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VISUAL FUNCTION AND FINE-MOTOR CONTROL IN SMALL-FOR-GESTATIONAL AGE INFANTS

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ABSTRACT - *Objective:* To compare visual function and fine-motor control of full-term infants small-for-gestational age (SGA) and appropriate for gestational age (AGA), in the first three months. *Method:* We evaluated prospectively 31 infants in the 1st month; 33 in the 2nd and 34 infants in the 3rd month, categorized as full-term; birth weight less than 10th percentile for SGA and 25th to 90th percentile for the AGA group. Genetic syndromes, infections, multiple congenital malformations were excluded. The Bayley Scales of Infant Development-II were used, especially items related to visual function and to fine-motor control outcomes. *Results:* The Motor Index Score (IS) was significantly lower in the SGA group in the 2nd month. The items "attempts to bring hands to mouth", in the 1st month and "reaches for suspended ring", in the 3rd month showed higher frequency in the SGA group. *Conclusion:* The Motor IS was lower in the 2nd month and items of fine-motor control in the 1st month and in the 3rd month showed higher frequency in the SGA group.

KEY WORDS: intrauterine growth retardation, neurodevelopment, visual function, fine-motor function.

Função visual e controle motor apendicular em lactentes pequenos para a idade gestacional

RESUMO - *Objetivo:* Comparar a função visual e o controle motor apendicular de lactentes nascidos a termo pequenos para a idade gestacional (PIG) com lactentes adequados para a idade gestacional (AIG), no primeiro trimestre. *Método:* Amostra de 31 lactentes no 1º mês, 33 no 2º e 34 lactentes no 3º mês, nascidos a termo; peso de nascimento < percentil 10 para o grupo PIG e percentil 25 a 90 para o grupo AIG. Síndromes genéticas, infecções ou malformações congênitas múltiplas foram excluídas. Foram utilizadas as Bayley Scales of Infant Development-II, especialmente itens relacionados com a evolução da função visual e controle motor apendicular. *Resultados:* Houve diferença significativa no Index Score (IS) Motor no 2º mês, havendo pontuação menor no grupo PIG. Os itens "tenta trazer mão à boca", no 1º mês e "alcança aro suspenso" no 3º mês foram mais freqüentes no grupo PIG. *Conclusão:* No grupo PIG, o IS Motor foi menor no 2º mês e maior número de lactentes executaram provas de controle motor apendicular no 1º e 3º meses.

PALAVRAS-CHAVE: retardo do crescimento intrauterino, neurodesenvolvimento, função visual, função motora apendicular.

Certain fetuses do not grow to normal size in uterus and manifest signs of chronic malnutrition. Their long-term growth and development may be impaired as a result of their intrauterine experience. These infants are most readily identified on a weight-for-gestation basis, and therefore the terms "intrauterine growth restriction" (IUGR) and "fetal growth restriction" (FGR) are different entity of "small-for-date" or "small-for-gestational age" (SGA). But at times the terms are used synonymously. The identification of newborns that present an abnormality of intrauterine growth remains a problem both from the multi-factorial aspect of fetal growth and from statistical definition[1]. Conceptually, a growth restricted newborn is defined as an infant who has not achieved its genetic growth potential in utero[2], in reference to the genetic growth potential of infants. The word IUGR supposes that the fetus was retarded in its growth and development by a pathological process during fetal life.

The term SGA is used for a fetus that has failed to achieve a specific and arbitrary anthropometrical or weight threshold by a specific gestational age; an infant who has a birth weight lower than a reference limit according to its gestational age. SGA describes a neonate whose birth weight or

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birth crown-heel length is at least 2 standard deviations bellow the mean for the infant's gestational age, based on data derived from a reference population. Also has been defined in some publications as birth weight or length below the 10th, 5th or 3rd percentile for gestational age[3]. The same statistical limits are used at birth to identify an infant as SGA or IUGR. Recently a new concept considered the estimation of an individualized birth weight limit, taking into account the genetic growth potential, under that a newborn must be considered as having FGR. This approach allowed to identify two new groups: a "constitutionally small" group, which should be considered as normal according to their low individual growth potential; and a non-SGA group, classically considered as having an appropriate weight, but which are growth restricted, considering their high individual growth potential[1]. Fetal malnutrition resulting in growth retardation may have consequences for the brain and the head circumference. The consequences of prenatal nutritional deprivation for the rapidly growing brain are dependent on the timing, duration and severity of the restriction[4]. In the human the phase of neuroblast multiplication occurs at a more highly protected early period of gestation. When the brain spurt begins, about the middle of gestation, the adult number of neurons has already been largely achieved. A deficit in particular regions of the cerebellum has been seen (with the late-dividing granular neurons) after undernutrition in the 3rd trimester of pregnancy. That early malnutrition in rats will curtail the rate of cell division if it occurs during the period of hiperplasia[5]. During the period of rapid cellular proliferation, undernutrition will affect the rate of cell division in any brain area where cells are dividing and in any cell type in the process of division. Regional growth in the human brain is somewhat different than in the rat brain; but it suggests that cell division can be curtailed by maternal undernutrition, which demonstrates that these changes are permanent, and may permanently reduce the number of brain cells in her offspring. Considering the number of SGA children at risk, few studies have been carried out in developing countries. The only well-documented reports we are aware of in Brazil showed that SGA full-term infants had poorer development than appropriate for gestational (AGA) infants at 6, 12 and 24 months[6,7,8] or abnormal neurological examination[9,10].

Cognitive functioning in American infants was similar between SGA and AGA term born children by age of 1 year, except for a lower Bayley Mental Development Index in SGA as measured by the Bayley Scales of Infant Development and the Fagan Test of Infant Intelligence[11,12]. Interest has now shifted to the outcome of infants from progressively lower birth weight groups in whom an increased incidence of more subtle problems, such as poor visual-motor integration, deficits in spatial relations, language disorders, reading and behavior problems has been reported[13]. More differences have been found in 3 to 5-years-old or older children[14,15,16].

Studies of the outcomes of low-birth weight children at school age have included measures of visual perception, fine motor skills and visual-motor integration. There has been no systematic investigation of the prevalence and nature of visual-motor integration dysfunction and the relation of the dysfunction to fine motor skills, visual perception and perinatal variables in apparently normal very low birth weight children at school age[17]. In the same way, there has been no systematic investigation of these functions in SGA infants. Variability in methodology, terminology, and assessments used makes it difficult to draw firm conclusions. Inconsistent terminology and definition such as visual-motor control, eye-hand coordination and visual-fine motor difficulties have been used for visual-motor integration, visual-perception and fine motor skill[17]. As noted in one of the only studies that differentiated these functions, a weakness with one of these components, in their reported fine-motor control, explained a significant part of the deficit in children at school age[17].

Visual-motor integration is defined as the degree to which visual (information) perception and limb movements, in this case finger-hand actions, are well coordinate. This rather general term, as frequently used in most of the research described, reflects in fact two separate and independent functions: visual perception and fine-motor control[18]. On the other hand, fine motor function may be described more specifically as the development status of finger/hand movements. Although the use of visual information may play a role in the task, assessment focus is on motor actions.

We are not aware of studies of the outcomes of measures of visual function and fine-motor control in apparently normal Brazilian SGA infants. This study aimed the investigation of visual functions (visual fixation and visual tracking) and fine-motor control in a group of full-term SGA compared with a control group full-term AGA infants in the first three months of life.

METHOD

The research design was a prospective cross-sectional study with two cohorts of full-term infants, a SGA group compared with a control AGA group. From September 2000 to August 2001, a neonatologist selected 42 full-term SGA and AGA neonates delivered at Neonatology Service at the Center of Integral Attention to the Woman's Health (CAISM) of the State University of Campinas (UNICAMP), São Paulo, Brazil. When a SGA neonate was chosen, the following two AGA neonates were selected. Ethical permission was obtained from the Research Ethics Committee of the Medical Faculty of UNICAMP and the mothers also gave the fully informed consent.

They were selected on the following criteria: 1) subjects living in Campinas metropolitan area, 2) neonates considered in good health for going home within 2 days of birth, 3) gestational age categorized as full-term (37-42 weeks) by the Capurro method[19], 4) expected birth weight used by Lubchenco method[20]: birth weight less than 10th percentile for the SGA group and between 25th and 90th percentile for the AGA group. Genetic syndromes, multiple congenital malformations and verified congenital infections (syphilis, toxoplasmosis, rubella, cytomegalovirus, herpes) were excluded.

Perinatal variables collected and examined were gender, gestational age, birth weight, birth weight centile. All children were scheduled for developmental evaluation and two professionals who were unaware of the classification of the neonate's group performed the assessments of the infants, in the presence of their mothers, at 1, 2 and 3 months of age. The Bayley Scales of Infant Development-II (BSID-II)[21] were used. The infant's score for each item was registered in the Mental and Motor Scale Record Form. The BSID-II index has a mean of 100 and a standard deviation of 15. The raw scores and index scores (IS) of the Mental and Motor Scales were considered. A system of well-defined terminology classified the Developmental IS as: accelerated performance (115 and above); within normal limits (85-114); mildly delayed performance (70-84); significantly delayed performance (69 and below). The Mental and Motor performance was classified as normal when the IS was equal or above 85 and altered performance when the IS was less than 85.

Infants were assessed once a month, between 7 days before or after their birthday. They should be in state of arousal, calm, alert to the environment. For the test procedure, the infant was lying on a padded surface, on an exam table in the supine position with the head at midline. The material used was a red ring with string.

Subtests were selected to investigate visual functions and fine-motor control. We devoted careful attention to the qualitative aspects of some items of the Mental and Motor Scales. Of great importance to us was the number of infants that performed them. In the 1st month, the visual functions assessed were visual fixation and visual tracking: "regards ring for 3 seconds" and "eyes follow ring (horizontal and vertical excursion)"; fine-motor control was assessed by the item "attempts to bring hands to mouth" (purposely attempts to place his hand in his mouth; the child need not actually place his hand in his mouth).

In the 2nd month, we evaluated the same visual functions as before and the fine motor control were "attempts to bring hands to mouth", "inspects own hand(s)" and "manipulates ring". In the 3rd month, all the items before plus "keeps hands open" and "reaches for suspended ring". The function "reaches for suspended ring" was considered while looking at the ring the infant purposely moved his arm in the ring's direction. This manipulative motor pattern was visually elicited and guided.

The data were registered in a database of the Epidemiological Information Program, version 6.02. The SSPS Package was used for statistical tests. The relation between categorical variables (visual and fine-motor control items, Mental and Motor performance classification) was investigated using Chi-Square or Fisher Tests. To determine the relation between continuous variables (birth weight, gestational age, IS of the Mental and Motor Scales) was used the Mann-Whitney test. The probability value was set at $p \leq 0.05$.

RESULTS

A total of 42 infants were studied. The sample for the cross-sectional study consisted of 31 infants in the 1st month, 33 in the 2nd month and 34 infants in 3rd month of life. Twenty infants were repeatedly evaluated all three months, 16 were evaluated two months and 6 in only one month (3 from the SGA group and 3 from the AGA group).

No differences were observed for gender (p=0.650) or gestational age (p=0.808). The birth weight in the SGA group ranged from 2125g to 2620g, median of 2370g. In the AGA group the birth weight ranged from 2765g to 3710g, median of 3220g. Comparison of birth weight between groups showed statistically significant difference (p=0.0001). It was concluded that the method for subject classification in each group was correct.

Table 1 shows the relation between chronological age, the number and percent of subjects with normal performance for Mental and Motor Scales and p-value. Fisher test were carried out to determine comparison between SGA and AGA groups in the three months.

In the Mental Scale, the groups responded differently in the 1st month (p=0.372) and in the 2nd month (p=0.450), but there was no significant difference ($p > 0.05$). In the 3rd month, both populations were similar (p=1.00). However, the SGA group has shown a proportionally greater number

Table 1. Chronological age, normal performance in the Mental and Motor Scale and p-values of SGA and control groups.

Chronological age	Group	n	Mental performance		Motor performance	
			f/%	p-value[a]	*f*/%	p-value[a]
1st month	AGA	20	14/70.00	0.372	17/85.00	1.000
	SGA	11	10/90.91		9/81.82	
2nd month	AGA	19	12/63.16	0.450	18/94.74	0.561
	SGA	14	7/50.00		12/85.71	
3rd month	AGA	21	18/85.71	1.000	12/57.14	0.725
	SGA	13	11/84.62		6/46.15	

[a]Fisher test; AGA, appropriate for gestational age; SGA, small-for-gestational age.

Table 2. Means and standard deviation of Index Score in the Mental and Motor Scales and p-values of the SGA and control groups.

Chronological age	Group	n	Minimum	Maximum	Mean	Standard deviation	p-value[b]
Mental Index Score							
1st month	AGA	20	64	104	92	10.93	0.834
	SGA	11	68	100	92	8.22	
2nd month	AGA	19	62	111	90	11.61	0.052*
	SGA	14	68	101	84	9.75	
3rd month	AGA	21	79	124	89	9.59	0.238
	SGA	13	73	103	87	7.19	
Motor Index Score							
1st month	AGA	20	76	107	94.5	7.88	0.627
	SGA	11	76	101	97	8.07	
2nd month	AGA	19	74	114	93	7.99	0.033**
	SGA	14	81	108	87	7.08	
3rd month	AGA	21	58	101	88	12.23	0.121
	SGA	13	67	91	82	8.08	

[b]Mann-Whitney test; AGA, appropriate for gestational age; SGA, age; *, near the limit to significant difference; **, significant difference.

of infants classified as normal in the Mental Scale, in the 1st month of life.

In the Motor Scale, both populations were similar (p=1.00) in the 1st month. The groups responded differently in the 2nd month (p=0.561) and in the 3rd month (p=0.725). The AGA group had shown a proportionally greater number of infants classified as normal in the Motor Scale, but there was no statiscally significant difference (p > 0.05).

Table 2 shows the relation between chronological age, IS in the Mental and Motor Scales and p-values. Mean comparisons using the Mann-Whitney test revealed near the limit to difference in Mental Scale and a statistically significant difference in Motor Scale, both in the 2nd month. The IS showed marked differences in the 2nd month.

Table 3 shows the results of the specific items of Mental and Motor Scales for the assessment of visual functions and fine - motor control in the groups. Table 4 shows p-values for comparison between SGA and AGA groups.

Tables 3 and 4 show that visual fixation evaluated by the item “regards ring for 3 seconds” and visual tracking evaluated by “eyes follow ring in ho-

Table 3. Cell frequency counts of the SGA and control groups in the visuomotor items.

Items	Groups	1st month f/%	2nd month f/%	3rd month f/%
Regards ring for 3 seconds	AGA	15/83.33	10/55.56	17/85.00
	SGA	10/90.91	6/50.00	9/81.82
Eyes follow ring (horizontal excursion)	AGA	13/76.47	15/83.33	
	SGA	9/90.00	10/76.92	
Eyes follow ring (vertical excursion)	AGA	10/58.82	11/61.11	
	SGA	4/40.00	6/46.15	
Manipulates ring	AGA		4/23.53	7/38.89
	SGA		2/14.29	4/36.36
Inspects own hand(s)	AGA		3/16.67	8/42.11
	SGA		4/28.57	3/25.00
Attempts to bring hands to mouth	AGA	6/30.00	9/50.00	12/60.00
	SGA	9/81.82	10/71.43	7/58.33
Keeps hands open	AGA			13/61.90
	SGA			3/27.27
Reaches for suspended ring	AGA			1/05.26
	SGA			4/40.00

AGA, appropriate for gestational age; SGA, small-for-gestational age.

Table 4. P-values in the visuomotor items for SGA and control group.

Item	1st month p-value[a]	2nd month p-value[a]	3rd month p-value[a]
Regards ring for 3 seconds	1.000	1.000	1.000
Eyes follow ring (horizontal excursion)	0.621	0.676	
Eyes follow ring (vertical excursion)	0.440	0.409	
Manipulates ring		0.664	1.000
Inspects own hand(s)		0.669	0.466
Attempts to bring hands to mouth	0.006**	0.221	1.000
Keeps hands open			0.063*
Reaches for suspended ring			0.036**

[a]Fisher test; *, near the limit to significant difference; **, significant difference; SGA, small-for-gestational age.

rizontal excursion", more frequently observed in the SGA group, in the 1st month, was not statistically significantly so. In addition, the item "attempts to bring hands to mouth" was more frequently observed in SGA infants in the 1st and 2nd months, with a statistically significant difference in the 1st month of life. Moreover, in this item, in the AGA group there was an increase with age for the proportion performing well the test and also for the SGA group falling from the 1st to the 3rd month.

In the 3rd month, the reaching movements for suspended ring were more frequently observed in the SGA group, with statiscally significant difference. The item "keeps hands open" was more frequent in the AGA group, near the limit to significant difference.

DISCUSSION

Since 1994, the Interdisciplinary Group of Studies in Infant Development (GIADI) have conducted studies at the Center of Studies and Research in Rehabilitation (CEPRE), in collaboration with the Department of Neurology and Division of Neonatology at the CAISM, State University of Campinas (UNICAMP) Sao Paulo, Brazil. This group works mainly in the study of infant neurodevelopment regarding aspects such as: visual and hearing functions, language, motor and neurological development. The team has professionals in the health areas: pediatric neurologist, pediatrician, occupational therapist, psychologist, speech pathologist, physical therapist and social worker. The present study comprises a group of 42 infants, 36 assessed at least twice and among these, 20 were assessed 3 times. So, the possibility of dropout-biased effect mentioned in the literature[6] is very small. However this selection of observations was a matter of supply and not of study design. The limitations in ensure the adequate monthly evaluation were formidable.

It was found significantly lower IS in the Motor Scale in SGA infants in the 2nd month of life. No differences were observed in the 3rd month. So at the age of two months the SGA infants were different from the AGA group but in the 3rd month the groups were equal. We conjectured that this may indicate the so called major transformation of neural function that occurs at about the end of the 2nd month posterm[22] and many neural functions change into a more adaptative condition than during the first 2 months after birth at term[23].

Prenatal maternal malnutrition (particularly in relation to the essential fatty acids, vitamin E and trace elements) may reduce total neuronal cell numbers and synapse formation and may also interfere with neuronal migration. Between 26 and 34 weeks of gestation, the normal process of neuron loss and axon retraction is at its height, with increased metabolic activity and increased vulnerability around the area of the basal ganglia, the caudate nucleus, the cerebellum and the optic radiations. These areas are implicated in critical aspects of motor control[24]. A triple watershed zone also affects the pathways between these areas, making them particularly vulnerable to hemorrhage, ischaemia and disturbances in cerebral blood flow. Interruption of these pathways is therefore likely to affect performance in a number of different domains.

The identification of poor performance in items of Mental and Motor Scales assessing particular skills might relate to specific deficits in the parts of the brain controlling the particular activity being tested. It was surprising to observe that functions of visual fixation in the midline and horizontal visual tracking were more frequently observed in the SGA group, in the 1st month of life, although not statistically significant. Those results suggest that the development of visual functions in SGA infants follow different patterns in comparison with AGA infants. We observed a qualitative tendency for diffuse observation of the environment, and an unsteady visual tracking in the SGA group. The administration and scoring directions of the BSID-II allows the examiners to repeat the same item a maximum of three times during the evaluation. So, infants with low visual focus concentration in a specific stimulus can perform successfully the item. It was referred in SGA neonates that although he comes to an alert state, his responsiveness is poor[25]. He does not lock into social stimuli easily and does not interact in a focused and modulated manner with the animate or inanimate environment.

Normally developing infants search and scan their environment in a consistent manner when they reach the age of three months[26]. It is referred in normal infants that few visual connections are found at birth (about 10% of the maximum), when visual alertness is yet very low and visual fixation and following are just beginning to be demonstrable. The rapid burst in synaptogenesis at the age of 4 months correlates with a sudden increase in visual alertness at about that time[27]. Clinical observations confirm the importance of the neurological maturation of the visual system. In the last two decades, advances have been considered in our understanding of the maturation of visual function and in the ways to assess it. It is now well accepted that the visual system functions mainly at a subcortical level in the newborn and in the first months after birth, and becomes progressively integrated with and dominated by cortical processes during the 1st year[28]. Longitudinal studies have followed the onset and the maturation of different aspects of visual function in normal infants thus providing age-dependent normative data[28,29].

We observed in the 1st and 2nd months the function “attempts to bring hands to mouth” (the child need not actually place his hand in his mouth) was more frequent in the SGA group, with significant difference in the 1st month. Both groups were equal in the 3rd month. The basic processes evaluated were the infant's ability to control motor behavior and to perform integrated motor actions. Items representing this dimension included hand to mouth coordination. Moreover, the results showed a gradient in neuromotor competence to attempts to bring hands to mouth: there was an increase in time in the AGA group and a decrease in the SGA group from the 1st to the 3rd month. We conjectured that those differences could be attributed to a greater occurrence of movement of the arms observed in SGA group, which purposely brought his hand to his mouth, mainly in the 1st month. It is plausible that those differences could be attributed to a greater speed and greater occurrence of movements observed in SGA group, mainly in the 1st month.

Studies have investigated the quality of general movements in fetuses and infants with intra-uterine growth retardation. Movements' quality was found to be impaired[30,31]. 'Slow motion' and 'chaotic' general movements are frequently observed in infants with growth retardation. Many infants with growth retardation have transiently abnormal general movements, indicating the importance of obtaining multiple observations. It has been suggested that abnormalities at a young age are related to lesions of neural subsystems whose role in motor control ceases after 2 to 3 months. These abnormalities may disappear if the new, post transformation set of neural functions is not impaired.

After birth, general movements of the normal infant are commonly referred to as writhing movements. At the age of 6 to 9 weeks post term, at about the end of the 2nd month, during the so-called major neural transformation[22], the general movements of the normal infant acquire a fidgety character. Fidgety general movements are circular movements of small amplitude, moderate speed, and variable acceleration of neck, trunk and limbs in all directions. All normally developing infants move their arms and legs with graceful, small movements[31]. Abnormal fidgety movements at this age resemble normal movements, but their amplitude, speed and jerkiness were moderately or greatly exaggerated. A very striking feature concerned a peculiar type of 'fidgety movements' in blind infants[26]: they were exaggerated in amplitude and jerky in character and their presence lasted until 8 to 10 months. The authors conjectured that exaggerated fidgety movements might indicate an attempt to compensate for the lack of integration of proprioception and vision.

The function "reaches for suspended ring" was more frequently observed in the SGA group in the 3rd month of life, with a statistically significant difference. These movements were exaggerated in speed and amplitude, despite of resemble normal movements.

The literature referred that the pattern of movement frequently observed in SGA and preterm infants[32], exists only indistinctly in normal full-term infants. Similar movement patterns were mentioned as "windmill motions of the arms"[33], or "wind-milling arms movement"[34], or "cicling movements"[35] or "arm movements in circles"[36].

Reaching behavior can be observed in normal infants since 3 month of life, but the visually controlled prehensile patterning emerges around the fourth or the fifth months[32]. It seems that during the early period of prehension development in human infants the initiation of reaching attempts is predominantly visually controlled, and the tactile-kinesthetic input associated with successful object capture appears to play a minor role in the regulation of early reaching behavior.

The techniques used for assessing visual and fine motor functions in these infants are non-invasive. It can be done without expensive equipments and an experienced observer does the assessment. It is important to mention that we have embarked on a further review of these infants at 12 months of age.

In conclusion, our results comparing the Index Score of the BSID-II in two groups of SGA and AGA infants showed significant difference in the Motor Index Score at 2 months of age. The item "attempts to bring hands to mouth" was more frequently observed in SGA infants in the 1st and 2nd, with statistically significant difference in the 1st month of life. The results showed a gradient in neuromotor competence to "attempts to bring hands to mouth": there was a decrease in time in the SGA group and an increase in the AGA group from the 1st to the 3rd month. In the 3rd month, the movements "reaches for suspended ring" were more frequently observed in the SGA group, with statiscally significant difference. The item "keeps hands open" was more frequent in the AGA group, near the limit to significant difference.

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