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ANGULAR ANALYSIS OF CORPUS CALLOSUM IN 18 PATIENTS WITH FRONTONASAL DYSPLASIA

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ABSTRACT - Considering the rarity of the frontonasal dysplasia (FD) and the few reports about it in a large casuistry using magnetic resonance image (MRI), we describe the results of the angular analysis of the corpus callosum of 18 individuals with FD (7 male, 11 female), using an easily-reproductive method. Group I had 12 individuals with isolated form and Group II had 6 individuals with FD syndromic with unknown etiology. The results are presented in set. Comparing with the control group, patients with FD presented alpha angle increase and beta and gamma angles reduction ($p<0.05$). Alpha and gamma angles express the relationship between the anterior portion of corpus callosum and the floor of 4th ventricle. Considering the embryonary development, these findings would occur secondarily to failure during the development of nasal capsula. Thus, angular anomaly in corpus callosum would be a usual finding, and not fortuitous in patients with FD.

KEY WORDS: corpus callosum, frontonasal dysplasia, magnetic resonance image, midline facial cleft.

Análise angular do corpo caloso em 18 pacientes com displasia frontonasal

RESUMO - Considerando a raridade da displasia frontonasal (DF) e os poucos estudos sobre esta condição clínica usando ressonância magnética (RM), descrevemos os resultados da análise angular do corpo caloso em 18 indivíduos com DF (7 homens, 11 mulheres), usando um método de fácil reprodução. O Grupo I foi formado por 12 indivíduos com DF isolada e o Grupo II, por 6 portadores de DF sindrômica de etiologia desconhecida. Não houve diferença entre os grupos, e os dados são apresentados em conjunto. Comparando com o grupo controle, houve aumento significativo do ângulo alfa e redução dos ângulos beta e gama ($p<0,05$) Os ângulos alfa e gama expressam a relação entre a porção anterior do corpo caloso e do piso do 4º ventrículo. Esses achados radiológicos poderiam ocorrer secundariamente à falência do desenvolvimento da cápsula nasal. Assim, as anomalias angulares no corpo caloso poderiam ser um achado usual, e não fortuito, na DF.

PALAVRAS-CHAVE: corpo caloso, displasia frontonasal, ressonancia magnética, fenda facial mediana.

Frontonasal dysplasia (FD) is a rare group of disorders, characterized by ocular hypertelorism and frontonasal process anomalies[1-3] in which clinical and etiological heterogeneity have been recognized since the first review[4]. Several central nervous system (CNS) anomalies are mentioned in this condition, such as frontal encephalocele, myelomeningocele, Chiari's malformation, hydrocephalus and Corpus callosum anomalies[5-9].

A morphometric method based on measurement of five angle in order to perform a morphological analysis of the *corpus callosum* in craniofacial malformative syndromes was described[10]. This method was used in 34 patients with different condition, including one with FD.

In this article, we describe the angular analysis of 18 individuals with FD.

METHOD

We evaluated 18 individuals (7 males and 11 females) affected by FD. Minimum inclusion criteria were ocular hypertelorism and frontonasal process anomalies. All individuals were evaluated by the same clinical geneticist and were divided in 2 groups based upon the presence or absence of extra-facial anomalies. Nine of them present-

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Table 1. Parameters for measurement of the corpus callosum angles[10].

Angles	Parameters
angle α	Between a line crossing the anterior commissure and touching the inferior margin of the genu of the corpus callosum and one tangencial to the upper surface of the anterior portion of its body
Angle β	Between the first line described alone and one tangential to the floor of the fourth ventricle
Angle γ	Between the line tangential to the convexity of the anterior portion of the body of the corpus callosum
Angle δ	Between the lines tangential to the floor of the 4th ventricle and that tangential to the convexity of the anterior and posterior parts of the corpus callosum
Angle ε	Between the lines tangential to the floor of the fourth ventricle and the convexity of the posterior portion of the body of the corpus callosum

ed an isolated form (Group I) and the others, FD associated to multiple congenital anomalies with unknown etiology (MCA) (Group II). The average age was 12.57 years.

Magnetic ressonance image (MRI) was performed without contrast at 2.0 T. The sequence was: Axial FSE double eco T2; Time echo (TE) = 16/128. Repetition time (TR) of 4600, 6 mm of thickness and 2% of space. Axial FSE double eco DP, TE = 16/128. TR = 4600, 6 mm of thickness and 2% of space. Sagittal SE T1; TE = 10. TR = 550, 4 mm of thickness and space of 0%. Axial SE T1; TE = 10. TR = 550, 6 mm of thickness and 2% of space. Coronal SE T1; TE = 10. TR = 550, 6 mm of thickness and 2% of space. Axial flair inverse recover TE = 90 on CSF. TR = 8100, TI = 2200, 6 mm of thickness and 2% of space. When necessary, MRI was performed with anesthesia, according to the American College of Emergency Physicians (1994). For analyses of corpus callosum, the best image of CNS midline in sagittal spin-eco T1 sequence was considered, based upon the following parameters: visibility of neurohypophysis, fastigium and one of the secondary structures, such as anterior commissure or mesencephalic aqueduct. Table 1 shows the parameters for measurement.

Angles α indicates the width of the genu of corpus callosum. The γ and ε angles indicate the position of the corpus callosum relative to the floor of the fourth ventricle (Fig 2). The control group used was the same described by Gabrielli[10] with volunteers (N=35) without dysmorphic features and neurological complaints (Group B). The normal angular average and standard deviation (SD) proposed by these authors were: α (38.4 ± 8.17), β (61 ± 6.4), ε (118.5 ± 8.07), γ (81 ± 8.9), δ (142.8 ± 11.55). The statistics evaluation was performed by Epidemiologic Program - Office version 6.0. For mean comparison the Student's T test (STT) was used[11]. The rejection level was fixed at 5%.

This study was approved by the Ethics Committee of the University Hospital / UNICAMP.

RESULTS

Comparing the data of Groups I and II, no statistical dif-

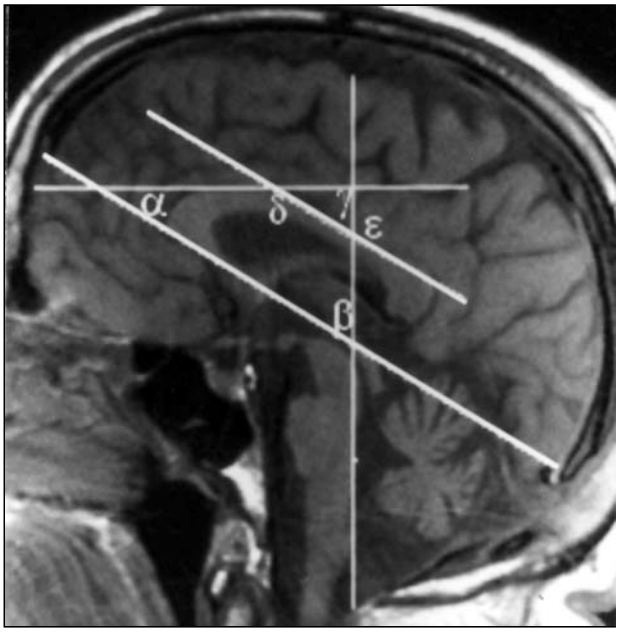

Fig 1. MRI showing angles of corpus callosum according to Gabrielli et al.[10].

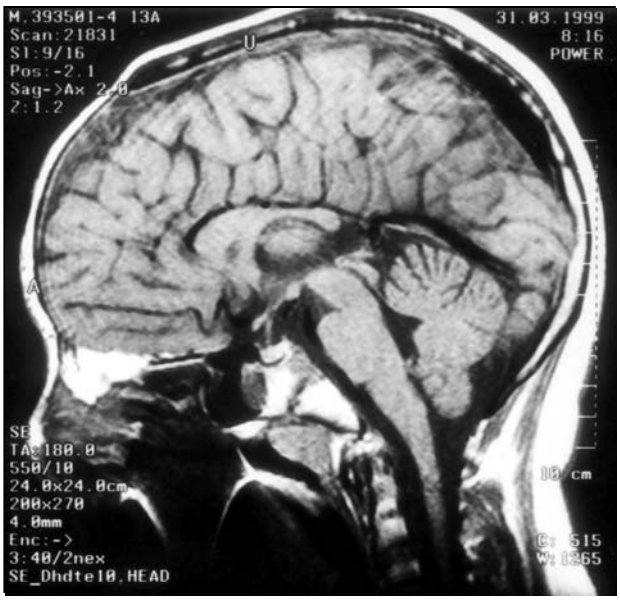

Fig 2. Corpus callosum of a FD patient showing a hypoplastic aspect and frontalization. It represents a increased of the alfa angle and reduced of beta and gama angles.

Table 2. Results of MRI avaliation in group I (n=12) and II (n=12).

MRI	Group I	Group II	EFT	χ2c	p
Corpus callosum anomalies	4	4	1	/	/
Ventricular alterations	4	4	1	/	/
Migration errors	5	2	/	0.81	0.37
Cerebellar hypoplasia	1	2	1	/	/

EFT, exact Fisher test; cχ2, corrected chi-square.

ference was found (Table 2) and the results of angular analyses of the corpus callosum in Groups I and II are presented in set (Group A). A comparative analysis with control group (Group B) was performed. These data revealed that patients affected by FD presented an increased α and decreased β and γ ($p< 0.05$) angles.

The results are presented in Table 3 (Figs 1 and 2).

Table 3. Comparison of the results of angular analysis of corpus callosum between Group A (FD patients) and Group B (control group).

Angles	Group A	Group B	Student T test	Significance level
Angle α	58.46	38.4	7.21	$p< 0.001$
Angle β	51.6	61	3.01	$p< 0.01$
Angle γ	70.57	81	3.15	$p< 0.01$
Angle δ	136.06	142.8	1.96	$p>0.05$
Angle ε	115.33	118.5	1.11	$p> 0.05$

DISCUSSION

FD usually presents clinical and etiological heterogeneity. In anyway, alterations in the nasal capsule formation, usually affect the frontal bone anatomy; as a consequence, the encephalic positional axis could be modified. Considering the rarity of FD and the few reports about it in a large casuistry using MRI, the method described by Gabrielli[10] could bring some more information about corpus callosum in this clinical condition. It is particularly interesting because of it is an easily-reproductive method in good quality MRI already done. This aspect is especially important, in view of the possibility to perform this analysis in old pre-surgical MRI and in patients from different hospitals.

The casuistry herein reported has some particularities that make the study uncommon in FD reports. This is the first report about this issue in which all MRI had the same parameters and all the individuals were evaluated by the same clinical geneticist for diagnosis. All individuals affected by a known genetic condition were excluded, in order to reduce the possibility of a pleiotropic gene effect.

In order to establish an objective parameter for participation of the corpus callosum in FD, the angle of implantation of the corpus callosum was measured and some significant alterations were observed: increase of α angle, decrease of β and γ angles, all with ($p<0.05$). GabrieIli[10] had just reported increased in α and β angles in his isolated patient with FD. However, he already proposed that alterations in the α angle be generally followed by alterations in β and γ angles.

Angles α and γ express the position of the anterior portion of the corpus callosum as regards the floor of the 4th ventricle.

This fact determines a frontal localization of the corpus callosum, evidenced by the increase in the α angle, which may be accompanied by decrease in β and γ angles. It this study, angular anomalies were detected even in individuals who had no visible MRI defects in corpus callosum. It might suggest that anatomic defects of the corpus callosum would be a usual finding, and not fortuitous, in patients with FD. Considering the easy method used, additional reports in different casuistry could bring complementary information.

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