ROLE OF DIFFUSION TENSOR IMAGING IN CHILDREN WITHDEVELOPMENTAL DELAY

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ABSTRACT

BACKGROUND

Delay in development is a frequent pediatric clinical issue that affects 10-15% of children. The use of an MRI scan is an important part of the thorough evaluation of children who have been diagnosed with developmental delay. The current study adapted DTI to analyze the brain morphology of children diagnosed with developmental delay based on developing evidence.

METHODOLOGY

In this cross sectional study we have studied 30 patients in Yenepoya Medical College Hospital, Mangalore who met the inclusion and exclusion criteria. Study tool used for the study is the use of Diffusion Tensor Imaging in addition to routine MR Sequences using 3T MRI. The quantitative analysis of FA and apparent diffusion coefficient (ADC) maps were generated automatically by the software and analysed.

RESULTS

The average age of the case group in our study was 4.97 ± 3.04, with a minimum of 1 and a maximum of 12. 26.7 percent of the children are between the ages of one and two years. Our findings revealed that children with developmental delay had significantly lower FA values than children without delay.Our study also showed that children with developmental delay has increased ADC values than children without developmental delay.ADC in the genu of the corpus

callosum was found to be significant, as were other areas and factors (higher in cases than in children without delay).

Keywords –Fractional anisotropy, developmental delay, Diffusion tensor imaging,Apparent diffusion coefficient, Magnetic Resonance imaging

INTRODUCTION

Development is defined as the growth of development of perceptual, emotional, intellectual, and behavioral skills and functioning. Maturation is directly linked to myelination in the central nervous system throughout development. Delay in development is a frequent paediatric clinical issue that affects 10-15% of children. The etiological insult that leads to embryological or fetal neuropathological alterations that eventually contribute to developmental delay can happen anytime between conception and birth. Because development occurs in various domains, a comprehensive developmental evaluation must appropriately include all areas of development, such as motor, cognitive, psychosocial and so on. The evaluation of both verbal and nonverbal skills provides a comprehensive picture of the child's development [1].

The use of MRI scan is an important part of the thorough evaluation of children who have been diagnosed with a developmental delay. Diffusion tensor imaging provides a view into brain microstructure at a scale not possible with other modalities, allowing for the detection and characterization of white matter abnormalities .Diffusion Tensor Imaging provides a comprehensive view of brain architecture, as well as the degree of communication between distinct brain regions. Because of the compactness and organization of white matter bundles, anisotropic diffusion may be measured on a macroscopic scale. Tractography, a post-processing technique for virtually dissecting white matter fibrebundles in vivo, takes advantage of this aspect of white matter organization. Fractional anisotropy and Apparent Diffusion Coefficient, two quantitative DTI measurements, show gradual changes with age and cerebral white matter maturity [2]. The apparent diffusion constant is a measurement of how much water diffusion restriction exists in brain tissue [3]. The orientation of white matter tracts is measured by anisotropy. The amount and severity of any identified differences in apparent diffusion constant and anisotropy measurements could be useful in determining the pathophysiologic characteristics

of developmental delay [4]. The current study adapted DTI to analyze the brain morphology of children diagnosed with developmental delay based on developing evidence. Hence the present study was designed to analyze the white matter tracts in children with developmental delay and to determine whether DTI can depict abnormalities in patients with a diagnosis of developmental delay. Further we evaluated the role of DTI – derived metrics for assessment of abnormalities of white matter fiber tracts in children with developmental delay.

MATERIALS AND METHODS

STUDY DESIGN

This study was designed as a Cross sectional study with patients attending Yenepoya Medical College Hospital, Mangalore who met the inclusion and exclusion criteria. The sample size was calculated using G* Power software. The total minimum sample size is 19 from the calculation derived. Hence 30 samples were taken. Sampling technique adapted was convenient sampling. Study tool used for the study is the use of Diffusion Tensor Imaging in addition to routine MR Sequences using 3.0 Tesla MRI machine (SIGNATM PIONEER-7O cm from General Electric). Pediatric patients (age group of 1-15 years) with developmental delay (Developmental Quotient < 85%) who are referred to MRI were included in this study.

IMAGING TECHNIQUE ADAPTED AND DATA PROCESSING

A 3T MR scanner (General Electric, Signa Pioneer) with a headneck 45 coil will be used for the MRI. Sagittal T1 weighted, transverse T2 weighted, transverse fluid attenuated inversion recovery (FLAIR), transverse T1 weighted, and transverse diffusion weighted imaging (DWI) sequences will also be done. One picture without diffusion weighting (b = 0 s/mm2) and six images with diffusion weighting (b0 = 1000 s/mm2) along six non-collinear directions should be obtained for each slice. To obtain DTI colour maps (RGB maps) from each patient, post processing and image analysis of DTI data will be performed on an AW Volume share GE workstation using Ready view Software.

The quantitative analysis of FA and apparent diffusion coefficient (ADC) maps generated automatically by the software will be done by drawing regions of interest (ROI) in the interactive

maps to include white matter tracts emanating from the most functionally active areas in the brain (these included genu, body, and splenium of corpus callosum, bilateral forceps minor and major, bilateral frontal and parietal lobes, bilateral pre and postcentral gyrus, bilateral genu, body, Each ROI has a diameter of 3 mm and is based on the average of three consecutive measurements taken at the same location. Data charted while calculating ROIs for various white matter locations is included in statistical analysis. The algebraic mean of all data will be calculated for each patient once the mean ADC and FA values for each ROI have been charted.

STATISTICAL ANALYSIS

Descriptive statistics will be reported for the required outcome variable and further statistical analysis will be applied by checking final data sheets. Statistical analysis will be done by comparing the resultant outcome variables/values (ADC and FA values) obtained in this study with standard reference values for age matched children without delay given in a standard article published by Christopher G. Filippi et al (2003).The basic descriptions and summary statistics will be used, SPSS version23 will be used to analyse the statistical data.
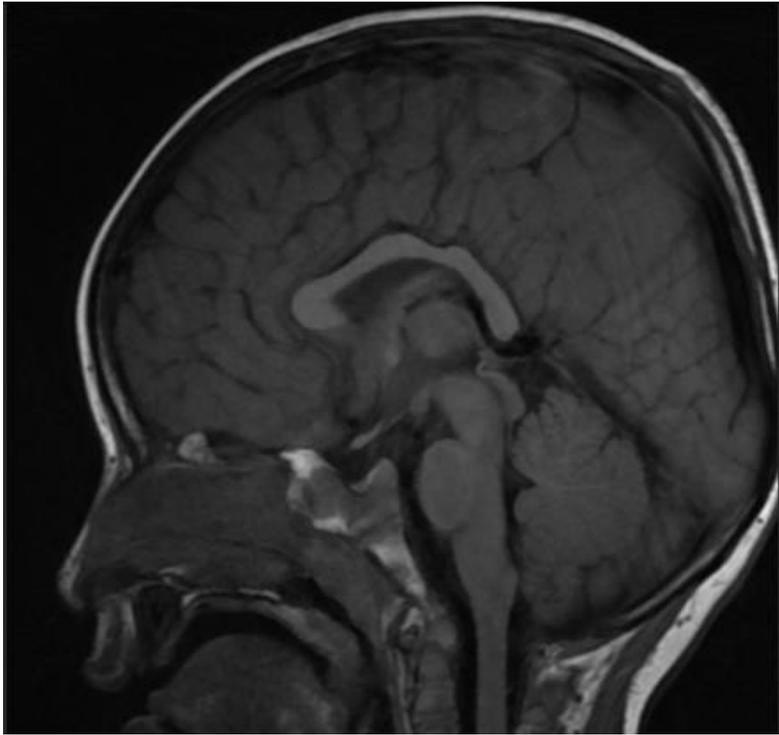
IMAGES

Serial DTI images showing association fibres in green color,projection fibres in blue colour and commissural fibres in red color.
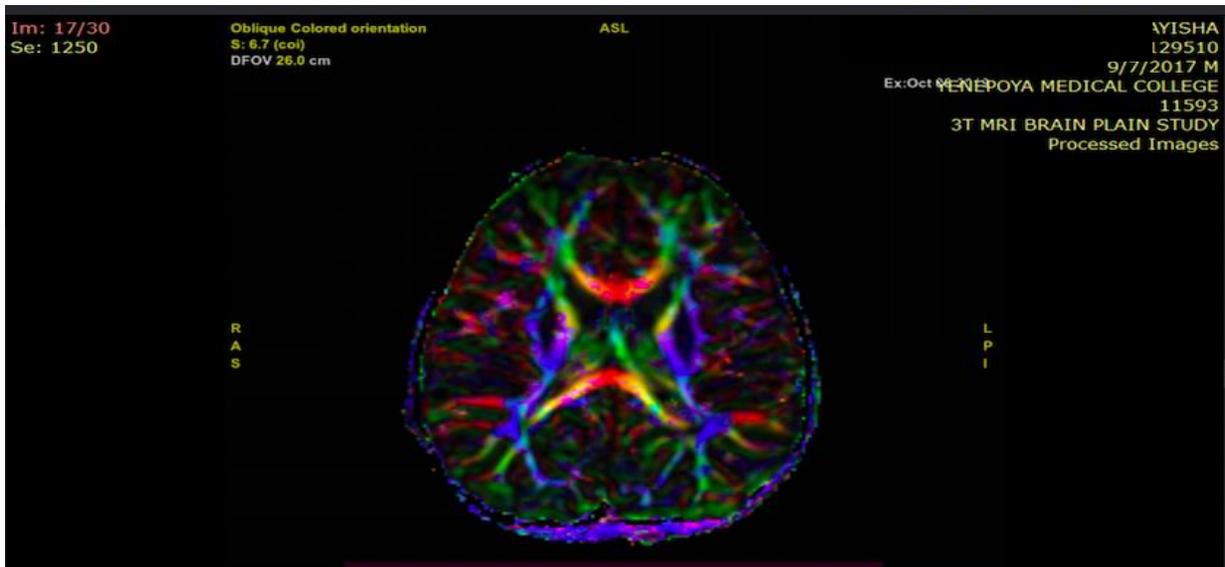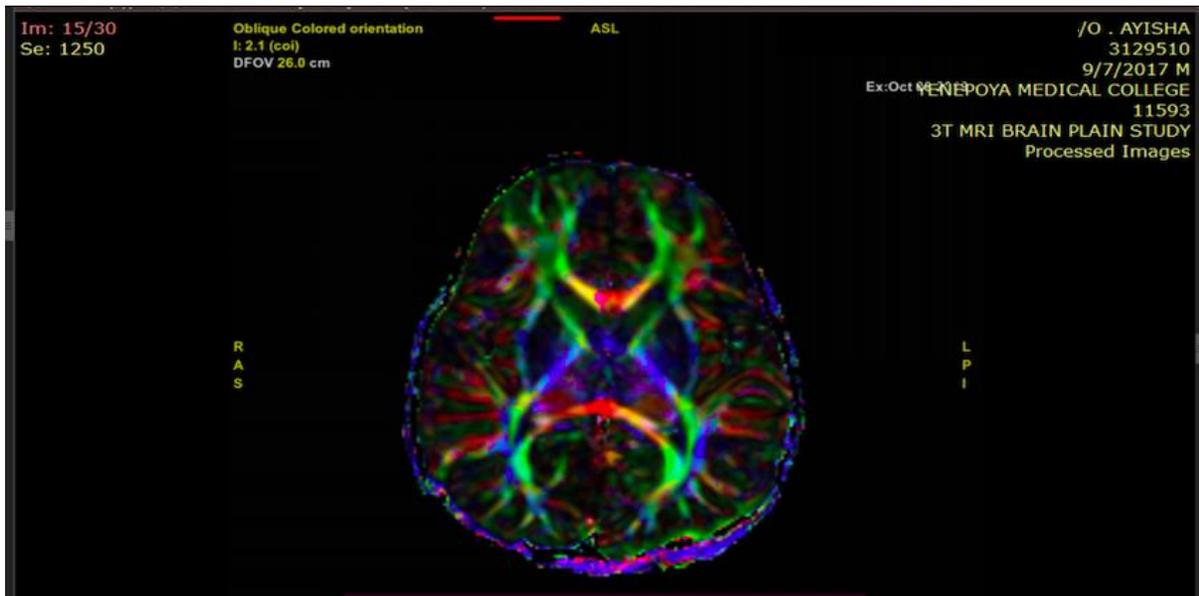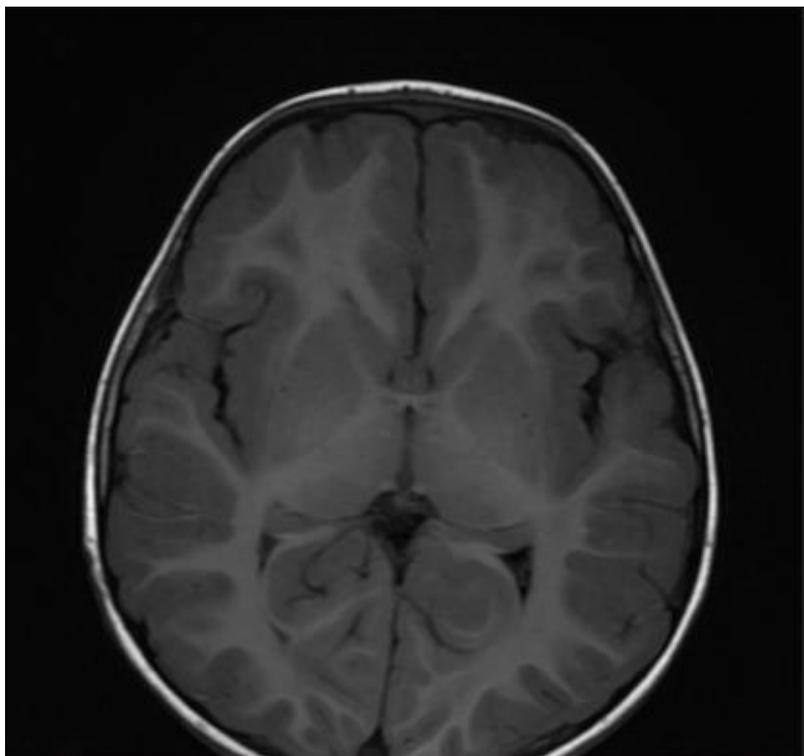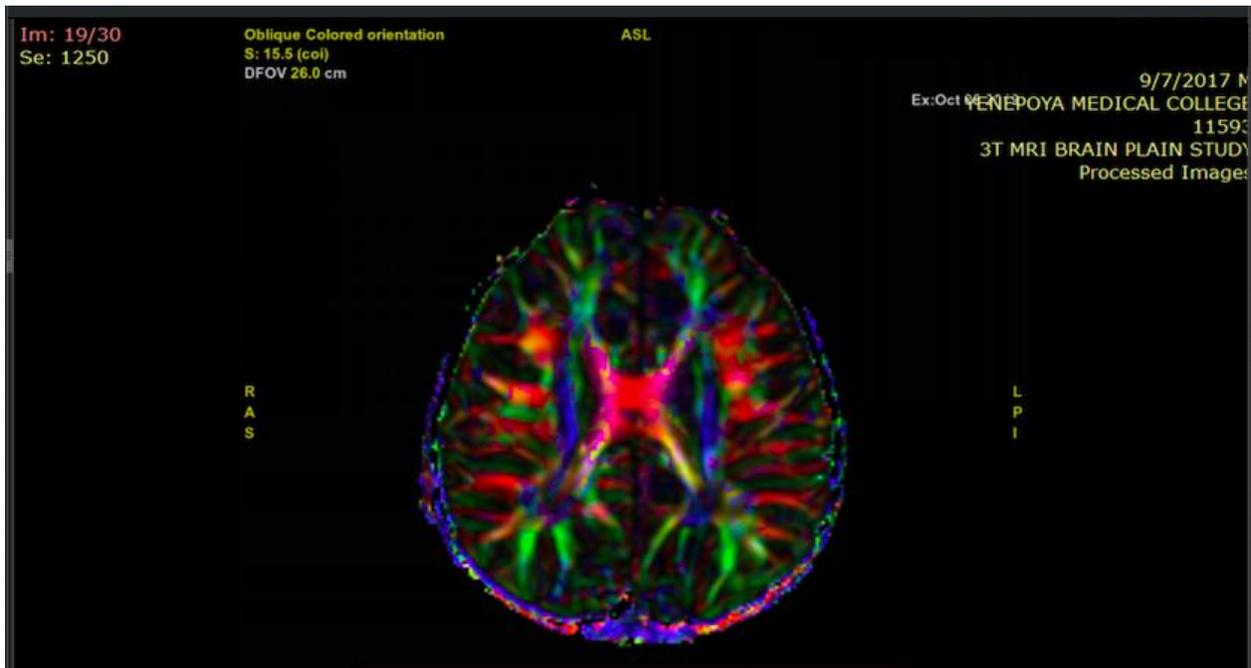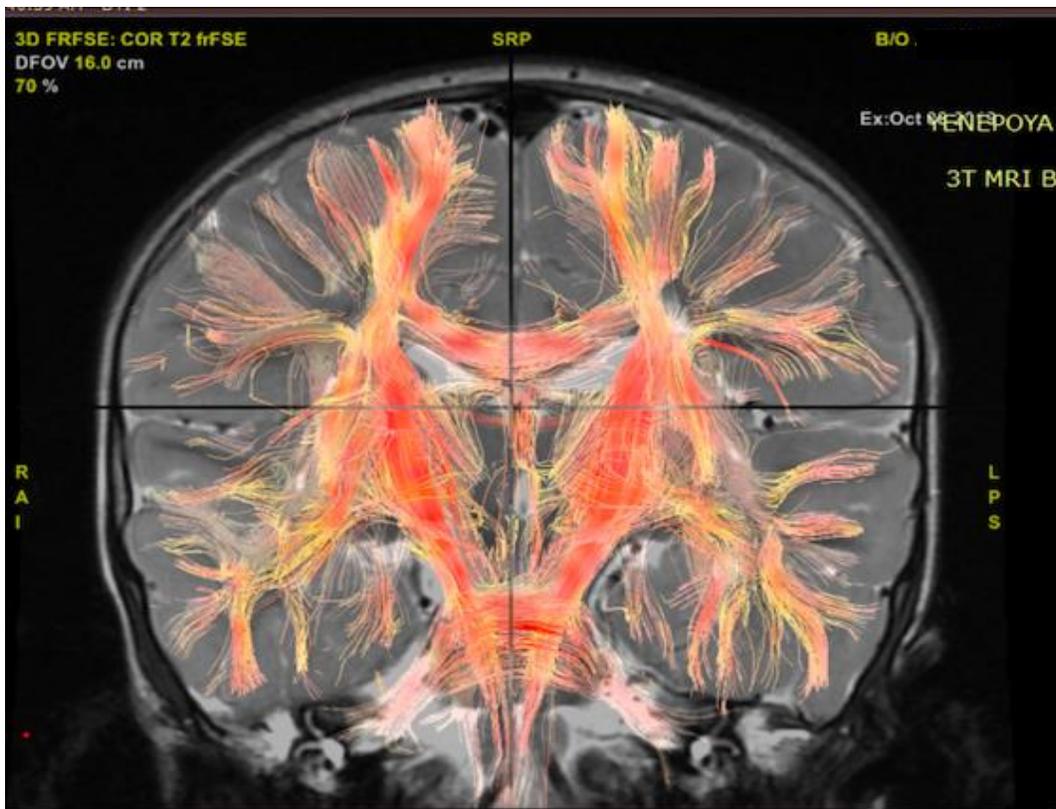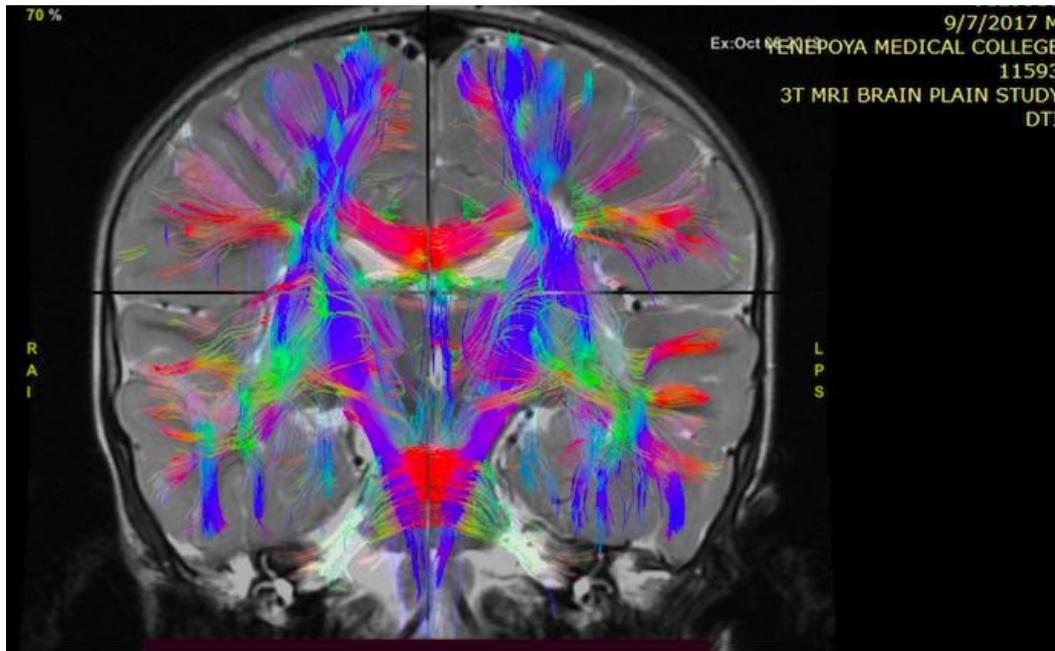
Axial T1 weighted image

Sagittal T1 weighted image

Color coded FA map in coronal plane

DTI -Tractography showing major white matter fibres in coronal plane

RESULTS

The current study adapted DTI to analyze the brain morphology of patients diagnosed with developmental delay.Cross sectional study was conducted in Yenepoya Medical College Hospital, Mangalore who met the inclusion and exclusion criteria. Study tool used for the study is the use of Diffusion Tensor Imaging in addition to routine MR Sequences using 3T MRI. The quantitative analysis of FA and apparent diffusion coefficient (ADC) maps generated automatically by the software will be done by drawing regions of interest (ROI) in the interactive maps to include white matter tracts emanating from the most functionally active areas in the brain. Statistical analysis done by comparing the resultant outcome variables /values (ADC and FA values) obtained in this study with standard reference values for children without delay.

Our findings revealed that children with developmental delayhad increased FA values and increased ADC values than children without delay.Diffusion tensor imaging provides a view into brain microstructure at a scale not possible with other modalities, allowing for the detection and characterization of white matter abnormalities.
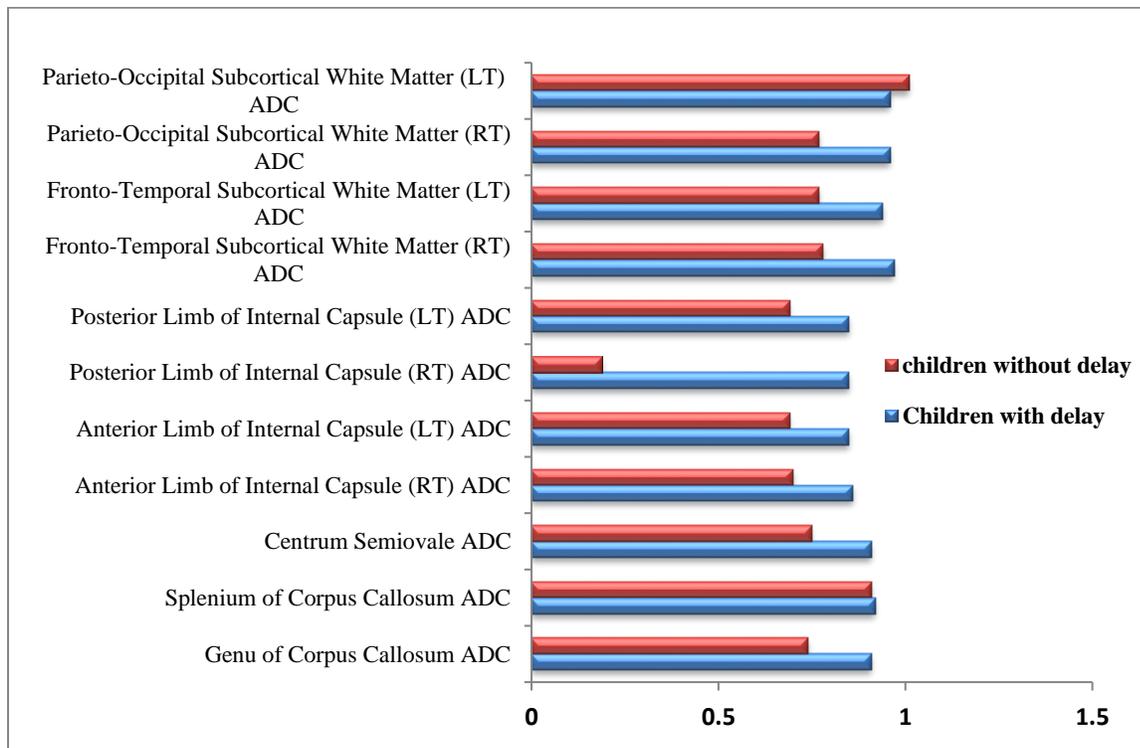
In this cross-sectional study, we have studied 30 patients in the age group between one year to twelve years referred to MRI from paediatric OP with clinical diagnosis of developmental delay .The average age of the case group in our study was 4.97± 3.04, with a minimum of 1 and a maximum of 12. 26.7 percent of the children are between the ages of one and two years. We chose an equal number of males and females for our study. In addition, the average development Quotient was 43.20 ± 8.65, with a minimum of 25 and a maximum of 56.00. The aspects of MR imaging were evaluated. Several more diffusion maps or indices can be constructed using DTI data. ADC in the genu of the corpus callosum was found to be significant, as were other areas and factors (higher in cases than in children without delay). The mean ADC of Genu of Corpus Callosum in cases is 0.91± 0.03, compared to 0.74± 0.05 in children without delay, with a p value of 0.0001. The FA of genu of the Corpus Callosum was found to be lower in children with delay (0.20± 0.03) than in children without delay (0.24± 0.03). Our findings revealed that children with developmental delay had significantly lower FA values than children without delay, as measured by mapped P values at the Posterior Limb of Internal Capsule (Left) FA (p value 0.0001), Fronto-Temporal Subcortical White Matter (Right) FA (p value 0.0001), Parieto-Occipital Subcortical White Matter (Right) FA, Fronto-Temporal Subcortical White Matter (Left) FA ((p value 0.0001).Our study also showed that children with developmental delay has increased ADC values than children without developmental delay.

Table 1 - Descriptive Statistics

Variable	Minimum	Maximum	Mean ± SD
Age	1.00	12.00	4.97 ± 3.04
Development Quotient	25.00	56.00	43.20 ± 8.65
Genu of Corpus Callosum ADC	0.66	0.97	0.82 ± 0.99
Genu of Corpus Callosum FA	0.15	0.29	0.22 ± 0.03
Splenium of Corpus Callosum ADC	0.78	0.99	0.90 ± 0.05
Splenium of Corpus Callosum FA	0.13	0.80	0.23 ± 0.09
Centrum Semiovale ADC	0.69	0.99	0.83 ± 0.09
Centrum Semiovale FA	0.04	0.24	0.13 ± 0.06
Anterior Limb of Internal Capsule (RT) ADC	0.69	0.91	0.78 ± 0.08
Anterior Limb of Internal Capsule (RT) FA	0.06	0.21	0.15 ± 0.04
Posterior Limb of Internal Capsule (RT) ADC	0.15	0.90	0.52 ± 0.33
Posterior Limb of Internal Capsule (RT) FA	0.10	0.72	0.42 ± 0.27
Anterior Limb of Internal Capsule (LT) ADC	0.69	0.90	0.77 ± 0.08

Anterior Limb of Internal Capsule (LT) FA	0.05	0.21	0.15 ± 0.04
Posterior Limb of Internal Capsule (LT) ADC	0.66	0.90	0.77 ± 0.08
Posterior Limb of Internal Capsule (LT) FA	0.10	0.26	0.18 ± 0.03
Fronto-Temporal Subcortical White Matter (RT) ADC	0.74	1.05	0.87 ± 0.10
Fronto-Temporal Subcortical White Matter (RT) FA	0.04	0.14	0.09 ± 0.03
Parieto-Occipital Subcortical White Matter (RT) ADC	0.74	1.00	0.86 ± 0.09
Parieto-Occipital Subcortical White Matter (RT) FA	0.05	0.14	0.09 ± 0.03
Fronto-Temporal Subcortical White Matter (LT) ADC	0.74	0.99	0.85 ± 0.09
Fronto-Temporal Subcortical White Matter (LT) FA	0.04	0.15	0.09 ± 0.03
Parieto-Occipital Subcortical White Matter (LT) ADC	0.74	1.00	0.87 ± 0.09
Parieto-Occipital Subcortical White Matter (LT) FA	0.05	0.24	0.09 ± 0.04

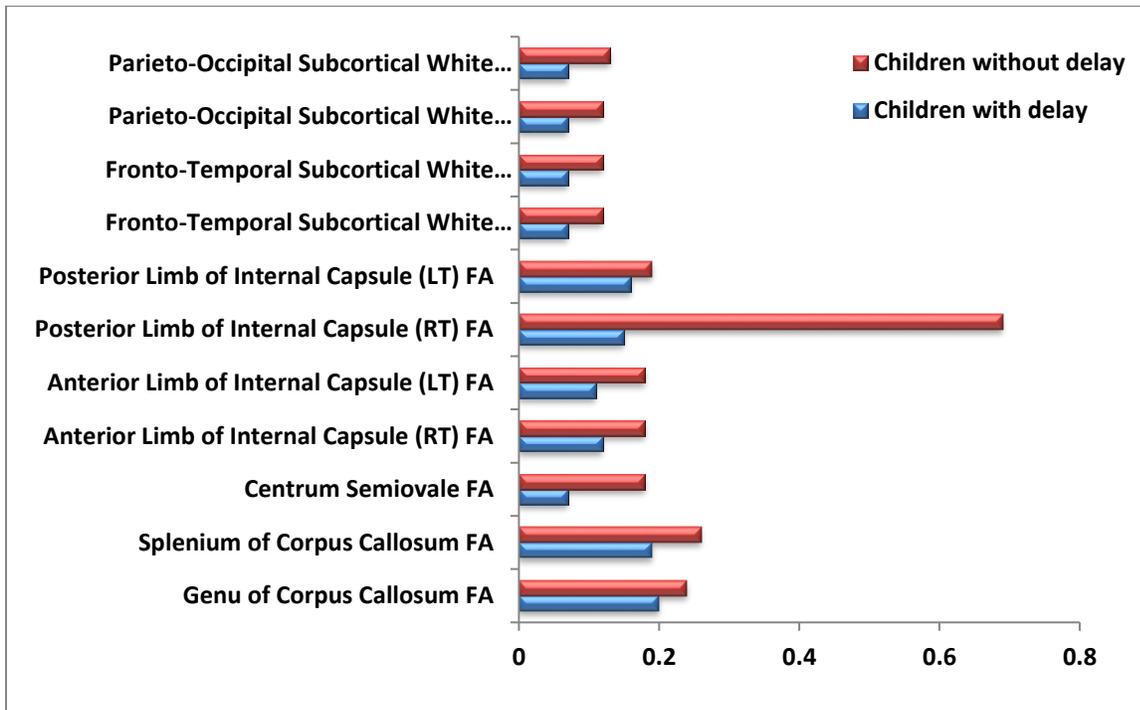**Figure 1 - Chart Overall ADC of children with developmental delay**

Figure 2-Chart Overall FA of children with developmental delay

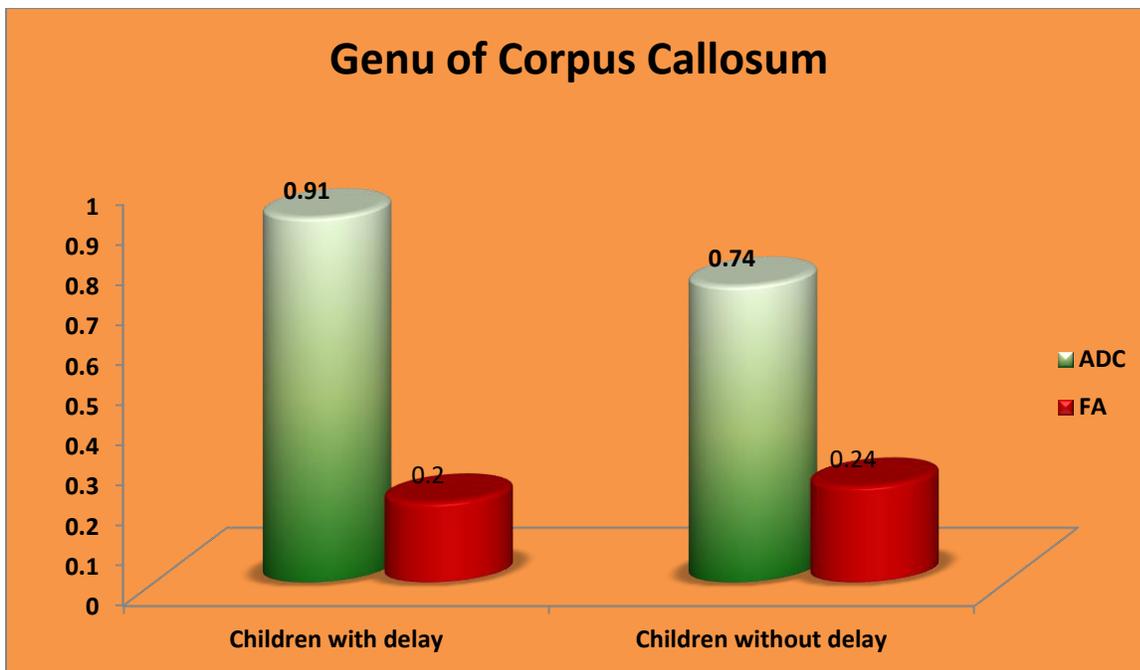Chart 1: Ge...

Chart   2:   Splenium   of   Corpus   Callosum

Splenium of Corpus Callosum
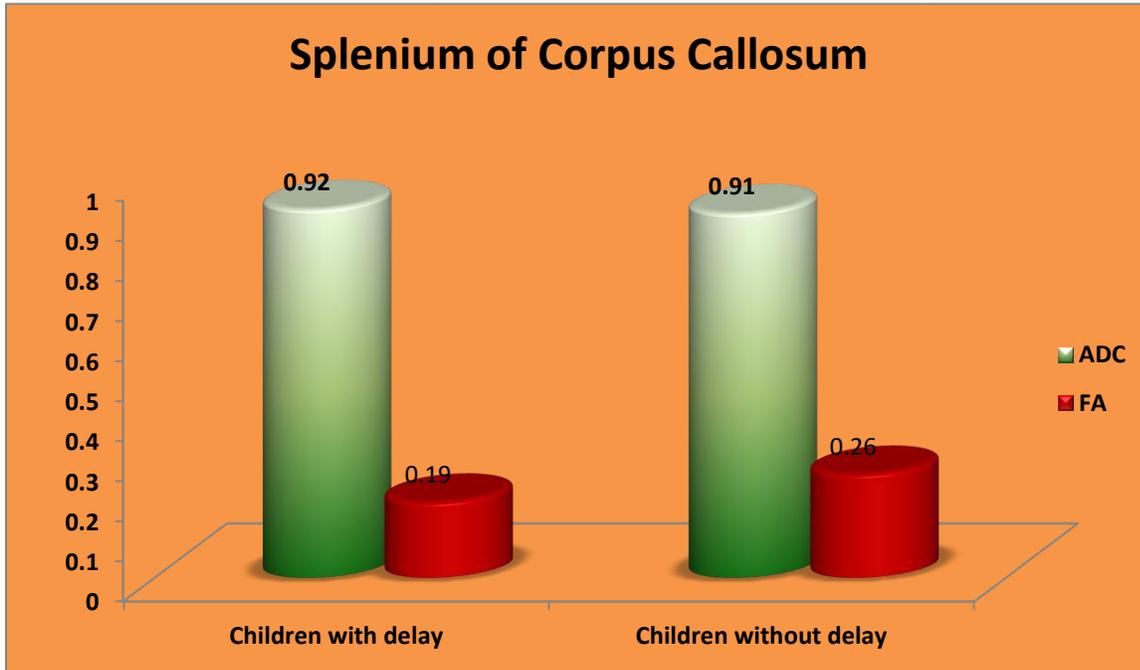

Chart 3: Anterior Limb of Internal Capsule (ADC)

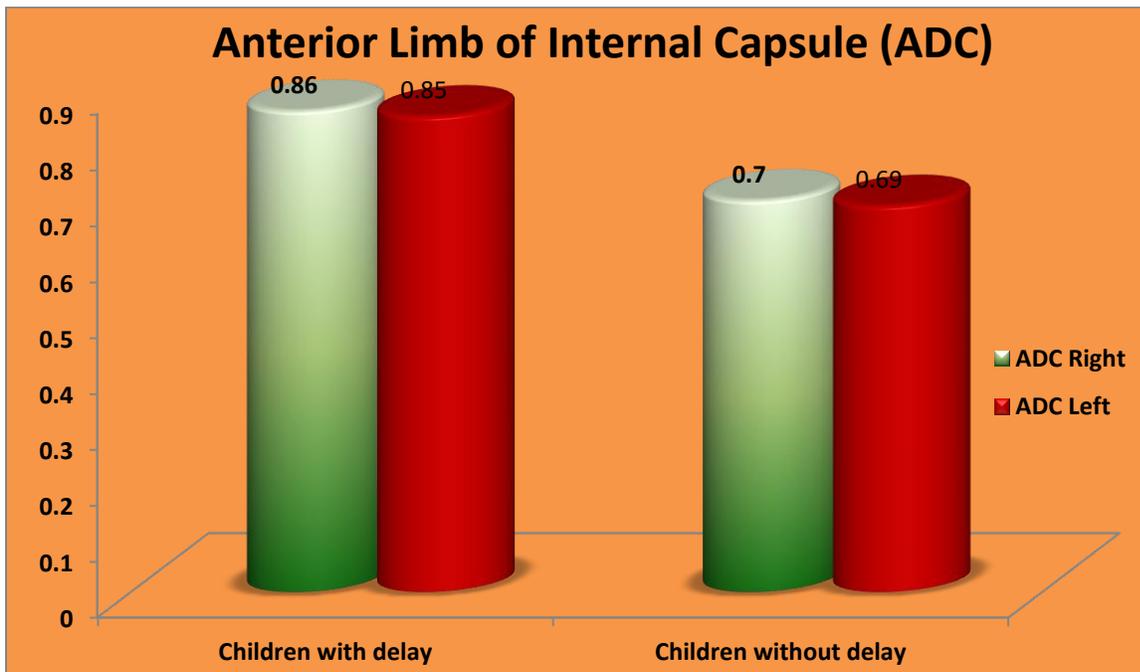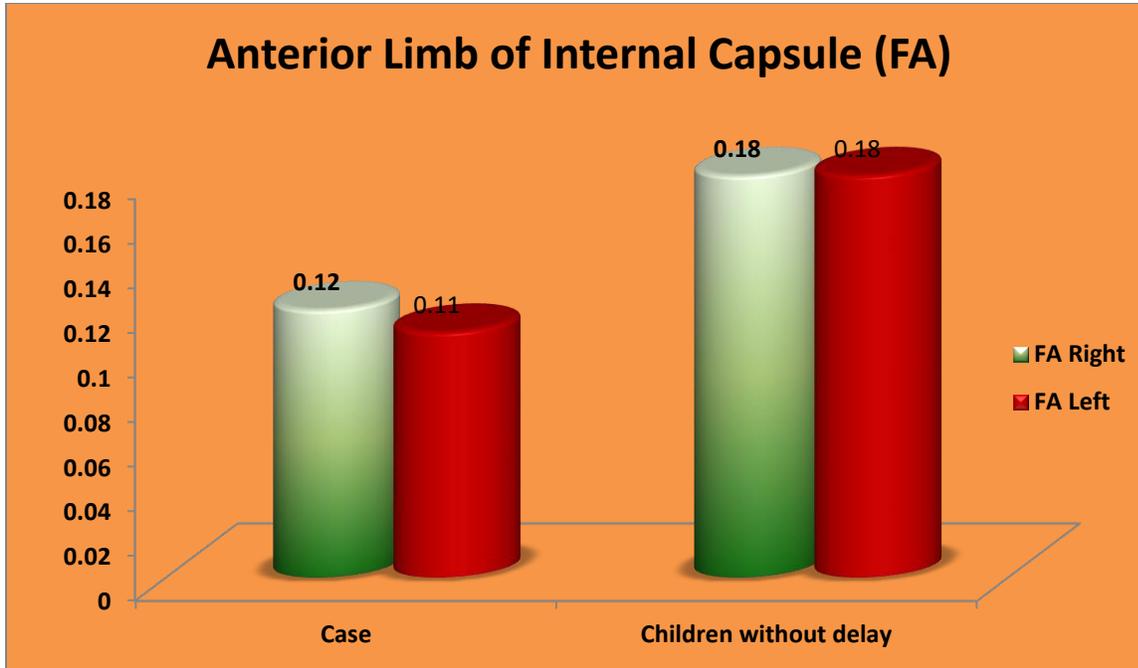**Anterior Limb of Internal Capsule (ADC)**

Chart 4: Anterior Limb of Internal Capsule (FA)

DISCUSSION

In this cross-sectional study, we have studied 30 children in the age group between one year to twelve years referred to MRI from paediatric OP with clinical diagnosis of developmental delay. The parents/guardians of these children gave their informed consent.The average age of the case group in our study was 4.97 ± 3.04, with a minimum of 1 and a maximum of 12. 26.7 percent of the children are between the ages of one and two years. We chose an equal number of males and females for our investigation.

In a study similar to ours, Ashish Verma and colleagues (2015) used diffusion tensor imaging of the brain in children (ages 2 to 12) with developmental delay who had morphologically normal MRI and discovered that DTI measures (FA and ADC) could detect anomalies in normal age-matched children without delay [5]. A comparable study was also conducted on 46 preterm new-borns by Huang [6]. In addition, the average development Quotient was 43.20 ± 8.65, with a minimum of 25 and a high of 56.00. Several more diffusion maps or indices can be constructed using DTI data. We mostly employed FA (fractional anisotropy), which is a quantitative measure

independent of imaging parameters, and ADC (apparent diffusion coefficient), which is a measure of voxel directionality. The total analysis contained ROIs (regions of interest) with 22 variables for each region, including an ADC value and FA value.

ADC in the genu of the corpus callosum was found to be significant, as were other areas and factors (higher in cases than in children without delay). The mean ADCof Genu of Corpus Callosum in cases is 0.91± 0.03, compared to 0.74± 0.05 in children without delay, with a p value of 0.0001. The FA of genu of the Corpus Callosum was found to be lower in children with delay (0.20± 0.03) than in children who did not have delay (0.24± 0.03).

Berman JI (2003) found a significant drop in FA values and increase in ADC in the corpus callosum's genu and splenium, frontal and parietal white matter, anterior limb of the internal capsule [7], and centrum semiovale. Neeraj B. Chepuri et al. (2002) used diffusion tensor imaging to analyse the anisotropy values in the corpus callosum in 200 normal people over the age of eighteen years, and found that there is a statistically significant rise across sex and age categories [8]. The anterior and posterior limbs of the Internal Capsule were found to differ between cases and children without delay. In both the anterior and posterior limbs of the internal capsule, FA revealed a statistically significant difference between cases and children without delay. In both the right and left anterior limbs of the internal capsule, ADC revealed a significant difference between cases and children without delay. In the current investigation, ADC in the posterior and anterior limbs in both directions remained significant with a p value of 0.0001.

Our findings revealed that children with developmental delay had significantly lower FA values than children without delay, as measured by mapped P values at the Posterior Limb of Internal Capsule (Left) FA (p value 0.0001), Fronto-Temporal Subcortical White Matter (Right) FA (p value 0.0001), Parieto-Occipital Subcortical White Matter (Right) FA, Fronto-Temporal Subcortical White Matter (Left) FA ((p value 0.0001).

Our study also showed that children with developmental delay has increased ADC values than children without developmental delay.

Our findings matched those of Christopher.G. Filippi et al. (2003), who found significant reductions in FA values and increase in ADC values in the corpus callosum's genu and splenium,

frontal and parietal white matter, anterior limb of the internal capsule, and centrum semiovale, respectively [7].

CONCLUSION

DTI aids in the quantification of white matter integrity and the qualitative alterations that can be employed in the development of specific rehabilitation measures when compared to the clinical data. In conclusion, despite normal-appearing brain conventional MR image findings, diffusion-tensor MR imaging revealed anisotropy and ADC variations in various white matter areas in children with developmental delay. More research is needed to see if the abnormalities found on diffusion-tensor MR imaging can be employed as diagnostic imaging markers of developmental delay. If followed up longitudinally, the amplitude and severity of aberrant diffusion-tensor MR imaging results may correlate with therapeutic or functional outcome and long-term prognosis. Furthermore, as more children with developmental delay are investigated using this developing technique, diffusion-tensor MR imaging may represent another method for objective and measurable assessment of neurodevelopment.

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