ORIGINAL ARTICLE

Association between the Size of Corpus Callosum and Developmental Delay in Children

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ABSTRACT

Background: Corpus callosum (CC) abnormalities are usually associated with abnormalities of cerebral cortex as they facilitate the communication between hemispheres. Developmental delays are associated with white matter abnormalities. The association between the developmental delays and CC thickness is less studied. **Aims:** To assess the difference in the sizes of various regions of corpus callosum in cases of children with developmental delay and children with normal milestones and to determine the association between different types of developmental delays with thinning of corpus callosum. **Methods:** This was a cross-sectional study conducted among children with developmental delay as cases and children without developmental delay as comparison group. Imaging of CC was performed with 3T MRI. Thicknesses of CC at its various regions were measured and mean thickness was compared among cases and comparison group. **Results:** The total number of children included were 102 (51 cases and 51 comparisons). Mean age of the children was 2.9 (±1.24) years and majority were male children (55%). The difference in the mean thicknesses of cases and comparison groups in various regions of CC were found to be statistically significant (p-value <0.001). The association between the thickness of anterior midbody and splenium of CC with motor milestone delay and language milestone delay respectively was also found to be statistically significant (p-value 0.003 and <0.001 respectively). **Conclusion:** Decrease in the thickness of CC is directly associated with developmental delays. Hence, developmental delays need to be evaluated in children with corpus callosum abnormalities and vice versa.

KEY WORDS: Developmental delays, corpus callosum, 3T MRI.

Introduction

Growth and development are unique phenomena among the pediatric population. Increase in the physical size of the body is growth and increase in skills and function is development. Growth and development are always considered as whole because the child grows and develops together.[1] While the sequence of events is similar across populations, the rates vary from child to child and age to age. This pattern of development is averaged across child population to obtain a set of milestones or markers which signal appropriate growth and development.[2]

The child is usually assessed across the major domains of gross motor, fine motor, social and language skills so as to ascertain whether the development was satisfactory.[3] When the child fails to attain skills or faculties within the reference range for the age, a delay is suspected and then the cause is sought out. The effects of delay maybe static following the restricted event in the history or it may be progressive with residual and recurring alternations in the development of the child.[4] The term developmental delay (DD) covers a heterogeneous group of conditions that start early in life and present with delay in development or an

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abnormal pattern of developmental progression. [5]

The largest white matter structure in the human brain is corpus callosum (CC) and it connects the right and left hemispheres. It has an important role of integration of the two hemispheres and facilitates the normal communication between them. [6] Abnormalities in development of the cerebral cortex may be reflected by abnormalities in the corpus callosum and vice-versa. [7]

The prevalence of the corpus callosal abnormalities is found to be 2-3% in individuals with developmental challenges and 0.3 to 0.7% among general population who undergo neuro-imaging. [8,9] There can be multiple conditions resulting in thinning of CC. They can be divided into primary and secondary causes. The primary cause can be due to abnormal or failed myelination resulting in hypomyelinating conditions like leukoencephalopathies, metabolic disorders or microcephaly. Secondary causes can be diffuse injuries like hypoxic-ischemic encephalopathy, hydrocephalus etc. [10]

The presence of hypoplastic CC is highly associated with cerebral dysgenesis as a cause of cerebral palsy. Corpus callosal alterations are noted in various psychiatric and neurodevelopmental disorders like autism [11], mental retardation, developmental dyslexia, attention deficit hyperactivity disorder [12], developmental language disorder, schizophrenia and Downs syndrome. The abnormalities found in CC in developmental dyslexia and developmental language disorder has been proven. [13]

Prevalence of DD among children has been reported as 5–10%. Based on the previous studies, around 60% cases have abnormal Magnetic Resonance Imaging (MRI) findings. [14] Brain MRI is an important modality for assessment of these patients and neuroimaging helps to reveal previous injuries or any other specific abnormalities. CC and its parts can be discretely identified and has shown to produce sharp images on MRI.

Thus, this study was conducted to assess the difference in the sizes of various regions of corpus callosum in cases of children with developmental delay and children with normal milestones. The other objective of the study was to determine the association between different types of developmental delays with thinning of corpus callosum.

Materials and methods

This cross-sectional study was conducted among patients referred to the department of radio diagnosis of a medical college hospital of coastal Karnataka. The data was collected from January 2018 to December 2018.

The patients who were diagnosed with DD and aged between 2 years to 5 years were included as study subjects/cases. Children who underwent MRI for other conditions (seizures/ acute trauma etc.) with DD being ruled out from their diagnosis were included in the comparison group. The cases and comparisons were age and gender matched. Patients who had undergone neurosurgery, lesions disturbing the anatomy of the CC, presence of complete/partial agenesis of CC, cerebral abnormalities, neuropsychological disorders, children with premature birth, pre and perinatal trauma/ hypoxic injury were excluded. Also children with motion artifacts and children whose parents did not give written informed consent were excluded from the study.

The development was evaluated by a pediatrician on four domains, gross motor, fine motor, social and language milestones. A detailed developmental history was taken in a pre-designed proforma. Children who were unable to gain the age appropriate developmental milestones were considered as having a DD which was performed using Denver Developmental Screening Test II (DDSTII).

The cases and comparison groups were imaged using 3 Tesla MRI (GE Signa Pioneer). Routine sequencing (T1, T2, Flair axial, T1 sagittal, diffusion weighted imaging and SWI axial) were used for imaging. Figure 1 depicts mid sagittal T1 weighted image, which were used to measure the thickness of CC (in millimeters) in its various segments according to Witelson's method as depicted in Figure 2. [15]

The anterior corpus collosum (ACC) and posterior corpus callosum (PCC) (Figure 2) indicate the anterior most and posterior most parts of the corpus callosum. M and M_1 are the superior and inferior points of the mid-point of corpus callosum. S and S_1 are the superior and inferior points on the splenium and G is the anterior most point on the inner convexity of CC. The dotted lines and solid lines divide the CC in to seven parts: rostrum, genu, rostral body, anterior midbody, posterior midbody, isthmus and splenium.

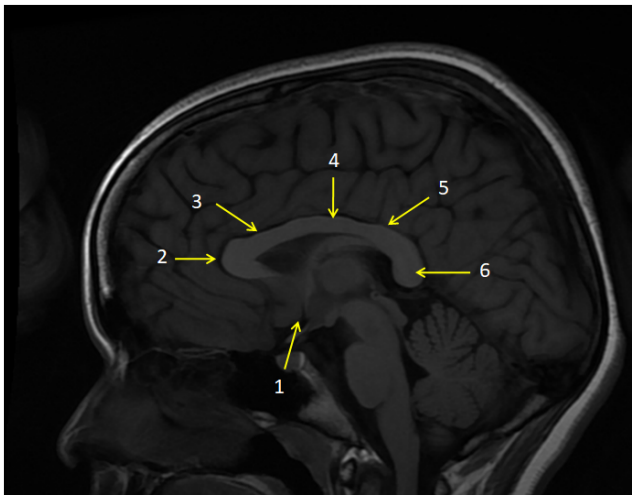

Figure 1: Mid sagittal T1 weighted image on 3T MRI shows normal segments of corpus callosum in 4 years old child in 1. Rostrum 2. Genu 3. Anterior body 4. Posterior body 5. Isthmus 6.Splenium

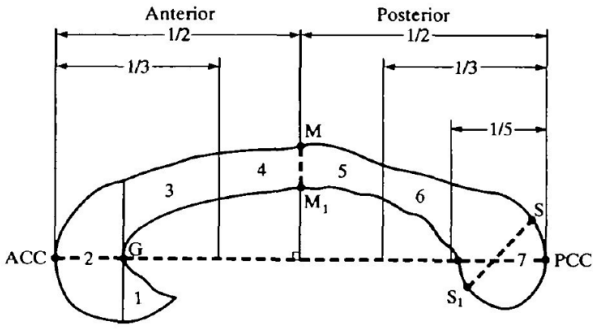

Figure 2: Subdivisions of corpus callosum according to the Witelson's method

IBM Statistical Package for Social Sciences (SPSS) (22 IBM, New York, USA) was used for analysis of data. The measurements were expressed as mean and standard deviation. The association between the mean sizes of the different regions of CC among the cases and comparison groups was assessed using student t-test. Also the associations between the different types of delays with thinning of CC were assessed using student t-test.

Institutional ethics committee approval was obtained for the study. Informed consent from the parents was obtained as the participants enrolled for the study were aged less than 5 years. Parents of children presenting with developmental delays were approached for enrollment into cases group. Parents of children who underwent MRI for other conditions were approached for enrollment in comparison group.

Results

A total of 102 children were included in the study, 51 each in case and control groups. Mean age of the children was 2.9 (±1.24) years. Among the study participants, 56 (55%) were male children. Figure 3 depicts the mean sizes of various areas of CC among cases and comparison subjects. The association between the mean values of sizes of CC among cases and comparison subjects were analyzed and it was found that the difference in the sizes of various subdivisions of CC was statistically significant ($p<0.001$). (Table 1)

The thickness of specific regions of CC was analyzed for the association with specific delays. The associations between the size of anterior midbody and splenium with motor milestone delay and language milestone delay were found to be statistically significant ($p<0.05$). (Table 2)

Table 1: Association between the size of corpus callosum and presence of developmental delays, N = 102

Sub-division of corpus callosum	Mean size (± SD)		t-test value	p-value
	Cases, n = 51	Comparison group, n = 51		
Rostrum	4.17 (1.87)	5.55 (0.52)	4.961	<0.001*
Genu	4.39 (2.44)	7.71 (1.06)	8.636	<0.001*
Rostral body	3.5 (1.8)	6.1 (1.23)	7.682	<0.001*
Anterior mid body	3.34 (2.29)	5.88 (0.57)	7.572	<0.001*
Posterior mid body	2.98 (2.3)	5.64 (0.49)	7.934	<0.001*
Isthmus	3.49 (1.9)	4.83 (0.24)	4.874	<0.001*
Splenium	4.33 (2.49)	6.04 (0.46)	4.73	<0.001*

*Statistically significant

Discussion

In this study, we analyzed the difference in the sizes of various regions of corpus callosum among children with developmental delays and without delays. The sizes of various regions of CC were found to be lower among the cases than among the comparison and these differences was found to be statistically significant. Figure 4 represents the diffuse thinning of corpus callosum.

Table 2: Association between size of specific areas of corpus callosum and presence of corresponding developmental delays, N = 51

Region	Predominantly motor milestone delay (n = 27)	Other forms of delays (n = 24)	t-test value	p-value
Anterior midbody size, Mean (± SD)	3.11 (0.24)	3.29 (0.17)	- 3.109	**0.003***
	Predominantly language milestone delay (n = 10)	**Other forms of delays (n = 41)**		
Splenium size, Mean (± SD)	3.96 (0.10)	4.38 (0.28)	-4.554	<0.001*

*Statistically significant

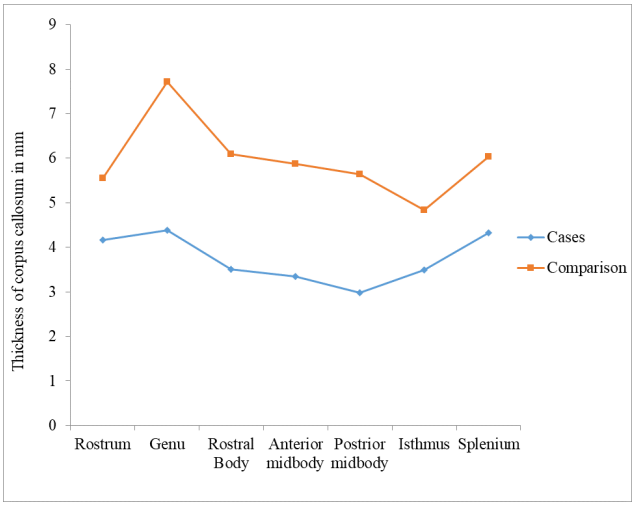

Figure 3: The mean sizes of various regions in corpus callosum among cases and comparison subjects, N = 102

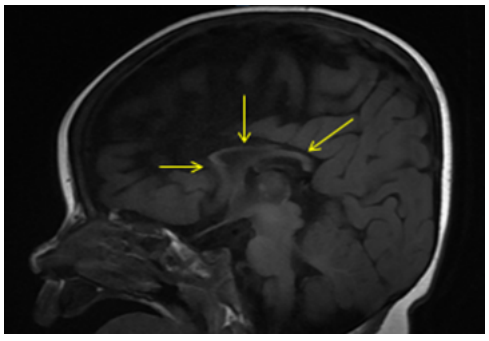

Figure 4: Mid sagittal T1 weighted image on 3T MRI shows diffuse thinning of the corpus callosum (depicted by arrows) in a 2 year old child

It is known fact that the thickness of the CC correlates with the cerebral white matter volume and hence, estimation of CC can help the radiologists to estimate the extent of volume loss in cases of children with peri-ventricular white matter injuries. And also, reduced volume of white matter in the brain is associated with DDs.[16] A study conducted by Ng WHA et al among Chinese school-going children to correlate between the size of the CC with academic performance concluded that mathematical skills and language may be related to general morphometry of CC.[17]

Different set of fibres pass through various regions of CC. The motor neurons predominantly pass through the anterior midbody.[15] Similarly, the speech and language related neurons are related to the splenium of CC.[18] Reduced thickness of CC in anterior midbody was associated with motor developmental delay in our study. Similar findings were observed in a Chinese study conducted by Chang CL et al, where the thickness of CC was positively associated with the 'rolling over' milestone of the babies.[6] Another study by Rademaker KJ et al to determine the association between CC and motor performance among prematurely born children in a population cohort found that the mean cross-sectional area of CC was significantly smaller among children born preterm compared to the term babies. The study concluded that among the children who were prematurely born and followed up for 7-8 years of age, larger CC, posterior region in particular was strongly associated with better motor functions.[19]

The difference in the means of splenium was compared among cases who had language milestone delay and others was found to be statistically significant indicating that the size of splenium could be associated with the language development. In a study conducted by Northon GB et al, the

inter-hemispheric connectivity was correlated with language impairment among adolescents who were born preterm. It was found that there was significant reduction in the volume of the white matter in the region of splenium among individuals with language impairments.[18] Similarly a systematic review conducted by Stipdonk et al found that oral language skills and verbal fluency were strongly related to volume of CC.[20] (Figure 5)

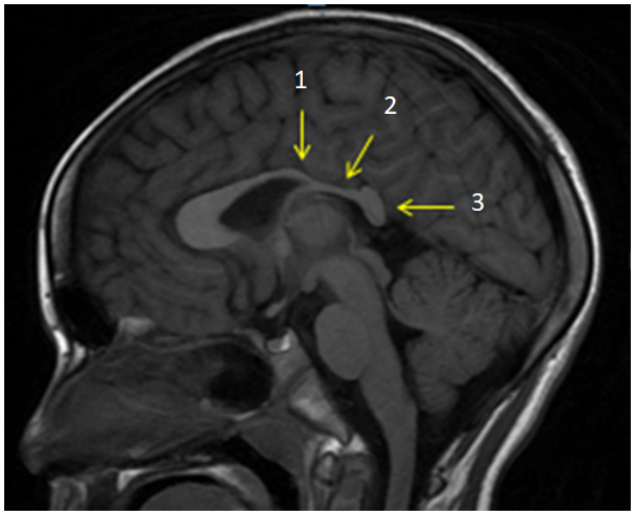

Figure 5: Mid sagittal T1 weighted image on 3T MRI shows thinning of the corpus callosum predominantly in 1. Posterior body 2. Isthmusand 3. Splenium in a 4 year old child

Thus, the CC thickness is found to be associated with the various delays in the attainment of developmental milestones. However, the routine workups for developmental delays do not consider screening of CC. Also, the incidental findings of thin CC necessitate evaluation of the child for presence of developmental delays.

The strengths of our study are that it was a novel idea to correlate the size of CC with developmental delay and cases and comparison groups were used for the same. Two regions of CC were analyzed with the specific type of delay based on the neurons that passed through them. Limitations of the study can be that the metabolic conditions like phenylketonuria/ maple syrup urine disease etc. that can be associated with developmental delays are not considered in this study. Also, a bigger sample size/ a multi-centric study would have provided more comprehensive results and hence, the study findings are not generalisable.

Conclusion

In our study, we have found that the decrease in the size of CC was associated with the developmental delays among children. The decrease in the size of anterior midbody and splenium regions were associated with motor milestone delay and language milestone delay respectively. The children with thin CC need evaluation for developmental delays.

References

1. and P. Park's textbook of preventive and social medicine. 25th ed. Banarsidas Bhanot publishers. 2019.
2. Rosa GD, Cavallaro T, Alibrandi A, Marseglia L, Lamberti M, Giaimo E, et al. Predictive role of early milestones-related psychomotor profiles and long-term neurodevelopmental pitfalls in preterm infants. Early Human Development. 2016;101:49–55. Available from: 10.1016/j.earlhumdev.2016.04.012.
3. Peyre H, Charkaluk ML, Forhan A, Heude B, Ramus F. Do developmental milestones at 4, 8, 12 and 24 months predict IQ at 5–6 years old? Results of the EDEN mother–child cohort. European Journal of Paediatric Neurology. 2017;21(2):272–279. Available from: 10.1016/j.ejpn.2016.11.001.
4. Prasad M, Hicks R, Mackay M, Nguyen CT, Campbell C. Developmental Milestones and Quality of Life Assessment in a Congenital Myotonic Dystrophy Cohort. Journal of Neuromuscular Diseases. 2016;3(3):405–412. Available from: 10.3233/jnd-160165.
5. Baird G, Simonoff E, Pickles A, Chandler S, Loucas T, Meldrum D, et al. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). The Lancet. 2006;368(9531):210–215. Available from: https://dx.doi.org/10.1016/s0140-6736(06)69041-7.
6. Chang CL, Hung KL, Yang YC, Ho CS, Chiu NC. Corpus Callosum and Motor Development in Healthy Term Infants. Pediatric Neurology. 2015;52(2):192–197. Available from: 10.1016/j.pediatrneurol.2014.10.012.
7. Hinkley LBN, Marco EJ, Findlay AM, Honma S, Jeremy RJ, Strominger Z, et al. The Role of Corpus Callosum Development in Functional Connectivity and Cognitive Processing. PLoS ONE. 2012;7(8):e39804. Available from: 10.1371/journal.pone.0039804.
8. Grogono JL. Children with Agenesis of the Corpus Callosum. Developmental Medicine & Child Neurology. 1968;10(5):613–616. Available from: 10.1111/j.1469-8749.1968.tb02944.x.
9. Jeret JS, Serur D, Wisniewski KE, Lubin RA. Clinicopathological Findings Associated with Agenesis of the Corpus Callosum. Brain and Development. 1987;9(3):255–264. Available from: 10.1016/s0387-7604(87)80042-6.

10. Andronikou S, Pillay T, Gabuza L, Mahomed N, Naidoo J, Hlabangana LT, et al. Corpus callosum thickness in children: an MR pattern-recognition approach on the midsagittal image. Pediatric Radiology. 2014;45(2):258–272. Available from: 10.1007/s00247-014-2998-9.
11. Nordahl CW, Iosif AM, Young GS, Perry LM, Dougherty R, Lee A, et al. Erratum: Sex differences in the corpus callosum in preschool-aged children with autism spectrum disorder. Molecular Autism. 2015;6(1):39. Available from: 10.1186/s13229-015-0030-3.
12. Semrud-Clikeman M, Filipek PA, Biederman J, Steingard R, Kennedy D, Renshaw P, et al. Attention-Deficit Hyperactivity Disorder: Magnetic Resonance Imaging Morphometric Analysis of the Corpus Callosum. Journal of the American Academy of Child & Adolescent Psychiatry. 1994;33(6):875–881. Available from: 10.1097/00004583-199407000-00014.
13. Paul LK. Developmental malformation of the corpus callosum: a review of typical callosal development and examples of developmental disorders with callosal involvement. Journal of Neurodevelopmental Disorders. 2010;3(1):3–27. Available from: 10.1007/s11689-010-9059-y.
14. Momen AA, Jelodar G, Dehdashti H. Brain Magnetic Resonance Imaging Findings in Developmentally Delayed Children. International Journal of Pediatrics. 2011;2011:1–4. Available from: 10.1155/2011/386984.
15. Witelson SF. Hand and sex differences in the isthmus and genu of the human corpus callosum: A postmortem morphological study. Brain. 1989;112(3):799–835. Available from: https://dx.doi.org/10.1093/brain/112.3.799.
16. Panigrahy A, Barnes PD, Robertson RL, Sleeper LA, Sayre JW. Quantitative analysis of the corpus callosum in children with cerebral palsy and developmental delay: correlation with cerebral white matter volume. Pediatric Radiology. 2005;35(12):1199–1207. Available from: 10.1007/s00247-005-1577-5.
17. Ng WHA, Chan YL, Au KSA, Yeung KWD, Kwan TF, To CY. Morphometry of the corpus callosum in Chinese children: relationship with gender and academic performance. Pediatric Radiology. 2004;35(6):565–571. Available from: 10.1007/s00247-004-1336-z.
18. Northam GB, Liégeois F, Tournier JD, Croft LJ, Johns PN, Chong WK, et al. Interhemispheric temporal lobe connectivity predicts language impairment in adolescents born preterm. Brain. 2012;135(12):3781–3798. Available from: 10.1093/brain/aws276.
19. Rademaker KJ, Lam JNGP, Van Haastert IC, Uiterwaal CSPM, Lieftink AF, Groenendaal F, et al. Larger corpus callosum size with better motor performance in prematurely born children. Seminars in Perinatology. 2004;28(4):279–287. Available from: 10.1053/j.semperi.2004.08.005.
20. Stipdonk LW, Franken MCJP, Dudink J. Language outcome related to brain structures in school-aged preterm children: A systematic review. PLOS ONE. 2018;13(6):e0196607. Available from: 10.1371/journal.pone.0196607.

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