POTENTIAL PHENOTYPIC SIGNS: PARTIAL ANALYSIS OF 42 PROBANDS WITH CORPUS CALLOSUM DYSGENESIS

Kossmann Ferraz, M.[1, 2] ; Gonçalves, Á. F. L. [1,3]; Oliveira-Szejnfeld, P. S. [1,4] ; Tovar-Moll, F. [1] ; Vargas, F. R. [1,3,5]

[1] D'Or Institute for Research and Education (IDOR), Rio de Janeiro, Brazil; [2] Hospital Universitário Gaffrée e Guinle, Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, Brazil; [3] Birth Defects Epidemiology Laboratory, Oswaldo Cruz Institute, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil; [4] Department of Radiology, Federal University of São Paulo, UNIFESP, São Paulo, Brazil; [5] Department of Genetics and Molecular Biology, Unirio, Rio de Janeiro, Brazil

Introduction: Corpus callosum dysgenesis (CCD) has a range of environmental and genetic aetiologies, among the latter being chromosomal anomalies being the most frequent cause. It is associated with a long list of phenotypic traits and syndromes. Phenotypic characteristics can be classified in those that vary in frequency within population, or as consequences of abnormal morphogenesis.

Objective: This ongoing study aims to describe and analyse the frequency of phenotypic characteristics and correlate them, in particular any abnormalities that might be associated with different types of CCD.

Methods: All recruited participants were diagnosed with CCD and were referred directly from our research institute, or from medical genetics or neurology clinics. This study was approved by the Institutional Review Board and written informed consent was obtained from the participants or their parents or legal guardians. All participants were examined by two investigators, except one, using a protocol with phenotypic characteristics adapted from Merks *et al.* 2003 that consisted of 686 items, in which 257 are classified as abnormalities. The participants underwent a body surface examination, measurements and photographic documentation. All data were collected and stored in RedCap® and statistically analysed using a χ^2 test with RStudio software.

Results: Forty-two probands with CCD were included in this study: 22 females (52.4%); with mean age at examination of 15 years old (8 months – 61 years old). Complete agenesis of the corpus callosum was present in 33.3% of the participants, partial agenesis in 21.4%, hypoplasia in 40.5% and, hyperplasia in 4.8%. 33 cases were sporadic cases and four were familial cases, two with discordance of type of CCD. When considering isolated cases of callosal malformation, or cases associated with other central nervous system (CNS) anomalies, we have a partial analysis of 33, of which 17 isolated.

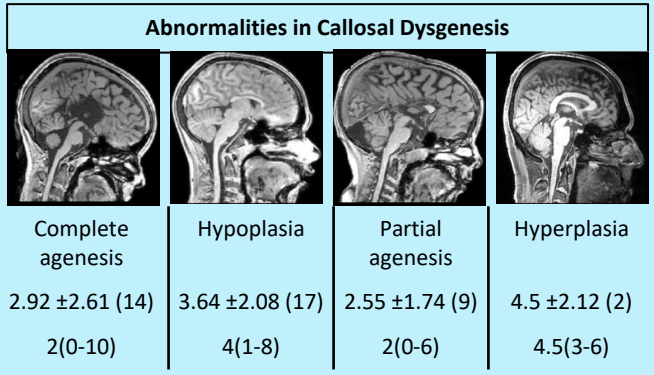

Figure 1. Sagital MR scans of CCD patients. Top number is mean abnormality findings with standard deviation (number of patients); bottom number is median findings (min-max).

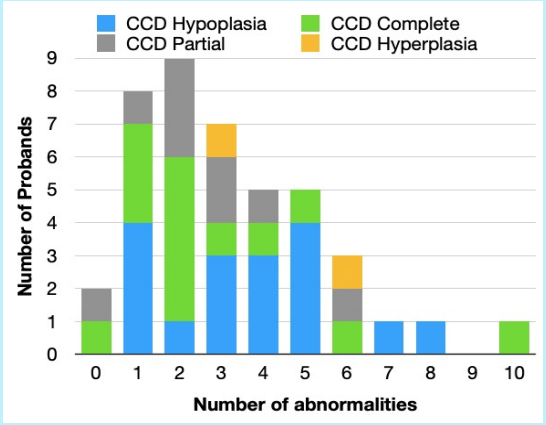

Figure 2. Distribution of abnormalities in the 42 probands (Mean = 3.21, SD = 2.20).

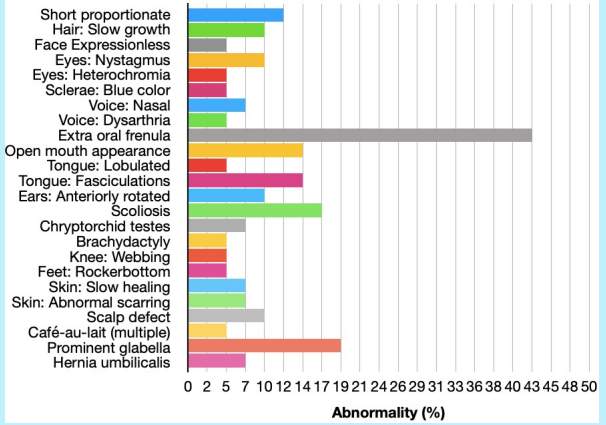

Figure 3. Percentage of abnormalities found in the patients. Only showing those present in at least two patients.

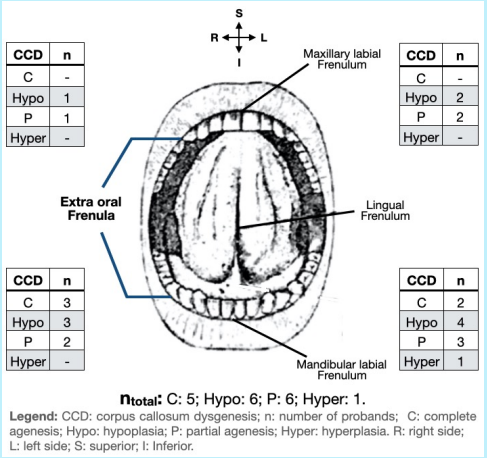

Figure 4. Location of Extra-oral frenula (n=16).

Of all the abnormalities, 60 were present in our cohort, the mean and median value for each CCD is listed in Figure 1. The frequency of abnormality in each proband is seen in Figure 2 and the percentage of abnormalities is seen in Figure3. 24 was present in more than one proband and extra-oral frenula were found in 18 probands, in two of them the site was not described (Figure 4). Absence of mandibular labial frenulum was present in 2 probands (1 partial agenesis and 1 hypoplasia).

Conclusion: A high frequency of extra-oral frenula was present in our cohort. This abnormality has been previously described in a few chromosomal anomalies and genetic conditions which may be associated with CNS malformations, such as holoprosencephaly [Mintz *et al.* 2005]. Preliminary results did not show significant difference in frequency of total abnormalities in the different types of CCD, or when isolated cases were compared to associated with other CNS abnormalities. Further analysis with a larger sample and identification of potential patterns of abnormalities are required.

References: Merks *et al.* (2003) Phenotypic abnormalities: Terminology and classification. Am J Med Genet. Mintz *et al.* (2005) An overview of oral frena and their association with multiple syndromic and nonsyndromic conditions. OOOO J.