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Original Article

Radiology Section

Diffusion Tensor MRI of Brain in Healthy Adult Population: Normative Fractional Anisotropy Values at 3 Tesla MRI

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ABSTRACT

Introduction: Diffusion Tensor Imaging (DTI) technique and its clinical application are increasing in clinical routine practice, still very less normative data is available. Awareness regarding regional differences in Fractional Anisotropy (FA) measurements is very important when routinely DTI is used in clinical Magnetic Resonance Imaging (MRI).

Aim: To determine the normative FA values data at 3 Tesla (3T) MRI and to determine the degradation of FA values in various regions of brain values with age.

Materials and Methods: This cross-sectional study involved a total of 52 participants without any abnormal findings (presence of tumour, stroke, infarct, degeneration, etc) and whose brain scanning was performed at 3T MRI, in the Department of Radiodiagnosis, Shree Krishna Hospital, and Pramukhswami Medical College, Karamsad, Anand, Gujarat, India. A DTI protocol was set for the healthy patient's brain scanning. The colour-coded DTI brain images were postprocessed carefully to draw a circular Region of Interest (ROI) in the required areas of white matter and FA values were noted. Descriptive statistics were used to find out the normative data in 11 regions of the brain on right and left side. Pearson correlation was used to check the correlation of FA values with age.

Results: There were 52 patients in the present study, with a male to female ratio of 1.7:1 and a mean age of 52 years. The highest FA values were observed in the splenium (0.809), genu (0.767), the body of the corpus callosum (0.627), and the posterior limb of the internal capsule (0.721), rest areas showed moderate to low FA values. Pearson correlation was used to find the variation in the FA values with age in three age groups 18-40, 41-60 and >60 years, where moderate changes in FA values with age were seen in a few regions of the brain such as genu (right side) with p-value=0.003 and foramen magnum at CVJ level (right side) with a p-value of 0.001.

Conclusion: Generally, FA values intend to change with the presence of multiple tract areas, field strength, coil sensitivity, and partial volume averaging. FA values were also found to be affected with respect to increasing age.

Keywords: Brain stem white matter, Central semiovale, Internal capsule, Magnetic resonance imaging

INTRODUCTION

The constant evolution in MRI techniques and its contrast mechanism has made MRI a powerful tool for the diagnosis of any abnormality related to brain. One of the recent applications of MRI is Diffusion Tensor Imaging (DTI). DTI may be used to plot and distinguish the three-dimensional diffusion of water as a function of spatial location [1,2]. Many developmental, aging, and pathologic conditions of the Central Nervous System (CNS) affect the microstructural architecture of the affected tissues. Diffusion-weighted (DW) MRI techniques, such as DTI and FA, are potent probes for evaluating the impact of disease and aging on microstructure because changes in tissue microstructure and organisation will affect the diffusion of water inside tissues. The most commonly applied quantitative parameters derived from DTI scans are Fractional Anisotropy (FA), which is a measure of the directionality of diffusion, and Apparent Diffusion Coefficient (ADC), which measures the magnitude of the diffusion [3].

As a matter of fact, the applications of DTI are rapidly growing because the technique is highly responsive to changes at the cellular and microstructural levels [4]. These parameters can be calculated by voxel-based morphometric and ROI based measurement. although voxel-wise analysis is not much operator dependent and more easily automated than ROI analysis, it requires inter-subject registration and image smoothing [5,6], which may cause errors in the acquired FA values. In the clinical setting, the ROI-based analysis is more readily applicable.

Despite the increase in the usage of DTI application, comparatively very low normal reference data is available which is measured on 3T MRI scanner. In researchers knowledge there are only three existed studies [7-9] in which FA and ADC values are measured at 3T MRI scanners. They have expanded the previous work by increasing the number of anatomical regions and a number of subjects with different age groups, hence the primary aim was to determine the normal FA values in 11 regions of the brain at 3T MRI. The secondary aim was to find out the correlation of FA values with age in healthy adult population.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Radiodiagnosis, Shree Krishna Hospital and Pramukhswami Medical College, Karamsad, Gujarat, India from April 2020 to August 2022. Institutional Ethical Committee (IEC approval no: IEC/HMPCMCE/117/Faculty/14/77/2020) approval was obtained. Participants were selected following a convenient sampling technique and informed consent was taken from all the participants. Total 52 adult patients were selected and were divided in three age groups: 18-40 years, 41-60 years, and >60 years.

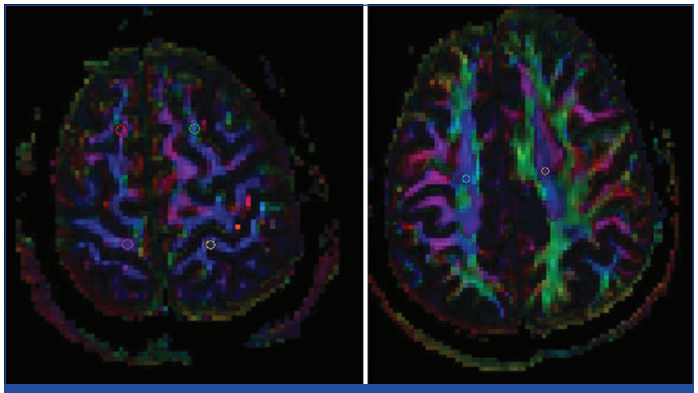
Inclusion and Exclusion criteria: Patients who were referred with clinical indication for MRI scan of brain (without and/or with contrast study} were included in the study as standard care of patient. Patients, who had given informed consent were included in an additional MRI DTI sequence for this research study; which took about 12 minutes of additional time. Patients below the age of 18 years and adults who had needed sedation or anaesthesia for MRI scans were excluded from the study.

Data Acquisition

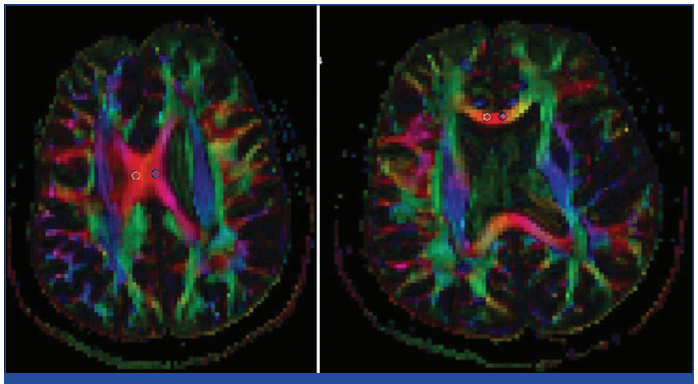
Brain MRI was performed on participants using 3T MRI Siemens spectra scanner, a head/neck 16 channel 3T Tim coil. First a 3D T1W Sagittal T1_mprage_sag_p2_iso, T2 weighted sequence, and coronal flair sequences were obtained for anatomical guidance and to ensure that there were no unexpected abnormal findings. Diffusion tensor MRI was performed using a single shot, spin echo, echo planar DT sequence named as Ep2d_diff_mddw_20p2_dti with TR=7500 ms, TE=103 ms, FOV=220 mm, number of averages=5, acquisition time=9 mins, bipolar gradients applied in 12 directions (max b factor=8000 s/mm^2). None of the subjects had significant abnormalities observed on conventional MRI sequences reported by certified radiologists.

DTI Image Analysis

Carefully and manually, a freehand ROI on colour coded directional maps was drawn, based on principal anisotropy, in 11 different regions on right and left side of brain. Regions were anterior and posterior side of frontal lobe [Table/Fig-1], centrum semiovale [Table/Fig-2], body of the corpus callosum [Table/Fig-3], genu [Table/Fig-4], splenium [Table/Fig-5], posterior limb of internal capsule [Table/Fig-6], midbrain [Table/Fig-7], pons [Table/Fig-8], medulla oblongata [Table/Fig-9] and foramen magnum [Table/Fig-10]. To minimise the influence of taking samples at random sites along the tract, researchers chose certain natural "crossroads or intermediate stations" that are simple to designate, only to ensure that the slices utilised for analysis were as near to the same level as feasible for all of the participants.



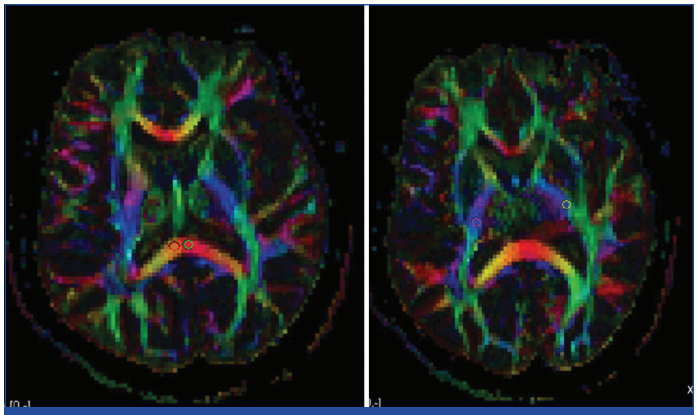
[Table/Fig-1]: Circular ROI at anterior and posterior part of frontal lobe (right and left side). **[Table/Fig-2]:** Circular ROI at centrum semiovale (right and left side). (Images from left to right)



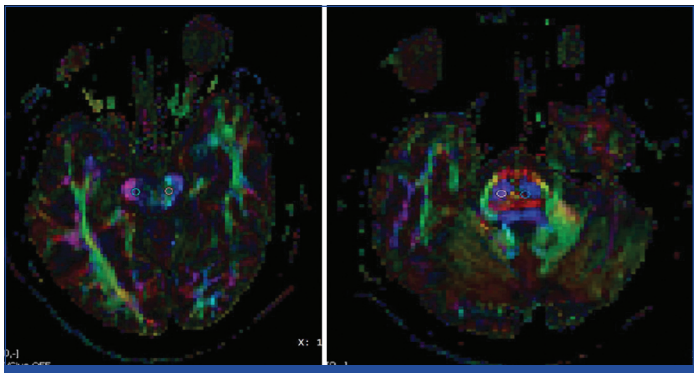
[Table/Fig-3]: Circular ROI at the body of the corpus callosum (right and left side).
[Table/Fig-4]: Circular ROI at the genu (right and left side). (Images from left to right)

STATISTICAL ANALYSIS

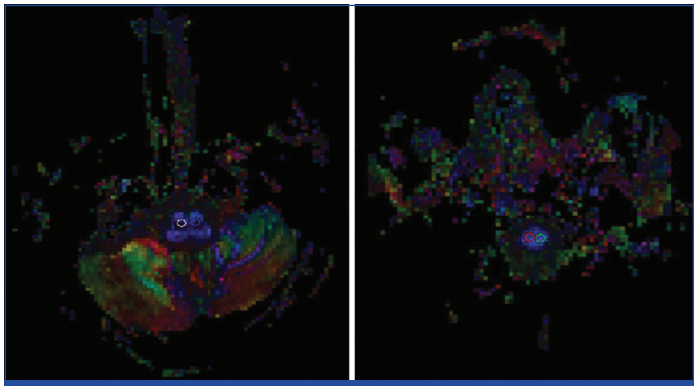
The mean FA and standard deviation for each region of the brain (right and left) were calculated and averaged using descriptive statistics. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software version 20. Pearson correlation was used to find out the correlation of FA values with different age groups.



[Table/Fig-5]: Circular ROI at splenium (right and left side).
[Table/Fig-6]: Circular ROI at posterior limb of internal capsule (right and left side). (Images from left to right)



[Table/Fig-7]: Circular ROI at midbrain (Right and left side).
[Table/Fig-8]: Circular ROI at pons (Right and left side). (Images from left to right)



[Table/Fig-9]: Circular ROI at medulla oblongata (Right and left side).
[Table/Fig-10]: Circular ROI at foramen magnum (Right and left side). (Images from left to right)

RESULTS

Total 52 adult patients were selected with 33 males and 19 females. The mean age of the study participants was 52 years. The majority of the data was normally distributed, so a parametric test was used to check the normality of FA values at 3T MRI. [Table/Fig-11] shows the mean FA values ranged from 0.280 on the right side of the medulla oblongata to 0.820 on the left side of the splenium.

Normally FA values are supposed to be less than one in normal patients and the same was observed in the present study, although minor regional differences were observed in FA values of a few regions which were moderate and within SD of 1. The [Table/Fig-12] shows combined averaged FA values of both sides.

Correlation values <0.5 reflects weak correlation, between 0.50 to 0.70 is moderate and >0.70 reflects strong correlation. In the 18-40 age group, strong positive correlations were observed in the midbrain on both sides (right and left) with statistical significance of 0.006 on right side [Table/Fig-13].

Brain region	Brain region	Standard deviation (SD)
Frontal lobe anterior right	0.413	0.120
Frontal lobe anterior left	0.376	0.154
Frontal lobe posterior right	0.487	0.125
Frontal lobe posterior left	0.441	0.133
Centrum semiovale right	0.430	0.101
Centrum semiovale left	0.444	0.107
Corpus callosum body right	0.624	0.196
Corpus callosum body left	0.630	0.198
Genu right	0.760	0.160
Genu left	0.772	0.140
Splenium right	0.798	0.162
Splenium left	0.820	0.141
Posterior limb of internal capsule right	0.729	0.110
Posterior limb of internal capsule left	0.712	0.117
Midbrain right	0.444	0.120
Midbrain left	0.420	0.125
Pons right	0.504	0.123
Pons left	0.509	0.100
Medulla oblongata right	0.280	0.104
Medulla oblongata left	0.298	0.117
Cervico-medullary junction (CMJ) at foramen magnum level right	0.549	0.131
Cervico-medullary junction (CMJ) at foramen magnum level left	0.556	0.143

[Table/Fig-11]: Descriptive statistics of FA values in different anatomic regions of brain.

Brain region	Average FA (mean±SD)
Frontal lobe anterior	0.395±0.139
Frontal lobe posterior	0.464±0.131
Centrum semiovale	0.437±0.104
Corpus callosum body	0.627±0.196
Genu	0.767±0.150
Splenium	0.809±0.152
Posterior limb of internal capsule	0.721±0.114
Midbrain	0.432±0.123
Pons	0.507±0.112
Medulla oblongata	0.289±0.111
Cervico-Medullary junction	0.553±0.137

[Table/Fig-12]: Averaged FA values of 11 regions of brain combining right and left side.

DISCUSSION

The FA does not cast any unique specific tissue quality, it is affected by tissue hydration, myelination, cell-packing density, and fibre diameter, as well as directional coherence, FA is often utilised as a barometer of white matter tissue integrity [10,11]. It is very well known that regional values of FA changes in healthy brain parenchyma [12]. In present study the FA values were found to be higher in all three parts of corpus callosum (body 0.627, genu 0.767, splenium 0.809) with least FA value in body of the callosum, similarly according to Brander A et al., [12], the body of the corpus callosum had a lower FA than the genu and splenium, which is likely due to its smaller size, which makes its measurement more susceptible to partial volume influence from neighbouring Cerebrospinal Fluid (CSF) gaps. The FA values observed in present study in the three parts of corpus callosum and posterior limb of internal capsule were slightly different from the findings of Lee CEC et al., [7], Huisman TAGM et al., [8], Husnche S et al., [9] [Table/Fig-14], possible reason could be precision and accuracy of the measurement.

The current study is the rarest one where FA values are measured in so many regions of white matter, and hence it was difficult to locate previous studies in which FA values in additional areas, such as the anterior or posterior part of the frontal lobe, centrum semiovale, midbrain, pons, medulla oblongata and cervico-medullary junction were measured at 3T MRI, however the present results [Table/Fig-14] were aligned with the findings of previous studies which showed that high FA values are typically found in white matter areas with constant fibre orientation and closely packed fibres such as corpus callosum, which is a dense bundle of mediolaterally oriented fibres connecting the cerebral hemispheres [12].

The present study findings were consistent with those of earlier studies which reflect that FA values significantly change as the human ages [7,13]. The existing study showed FA values in the posterior limb of the internal capsule in the 19-35 age group were 0.714±0.04, 0.676±0.081 in the 40-65 age group, in the genu of the corpus callosum were 0.806±0.065 in the 19-35 age group and 0.786±0.076 in the 45-60 age group. In Splenium of Corpus Callosum FA values were 0.775±0.052 in the 19-35 age group and 0.777±0.085 in the 45-65 age group [7], however these investigations were restricted to a small number of brain areas.

Lee CEC et al., [7] and Bisdas S et al., [6] investigated age-related changes in white matter microstructure using diffusion tensor imaging and discovered that FA of inferior frontal white matter decreased with age, their finding points to a regional acceleration of white matter degradation as people get older. In 40-60 age group FA values are highly affected in posterior limb of internal capsule. Reduction in FA values suggested that white matter alterations are not limited to prefrontal white matter and that they occur more frequently in the

Brain regions	Correlation coefficient (Age 18-40), n=15	Sig. (2-tailed)	Correlation coefficient (Age 41-60), n=22	Sig. (2-tailed)	Correlation coefficient (Age above 60), n=15	Sig. (2-tailed)
Frontal lobe anterior (right)	-0.093	0.682	-0.264	0.408	0.041	0.884
Frontal lobe anterior (left)	-0.055	0.809	-0.520	0.083	0.029	0.919
Frontal lobe posterior (right)	-0.0264	0.236	-0.373	0.233	-0.097	0.731
Frontal lobe posterior (left)	-0.037	0.870	-0.275	0.388	0.031	0.914
Centrum semiovale (right)	-0.147	0.514	-0.422	0.172	-0.208	0.458
Centrum semiovale (left)	0.284	0.200	-0.626*	0.030	-0.426	0.113
Corpus callosum body (right)	-0.038	0.866	-0.756**	0.004	0.56	0.844
Corpus callosum body (left)	-0.170	0.448	-0.794**	0.002	0.66	0.814
Genu (right)	-0.066	0.770	-0.612*	0.035	-0.703**	0.003
Genu (left)	-0.081	0.719	-0.562	0.057	-0.598*	0.018
Splenium (right)	-0.103	0.944	-0.288	0.364	0.341	0.213
Splenium (left)	-0.291	0.650	0.141	0.663	0.197	0.483
Posterior limb of internal capsule (right)	0.247	0.190	0.155	0.631	-0.129	0.646

Posterior limb of internal capsule (left)	0.565**	0.268	0.158	0.623	-0.456	0.087
Midbrain (right)	0.082	0.006	0.243	0.448	-0.081	0.775
Midbrain (left)	0.174	0.716	0.362	0.247	-0.126	0.655
Pons (right)	0.188	0.440	-0.221	0.489	.009	0.975
Pons (left)	0.255	0.402	0.330	0.294	-0.492	0.062
Medulla oblongata (right)	0.255	0.251	-0.007	0.983	-0.445	0.096
Medulla oblongata (left)	0.018	0.938	0.278	0.382	-0.640*	0.010
Cervico-medullary junction (CMJ) at foramen magnum level right	0.383	0.078	-0.390	0.210	0.767**	0.001
Cervico-medullary junction (CMJ) at foramen magnum level left	0.380	0.081	0.228	0.475	0.499	0.093

[Table/Fig-13]: Correlation of FA values in different regions of brain with three age groups.

Brain region	Current study (n=52)	Lee CEC et al., 3T (n=19) [7]	Huisman TAGM et al., 3T (n=12) [8]	Husnche S et al., 3T (n=7) [9]
Genu	0.767±0.150	0.086±0.065	0.80±0.08	
Splenium	0.809±0.152	0.775±0.052	0.800±0.034	0.77±0.07
Posterior limb of internal capsule	0.721±0.114	0.714±0.049	0.722±0.024	

[Table/Fig-14]: Comparison between FA (mean±SD) measured in the study, and results from published studies at 3T MRI Scan [7-9].

posterior limb of internal capsule than in specific frontal white matter regions [14], however mild to moderate correlation of few areas of brain was observed in 60 above age group. The present study also came up with the DTI protocol which could be utilised for 3T MRI for brain imaging.

Limitation(s)

Limited number of participants in each age group would be less to confirm the degradation of FA values with age.

CONCLUSION(S)

In present study FA values are found to be higher in splenium, genu and body of corpus callosum as compared to the other parts of White Matter that could be due to the composition of multiple and histologically heterogeneous tracts. Moderate correlation of FA values in different age groups are also observed in the study which reflects FA values are found to be significantly affected as the human ages.

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