



ASSESSMENT OF WHITE MATTER OF BRAIN IN REFRACTORY EPILEPSY PATIENTS WITH DIFFUSION TENSOR IMAGING

Radiodiagnosis

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ABSTRACT

Objective: Present study was planned to assess the normal appearing white matter in refractory epilepsy cases and to look for any difference in these areas as compared to age matched healthy control.

Material and method: This was observational study done in tertiary care centre after approval of ethical committee. DTI was done to assess the normal appearing white matter in all lobes of brain in both cases and control. Fractional anisotropy and mean diffusivity were measured in frontal, parietal and temporal lobe white matter.

Results: Fractional anisotropy [FA] of patients with seizures was found to be higher than those with no seizures at both the sides [Right and Left] of frontal, parietal and temporal lobes of the brain. Differences in fractional anisotropy & mean diffusivity between patients with or without seizures were not found to be significant for any of the observation.

Conclusion: Refractory epilepsy being a disease with manifestations appearing early in the disease. DTI is a noninvasively procedure includes no risk to patients. DTI of the patients with and without epilepsy did not show any significant difference in the FA and MD of the normal-appearing white matter in present study. Although further research is needed to evaluate the role of DTI in refractory epilepsy.

KEYWORDS

Fractional anisotropy (FA), mean diffusivity (MD), DTI, refractory epilepsy

INTRODUCTION

Epilepsy is one of the most common neurological conditions in India as well as globally accounting for 1% of the world's burden of disease resembling lung cancer in men and breast cancer in females. [1]. Refractory epilepsy is defined as- "failure of adequate trials of two tolerated, appropriately chosen, and used antiepileptic drug schedules [whether as monotherapies or in combination] to achieve sustained seizure freedom". (1) Failure of first antiseizure drug is one of the predictor for refractory epilepsy. (2)

Some cases with refractory epilepsy show focal or diffuse abnormality on conventional MRI, however majority of case did not show any abnormality on MRI. Diffusion tensor imaging is new MRI technique that assess the functional and structural organization of the brain. It based on the principle of diffusion of water molecules in the brain.

DTI measures directionality and rate of the displacement of water molecules in the brain. (3) The Fractional Anisotropy (FA) and mean diffusivity (MD) are two parameter that are derived by DTI data.

The fractional anisotropy (FA) assess the degree of anisotropic diffusion occurring within a region. FA measure the functional integrity and specific organization of myelinated axonal fibers. Zero FA denotes the equal diffusion in all directions. FA values of one denotes the diffusion in only one direction. Due to the presence of myelinated fiber bundles, anisotropy tends to be higher in the white matter compared with the gray matter, and greater in parallel running white matter fiber, such as the corpus callosum. (3, 4) Present study was planned to see the changes in white matter of the refractory epilepsy.

MATERIALS AND METHODS

This present research took place at the Department of Radiodiagnosis, at tertiary care hospital. This is an observational study which included the 10 cases of refractory epilepsy & 25 control subject. Conventional MRI with diffusion tensor imaging of all cases and control done. Institutional ethic committee approved the study. Informed consent was taken from all patients.

Equipment used

- 3 Tesla Signa HDxt MRI [General Electric, Milwaukee, WI] with Nordic neuro lab's functional MRI.

INCLUSION CRITERIA

- Patients diagnosed with refractory epilepsy.

- Patients with normal conventional brain MRI.

EXCLUSION CRITERIA

- Patients with metallic implants or any other contraindication of MRI.
- Patients unwilling to undergo MRI.

The study was done in patients diagnosed with refractory epilepsy in Neurology OPD and were sent to the Department of Radiodiagnosis for MRI evaluation. All the patients who came for an MRI brain fulfilling the inclusion criteria were explained about the study and their consent was taken. The patients with metallic implants incompatible with MRI were excluded from the study. Patients unwilling to undergo MRI patients were also excluded from the study.

The patients were explained in detail about the procedure and consent was taken. Total of 35 cases (10 cases and 25 controls) underwent DTI sequence along with other conventional MRI sequences. Closely matched patients with no history of epilepsy who came for some other cause (mostly headache) and did not have any apparent lesion on MRI underwent DTI evaluation as a control subject. DTI sequences of the patient was evaluated on GE console. The fractional anisotropy and average diffusion maps were evaluated simultaneously with ROI of 30 mm². The fractional anisotropy and average diffusion coefficient were measured from white matter of bilateral frontal white matter above the level of lateral ventricles, bilateral high parietal white matter and bilateral temporal lobe white matter. During all the sequences the patient was monitored and guided, if required from the console through a transparent mirror.

OBSERVATION & RESULT

The present study was conducted in the Department of Radiodiagnosis, Ram Manohar Lohia Institute of Medical Sciences, Lucknow to study the changes on DTI in patients of refractory epilepsy and to compare the changes with control. Patients with history of refractory epilepsy underwent DTI and FA & Mean diffusivity was measured. Closely matched patients with no history of epilepsy were taken as control and underwent DTI.

Table 1: Association of Seizure and Demographic Profile

SN		No seizure [n=25]	With seizure [n=10]	Total [N=35]
1-	Mean age±SD [Range]	47.88±18.42 [16-85]	31.00±17.19 [11-65]	43.06±19.43 [11-85]

	t'=2.493; p=0.018 [Sig]						
		No.	%	No.	%	No.	%
2-	Gender						
	Female	11	44.0	5	50.0	16	45.7
	Male	14	56.0	5	50.0	19	54.3
	X ² =0.104; p=0.748						

Age of patients enrolled in the study ranged from 11 to 85 years, mean age was 43.06±19.43 years. Mean age of patients with seizures was found to be significantly lower than that without seizures (31.00±17.19 vs. 47.88±18.42 years).

Out of 35 cases, 19 [54.3%] were male and rest 16 [45.7%] were female. Patients of refractory epilepsy without seizure comprised 56.0% males and rest females while those with seizures had equal representation of males and females (50% each) (table-1

Table 2: Association of Seizure with Average Fractional Anisotropy [FA] at different locations of brain

Location	Seizure	No.	Mean	SD	Range	
					Min.	Max
Frontal Lobe						
Right	No seizure	25	0.26	0.09	0.04	0.48
	Seizure	10	0.31	0.08	0.20	0.49
	t'=-0.659; p=0.515					
Left	No seizure	25	0.23	0.08	0.13	0.50
	Seizure	10	0.28	0.07	0.17	0.42
	t'=-1.079; p=0.289					
Parietal Lobe						
Right	No seizure	25	0.35	0.10	0.18	0.59
	Seizure	10	0.40	0.09	0.29	0.57
	t'=-0.865; p=0.393					
Left	No seizure	24	0.34	0.08	0.21	0.60
	Seizure	10	0.37	0.07	0.25	0.52
	t'=-1.662; p=0.106					
Temporal Lobe						
Right	No seizure	25	0.28	0.06	0.17	0.45
	Seizure	10	0.32	0.10	0.18	0.49
	t'=-0.619; p=0.540					
Left	No seizure	25	0.27	0.06	0.16	0.37
	Seizure	10	0.24	0.07	0.16	0.35
	t'=1.299; p=0.203					

Fractional anisotropy [FA] of patients with seizures was found to be higher than those with no seizures at both the sides [Right and Left] of frontal, parietal and temporal lobes of the brain. Differences in fractional anisotropy between patients with or without seizures were not found to be significant for any of the observation. (table-2). Mean Diffusivity of patients with seizure were found to be higher than that of with no seizures at both sides [Right and Left] of frontal lobe, parietal lobe and on left side of temporal lobe however without any significant difference. (p value-0.5)

DISCUSSION:

Refractory epilepsy is defined as- "failure of adequate trials of two tolerated, appropriately chosen, and used antiepileptic drug schedules to achieve sustained seizure freedom". This definition was developed primarily to provide an operational definition to guide the clinical management of patients. (5,6).

In a study by Gesche et al. in 2008, 499 patients of refractory epilepsy were included in the study to study the epidemiology of the disease. About 92.1% of the refractory epilepsy patients were diagnosed before the age of 25 years. (7) In the present study, the mean age patients with seizure was found to be significantly lower than the control group without seizure (31.00±17.19 vs. 47.88±18.42 years).

In a study by Laboto et al. in 2018 (8), 40 adults with idiopathic epilepsy syndrome were grouped into refractory and non-refractory epilepsy group and underwent DTI. The study measured fractional anisotropy and mean diffusivity of various white matter tracts. The study concluded that there was no significant difference in fractional anisotropy values and mean diffusivity between refractory and non-refractory epilepsy patients. Similar to the findings of our study they concluded a uniform increase in mean diffusivity in epilepsy groups. However, unlike our study which showed a small increase in FA of

white matter in the epilepsy cases, Laboto et al. noticed a decrease in fractional anisotropy in both the groups. (8)

In a study by Liang et al. in 2016, (9) 18 case of absence seizure and 10 controls were evaluated using fractional anisotropy, mean diffusivity, parallel and perpendicular diffusivity. The study did not find and significant difference in FA and MD in the white matter of the brain except genu corpus callosum. This study also found similar results with no significant difference in FA and MD in bilateral white matter tracts in all the 3 lobes of cerebral hemispheres. Result of present studies matches with studies done previously, however few studies showed significant changes in specific brain areas, that need to be evaluated further.

CONCLUSION :

DTI of patients with and without refractory epilepsy did not show any significant difference in the FA and MD of the white matter in present study. However few studies showed changes in specific brain areas like corpus callosum. Further research is needed to evaluate the role of DTI in refractory epilepsy in specific brain areas.

Acknowledgment : none

Conflict of interest : none

REFERENCES

1. Chaudhary K, Kumaran SS, Chandra SP, Wadhawan AN, Tripathi M. Mapping of cognitive functions in chronic intractable epilepsy: Role of fMRI. Indian J Radiol Imaging. 2014;24[1]:51-6.
2. Madden DJ, Whiting WL, Huettel SA, White LE, MacFall JR, Provenzale JM. Diffusion tensor imaging of adult age differences in cerebral white matter: relation to response time. NeuroImage. 2004 Mar;21[3]:1174-81.
3. Sridharan R, Murthy BN. Prevalence and pattern of epilepsy in India. Epilepsia. 1999 May;40[5]:631-6.
4. Granados AM, Orejuela JF, Rodriguez-Takeuchi SY. Neuroimaging evaluation in refractory epilepsy. Neuroradiol J. 2015 Oct;28[5]:529-35.
5. Kalilani L, Sun X, Pelgrims B, Noack R, Rink M, Villanueva V. The epidemiology of drug-resistant epilepsy: A systematic review and meta-analysis. Epilepsia. 2018;59 [12]: 2179-93.
6. Chen Z, An Y, Zhao B, Yang W, Yu Q, Cai L, et al. The value of resting-state functional magnetic resonance imaging for detecting epileptogenic zones in patients with focal epilepsy. PLOS ONE. 2017 Feb 15;12[2]:e0172094.
7. Gesche J, Christensen J, Hjalgrim H, Rubboli G, Beier CP. Epidemiology and outcome of idiopathic generalized epilepsy in adults. Eur J Neurol. 2020 Apr;27[4]:676-84.
8. Lobato M, Garcia L, Amaro E, Otaduy M, Jorge C, Castro LH. Analysis of fractional anisotropy and mean diffusivity in refractory and non-refractory idiopathic generalized epilepsies. Seizure - Eur J Epilepsy. 2018 Nov 1;62:33-7.
9. Liang J-S, Lee S-P, Pulli B, Chen JW, Kao S-C, Tsang Y-M, et al. Microstructural Changes in Absence Seizure Children: A Diffusion Tensor Magnetic Resonance Imaging Study. Pediatr Neonatol. 2016 Aug 1;57[4]:318-25.