high scores in some items and low ones in others.

Keywords:
Extreme prematurity; neuropsychological functions; schoolchildren; preterm infants

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Introduction

Growth alterations seen in children with history of extreme prematurity (EP) have been widely studied in developed countries. Approximately 10% of these children may grow with significant neurological deficits and 25-50% of them may present cognitive, motor, behavioral and academic problems at preschool and school age[1,2]. The incidence and severity of these consequences increase as the gestational age decreases and interfere at different levels in the development of social skills and the normal school performance, which may last into adolescence and early adulthood. It has been suggested that the neuromotor difficulties in extremely preterm infants have decreased in recent decades, while their cognitive and perceptual problems have increased[3].

Among the cognitive factors that can be affected by the EP are the neuropsychological functions (NPF), those related to the cerebral organization of the cognitive behavioral activity (memory, visuospatial skills, perceptual skills, attention, executive functions, and language, among others). The executive functions (EF), in turn, include inhibition, working memory, planning, fluency and cognitive flexibility, which are interrelated processes that facilitate having a coherent and consistent plan for the achievement of specific goals.

Schoolchildren with history of EP perform significantly worse than their peers born at term when evaluating neuropsychological variables[4-6]. These children would have a worse performance than their peers born at term in memory assessments[7]; visual attention, visual-motor skill, designs copy, phonological processing[8]; visuospatial processing, and language[9]. EF assessment in EP children shows a lower performance than the control group in cognitive flexibility, but not in working memory and inhibition capacity[10]. In some studies, it has been found that premature children have similar results to term children in working memory but using different brain areas. Younger preterm children, with a lower performance, show atypical work styles, while older preterm children, with better performance, show work schemes similar to term children[11]. In the last years, it has been observed an improvement in the performance in EP children in cognitive and neuropsychological tests[8], however, newborns with lower gestation age did not necessarily obtain lower scores. It seems like there is a wide variability in the performance of these children depending on the interaction between prematurity level, medical complications, and environmental or social factors[12].

The data related to this topic are still insufficient in our sphere. Since the Guillermo Grant Benavente Hospital (GGBH) in Concepción, Chile, is a reference center for the care of extreme and very extreme premature children, it is appropriate to know the evolution of children who were born and received their first attention there. The objective of this research was to describe the neuropsychological functions in schoolchildren with history of extreme prematurity, who were born at the GGBH during 2006 and 2007 and to compare them with term children of the same age.

Patients and Method

Non-experimental, quantitative and correlational research with non-probabilistic sample. The following inclusion criteria for the study group were established: children born at the GGBH in 2006 and 2007 with less than 1,500grs of weight and/or less than 32 weeks of gestation at birth, residents in the Concepción or Arauco province, without neurological disability diagnosis that implies motor deficit, congenital or metabolic disease, and without sensory or cognitive deficits. These data were confirmed with the clinical records and information provided by the parents. During 2006 and 2007 it was recorded the birth of 143 children with less than 1,500grs of weight and/or less than 32 weeks of gestation. 23 of these children did not meet the inclusion criteria (18 of them had important neurological problems, cognitive or sensory deficit and five lived outside Concepción and Arauco). Out of the remaining 120 children, 47 were not located, 12 refused to participate and 18 agreed to participate but dropped out before concluding the evaluation process. The final sample consisted of 43 children (19 females and 24 males), residents in the Concepción province, average gestational age of 29.5 weeks (range 25-33 weeks, median 30 weeks), average weight 1,121.5 grs (range 620-1,880 grs, sd 294.9 grs). Out of these children, 35 (81.4%) had attended early stimulation programs in the physical medicine and rehabilitation service during their infant years. The sample was compared with a control group (40 patients), which met the following inclusion criteria: classmates of the sample members, of the same chronological age, gender, and socioeconomic status. Premature children, as well as those with a history of cognitive or sensory deficit or neurological disorders that imply motor deficit were excluded. These data were confirmed with the clinical records and information provided by the parents.

At the beginning of the process, an interview was conducted with the parents requesting the signature of an Informed Consent. The evaluation process was completed in three consecutive sessions. The data collection was performed through the Neuropsychological Assessment of Children 2 (ENI)[13] which assesses the neuropsychological characteristic of children between

five and 16 years of age. It includes the evaluation of 14 neuropsychological processes: constructional skills, memory, perceptual skills, language, metalinguistic skills, reading, writing, arithmetic, spatial skills, attention, conceptual skills, fluency, cognitive flexibility, and planning. It is possible to apply it totally or partially. For the purpose of this research, tests for cognitive and executive functions were applied since they determine factors that support or reduce the ability of the child to successfully participate in school activities, daily living, and activities of interest. The normative data of this instrument were obtained from its application in Mexican and Colombian children. It establishes a failure criteria standard score of 85 or lower. It includes guidelines to execute a qualitative performance evaluation of the patients, in parallel with the test itself.

According to the characteristics of the study, an analysis of the variance was carried out applying the Kruskal Wallis test, which established a p-value of 0.05. For the data analysis, the premature group was classified according to WHO classification as very extremely preterm (less than 28 gestation weeks – Group A, 11 subjects), extremely preterm (between 28 and 31 gestation weeks – Group B, 22 subjects), and late preterm (between 32 and 36 gestation weeks – Group C, 10 subjects).

Results

Table 1 shows the socio-demographic background of preterm and term children. There is a significant difference in the birth weight variable between group 1 and groups 2, 3 and 4. There is also a significant difference in the gestational age variable between group 1 and 2, and between group 2 and 4. No significant difference is observed in the variables level of education of the parents and children age at the time of the evaluation.

The average age of the sample group and the control group was eight years (range 7 years – 9 years 5 months) at the time of the evaluation. 74% of the children in the sample group and 63% of the control group began their education in kindergarten. Table 2 summarizes the global results. Group A achieved lower-than-normal scores in three sub-tests (auditory memory evocation, visual attention, and verbal fluency), and the Group B achieved low scores in two sub-tests (auditory memory evocation, and number of administered tests). Group C and D obtained standard scores in a normal range in all sub-tests; however, Group C had comparatively lower scores than Group D (control). An analysis of the parametric variance was performed for sub-tests of graphic skills, verbal fluency, and graphic fluency, where there was a significant difference (p – 0.0209) in graphic skills sub-tests between group A and B, and group A and D. An analysis of the non-parametric variance was performed for the remaining sub-tests, where there was a significant difference (value p – 0.042) in the auditory perception between group B and D, in the auditory attention (value p – 0.0282) between group B and D, and in the total amount of correct answers (value p – 0.0281) between group A and B, and B and D. However, in all cases the scores were in the normal range. There were no significant differences in those subtests in which groups A and B obtained average standard scores under normal range.

Table 1. Sociodemographic background

Parents educational level	Group A		Group B		Group C		Group D			
Education	n	%	n	%	n	%	n	%	p-value	Statistics
Elementary	1	9	4	18.1	-	-	4	10	0.828	Fisher
High school	5	45.5	8	36.4	6	60	12	30		
Graduate	5	45.5	10	45.5	4	40	24	60		
Total	11	100	22	100	10	100	40	100		

	Group A		Group B		Group C		Group D			
	Media	SD	Media	SD	Media	SD	Media	SD	p-value	Statistics
Birth weight	825.7	126.9	1.249.5	138.6	1.672.5	138.4	3.240.6	440.9	< 0.0001	Anova
Gestational age	27.8	1.9	30.6	2.1	30.3	2.5	38.6	1.4	< 0.0001	Kruskal Wallis
Children age (months)	102.6	11.6	97.8	7.8	98.8	11	84.4	36.5	0.4847	Kruskal Wallis

There is a significant difference in birth weigth variable between group 1 and groups 2, 3 and 4. There is also significant difference in gestational age variable between group 1 and group 2 and between groups 2 and 4. Not significant difference is observed in the variables parents educational level and children age at time of the evaluation.

Table 2. Test ENI Results

Test	Group A		Group B		Group C		Group D-Controls			
	Average	SD	Average	SD	Average	SD	Average	SD	Statistics	p-value
Cognitive functions										
Construction with chopsticks	100	15.6	95	8.8	92	10	101	16	K. Wallis	0.3218
Graphic Skills	**96***	18.5	**106***	9.8	105	12	**109***	10.9	Anova	**0.0209**
Auditory coding memory	86	22.3	86	19.7	88	15.2	90	17.0	K. Wallis	0.7311
Visual coding memory	90	12.7	94	14.4	101	17.1	99	15.9	K. Wallis	0.1418
Auditory evocation memory	80	24.1	82	21.5	88	19.5	93	23.1	K. Wallis	0.2202
Visual evocation memory	86	18.8	89	16	91	17.1	99	21.7	K. Wallis	0.0625
Tactile perception	92	12.2	91	11.4	90	14.1	96	8.7	K. Wallis	0.2209
Visual perception	111	11.2	116	10.3	109	9.1	118	12.2	K. Wallis	0.0661
Auditory perception	107	6.1	**101**$^{\alpha}$	19.7	106	12.6	**112**$^{\alpha}$	15.2	K.Wallis	0.0421
Spatial skills	97	17.1	98	12.7	102	14.9	103	13.8	K Wallis	0.3181
Visual attention	84	19.6	88	13.1	97	9.9	93	16.2	K. Wallis	0.0980
Auditory attention	93	14.8	**89**$^{\alpha}$	12.4	96	15.6	**100**$^{\alpha}$	16.4	K. Wallis	**0.0282**
Conceptual Skills	97	23.3	103	13.2	98	17.6	107	16.7	K. Wallis	0.2761
Executive functions									K Wallis	
Verbal fluency	82	11.9	93	13.7	93	7.1	90	11.5	Anova	0.0966
Graphic fluency	95	13.6	105	19	104	11.1	96	16.6	Anova	0.4192
Cognitive Flexibility - Number of trials administered	88	6.7	85	8.4	90	9.1	91	12.5	K. Wallis	0.4909
Cognitive Flexibility - Total of correct answers	**98***	11.5	**87**$^{\mu}$	12.5	96	14.4	**98**$^{\mu}$	13.3	K .Wallis	**0.0281**
Cognitive Flexibility - Correct answers averege	92	10.1	86	10.9	92	13.3	92	15.1	K. Wallis	0.1644
Cognitive Flexibility - Number of categories	99	10.4	98	13.9	100	10.7	101	10.8	K. Wallis	0.5314
Planning - correct designs	91	13.2	97	9.6	99	6.7	98	11.6	K. Wallis	0.2122
Planning - correct designs with minimal movement	100	15.0	97	10.2	95	16.3	101	13.3	K. Wallis	0.1674

(*) significant difference between group A and groups B and D, p-value = 0,0209. (α) significant difference between group B and group D, p-value = 0,0421. (α) significant difference between group B and group D, p-value = 0,0282. (μ) significant difference between group B and groups A and D, p-value= 0,0281.

Individually, seven children (67%) from group A, 13 (59%) from group B, five (50%) from group C, and 16 (40%) from group D had lower-than-normal scores in between three to ten sub-tests.

In a global appreciation, the average score decreases as the gestational age decreases, although with significant variability between groups when comparing sub-tests. The four groups coincided in low averages (although within normal range) in memory and auditory attention sub-tests. Group A had higher scores than group B and C in the sub-tests of stick construction, tactile perception, auditory perception, total amount of correct answers, percentage of correct answers, number of categories and correct designs with minimal movement.

The qualitative evolution of the ENI, regarding the evaluation of capacity of paying attention to a task, showed that 73% of the group A repeatedly showed between two to five behaviors suggestive of attentional lability (hyperactivity, making irrelevant associations, require task reformulation, provide impulsive answers, being impersistent, exhibit fatigue, and excessive talking), in comparison with group B (59%), group C (60%), and group D (33%).

Discussion

The results partially coincide with reviewed studies regarding neuropsychological functions[5,8]. Attention is emerging as an area with high deterioration. It is suggested[14] that from a neurological point of view, the attention would have three components: a warning system for the reception of stimuli, a system of spatial orientation towards stimuli, and an executive attentional system designed to organize the required brain areas to execute complex actions. The attention deficit shown by the premature group allows presuming that these children have difficulties in the three components of this process. Likewise, the memory shows a significant deficit. There is a close relationship between memory and attention. As a consequence of poor capacity of global attention, subjects will have limited memory capacities, which means a lower ability to retain and later use important information in a specific situation. This condition could affect the low performance compared to other reagents of the evaluation.

Likewise, these results match with published reports that indicate deficits in the EF. In our case, group A (extremely preterm) shows lower-than-normal scores in the verbal fluency sub-test, with a tendency towards lower scores as the gestational age diminishes. In line with the work of Ritter[10], there is a statistically significant difference in the cognitive flexibility subtest (total item of correct answers).

The EF have been defined[15] as "*those central regulatory skills that articulate basic procedures… in order to achieve flexibly an objective*". Among them are the planning, the inhibition of an irrelevant scheme and the change. The inhibition of an inefficient action leads to persisting. These abilities are important in the attention control, in the establishment and maintenance of an objective, and in the flexibility. This would allow understanding the difficulties demonstrated in the study group, given the limitations in attention previously described and considering that perseverance is one of the behavioral indicators of attentional lability, which appeared in the three groups during the evaluation process.

Although these results can be considered as evidence of deficits in extremely preterm and very preterm children in neuropsychological functions, the high standard deviations reported indicate a high heterogeneity in the performance of the groups, therefore it is not possible to establish in advance that the performance of the premature group is deficient. In an individual analysis, it was found that most of the subjects had normal scores in some items and very low scores in other ones. There are no differences related to the socioeconomic status, educational level or gender of the subjects. In the codification memory and auditory and visual evocation memory tests, as well as in auditory and visual attention tests, a high percentage of preterm and term children obtained low scores (although the average of the group is in the normal range).

Sub-tests where the significant differences were detected, did not show standard scores necessarily lower than normal. Both groups (premature and control) presented better scores in visual and auditory perception sub-tests and worse scores in memory and attention sub-tests.

The obtained results allow proposing that effectively the minor neurological sequelae in EP children have decreased as consequence of the preterm follow-up program of the Ministry of Health, monitoring by specialists, and the subsequent referral to specific therapies. Even so, it is important to increase the knowledge regarding the performance of premature children and to perform a specific follow-up not only of their medical condition throughout childhood but also the rate of acquisition of the skills under study. This report is a contribution to the knowledge of a subject that is still insufficiently analyzed in our sphere and which needs to be studied in greater depth given the increase of preterm births. Due to the incidence of neuropsychological functions in the functional performance of the subjects, learning, school performance, and overall quality of life, it is relevant to investigate these topics in the preschool and school population of our region, particularly in those patients from rural areas. The next step in this work line should lead to preventive strategies or corrective proposals in order to decrease the future percentage of neuropsychological deficits, mainly in attention and memory, in the studied group. Limitations of this study are the small sample (36% of those born in the period and who met the inclusion criteria), children from rural areas did not participate, high dispersion of the data, and the fact that the evaluators knew which evaluated child was term or preterm.

Conclusions

Children with history of prematurity, who participated in the research, show a variety of neuropsychological functions deficits, despite the fact that their performance is disharmonic, with normal and high scores in some items along with lower-than-normal scores in others. The performance of the control group is also disharmonic.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World

Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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