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Research Paper

Mapping of motor and visual areas in refractory epilepsy by functional MRI

AUTHOR

ABSTRACT
Introduction *Functional MRI (fMRI) has been used to enhance the understanding of neuroanatomy and functions of the brain and is becoming an accepted brain-mapping tool for clinicians and researchers . One of major use of fMRI in presurgical mapping of motor, language and memory functions, It is a noninvasively procedure includes no risk to patients*
Objective *present study was planned to map the cortical motor and visual areas in refractory epilepsy cases and to look for any difference in these activated areas as compared to age matched healthy control.*
Material and method *This was observational study done in tertiary care centre. Study include the 15 cases and 15 control fMRI was done to map the visual and motor areas. Specific task was given to activate motor and visual areas during fMRI.*
Results *FMRI accurately map the visual and motor areas in brain after giving particular specific task. Right and left hand motor areas activation were seen precentral gyrus. Visual areas activation was seen in occipital cortex. No difference in cases and control noted regarding pattern of motor and visual areas activation.*
Conclusion: *FMRI is noninvasive tool to map the motor and visual areas in refractory epilepsy cases. These mapping are important for presurgical planning . Major limitation of study includes the cases who can not performed these task due to neurological deficit or cognitive impairment .*

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I. INTRODUCTION

Among the very common neurological cases in our country, Epilepsy is included as it globally accounts to 1% of the world's burden of disease resembling lung cancer in males and breast cancer in females [1]. One study estimates the worldwide affected population to be about 50 million [2]. World's 10% population will suffer from at least 1 seizure in their lifetime [1]. Epilepsy commonness in our country is around 5.59/1000 [3] Antiepileptic drugs are the 1st line medications used primarily to control seizures. However, out of 10 patients are refractory to treatment [4]. Pharmaco -resistant epilepsy cannot be taken literally as it is almost impossible to try all the permutations and combinations of anti-epileptic drugs on a patient to label his/her epilepsy as refractory [1]. Refractory epilepsy **-** "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 1st appropriate antiseizure drug, due to its efficacy and not due to intolerance, is the best predictor for refractory epilepsy.

India refractory epilepsy is estimated to constitute 20-30% of the epilepsy. Epilepsy with no obvious identifiable cause is expected to be 6/100,000/year and commonness of 2-3 per 1000 (>1 episode/year). The objectives for the treatment of epilepsy are no side effects along with no seizure as soon as possible.

It is important to do a presurgical evaluation to demonstrate that epileptogenic seizures are originating within the area planned to be resected and to localize the epileptogenic region. fMRI has a contributory part in the presurgical planning as it helps to correlate the anatomical structures with their function [4].

The primary contrast used in fMRI is blood oxygen level-dependent [BOLD]. BOLD contrast is easily obtained and provides a high signal to noise ratio. Thus, it is the method of choice for functional MRI. Stimulation of neurons increases energy and oxygen consumption in operational regions. Subsequently fMRI measures changes in hemodynamics due to neurovascular coupling [12]. Oxy and deoxy haemoglobin have differences in their magnetic features and thus they are basis of BOLD technique [13, 14].

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Almost each and every fMRI research comprises of time-series information that is gathered with the use of snapshot imaging techniques where volume of the brain is sampled in the interval of 1-3 sec [7]. Most fMRIs use block design (fig-2) which employs 2 states of 'active' and 'resting' alternating with each other (resting; Task; resting; task….). Each state is of specified time period together forming a particular duration of the sequence being done. As large signal changes are sustained, this approach maximizes sensitivity [7].

fMRI in epilepsy is useful due to a variety of reasons. Motor, visual, memory and language regions of pre-surgical motor mapping are the most researched clinical applications in fMRI of intractable epilepsy [2] [7]. fMRI can recognize, plot and help in preserving crucial regions of brain that are related to presurgical assessment.

A surgeon can make use of preoperative fMRI by describing the motor, language and memory regions for optimization of perioperative planning for increasing the tumor resection [8-10]. At the same time, it decreases the harm in the regions nearby. Determining a surgical resection is dependent largely upon the anatomic areas of tumor in expressive cortices. People have functional cortices situated in the different places and they can be impacted from lesion and/or related cortical rearrangement. Therefore, it might not be the same as estimated anatomic locations [11]. Through fMRI, it is possible to clear the anatomy in certain patients and identify the non-uniformities. When a tumor invades eloquent cortices, all such details can prove to be increasingly significant [11].

We can depend on functional plotting of sensory and motor systems more in comparison to language plotting. Somatosensory cortex is situated at the postcentral gyrus behind the central sulcus. Motor cortex is situated in precentral gyrus in front of central sulcus. Electrocortical stimulation helps in recognizing central sulcus at the time of the surgery. fMRI can be helpful before the surgery and later help in changing the surgical planning.

Present study was done for cortical mapping of motor and visual areas in patients of refractory epilepsy.

II. MATERIAL AND METHOD

This present research took place at the Department of Radiodiagnosis, at tertiary care hospital .This is an observational study which included the 15 cases of refractory epilepsy . Functional MRI of cases done by giving motor and visual task for the mapping of cortical motor and visual areas. Institutional ethic committee approved the study. Informed consent was taken from all patients. A total 15 age matched control were also taken who had normal conventional MRI brain. fMRI of control was done in similar way.

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 no significant abnormality in routine blood or any other investigation suggestive of cause for behavioural abnormality in epilepsy.
- A patient who is willing to undergo f-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 Radio diagnosis 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.

Patient was taken into the MRI room after checking for any metallic object in or on the patient's clothing. The patient was once again briefly explained about the procedure inside the MRI room with patient's display in front of the MRI table. The patient was asked to lie down on the MRI table with HNS brain coil placed on the head. A reflecting mirror as used to reflect the image of the patient's display to the patient's eyes. Patient's comfort was ensured so as to prevent any motion due to discomfort during the MRI.

The patient while undergoing MRI could see the display placed in front of the patient through a mirror fixed on the brain coil. The patient on seeing the cue on the screen would start to respond to it accordingly, for example in case of motor fMRI the patient would start pressing the response box buttons or just clench his fists. Block design method was used with 30 seconds of activation phase and 30 seconds of baseline phase for a total of 4mins 30 seconds. The sequences used in the study include-

1. Right hand motor

2. Left hand motor
3. Visual checkerboard

After running a structural sequence (here SPGR3D) (TR- 7.8, TE- minimum-3 and maximum -12, FOV- 24, Thickness- 1.2. scan time of 4min 59 sec) the motor sequence was done, first right and then left hand. The BOLD sequence was done with specifications as follows- gradient echo- echo planar imaging, TR- 3000 ms, TE- 35 ms, FOV- 26, Thickness- 5mm, spacing - .5mm, total slices-25, NEX- 1.00, flip angle- 90-degrees, acquisition time- 4min 30 sec

During the motor sequence the patient was asked to open and close the fist when the green light blinks on the screen and to stop when it disappears. The hand corresponded to the side of screen on which the light blinks i.e. right hand when the light blinks on right side of the screen (fig 1a & b) and left hand when it blinks on the left. The whole sequence was of 4 minutes and 30 seconds-30 seconds of active phase alternating with 30 seconds of baseline phase. At the end the results were saved and next sequence was started.

For visual assessment checkboard method was used. The patient was asked to look at the screen. The screen displayed a checkerboard during the active phase and a black screen during the baseline phase. (Fig 2)

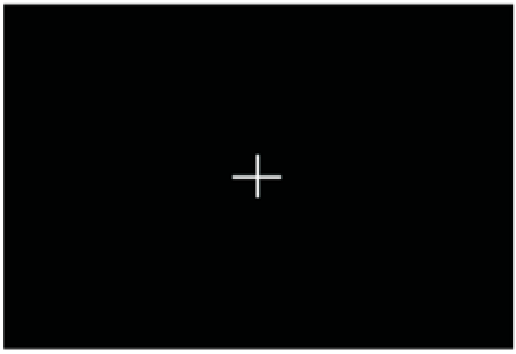


Fig1a

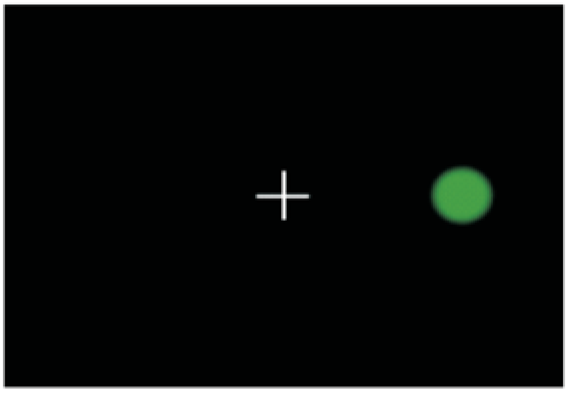


Fig 1 b

Screen during baseline phase of motor (fig 1 a). Screen during the active phase of right hand motor (fig 1 b)

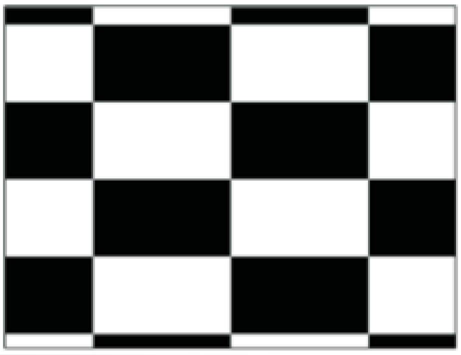


Fig 2 – Screen during the active phase of visual (visual checkerboard)

III. RESULTS

Out of 30 subjects enrolled for assessment of BOLD fMRI, 15 [50.0%] subjects were diagnosed cases of refractory epilepsy and 15 [50.0%] were controls. Mean age of Cases was 26.27±8.05 years while that of Controls was 26.20±1.15 years. Difference in age of Cases and Controls was not significant statistically. (Table-1,)

Table 1: Comparison of Demographic Profile of Cases and Controls

SN		Cases [n=15]		Controls [n=15]		Total [N=30]	
1-	Mean age±SD [Range]	26.27±8.05 [17-38]		26.20±1.15 [23-28]		26.23±5.65 [17-38]	
	‘t’=0.032; p=0.975						
		No.	%	No.	%	No.	%
2-	Gender						

	Female	4	26.7	7	46.7	11	36.7
	Male	11	73.3	8	53.3	19	63.3
	χ^2=1.292; p=0.256						

Out of 15 cases of refractory epilepsy only 4[26.7%] were females and rest were males [73.3%] while among controls 7 [46.7%] were females and rest 8 [53.3%] were male. Despite difference in Gender ratio of cases and controls, the difference was statistically insignificant. (Table-2,)

No abnormality on MRI was observed in any of the control subjects. Abnormal MRI was found in 6 [40.0%] out of 15 cases and all of them had abnormality in the form of some focal lesion (example cavernous hemangioma, NCC etc.) (Table -2).

Table 2: Comparison of radiological features of Cases and Controls

SN		**Total [n=30]**	**Cases [n=15]**		**Controls [n=15]**		**Statistical significance**	
			No.	**%**	**No.**	**%**	**χ^2**	**'p'**
1-	Focal lesion present	6	6	40.0	0	0.0	7.500	0.006
2-	Bold Signals at lesion	[n=6]	[n=6]					
	Abnormal	0	0	0.0				
	Normal	6	6	100.0				

fMRI was able to localize right and left motor areas in premotor cortex of contralateral sides on BOLD scans in all the cases and controls [Fig-3 & 4]. Similarly, visual area was localized normally in occipital cortex in all cases and controls (Fig 5). No case with focal lesion on MRI showed any abnormal BOLD signal at the site of the lesion. Moreover, none of the refractory epilepsy cases showed any abnormal BOLD signal on fMRI.

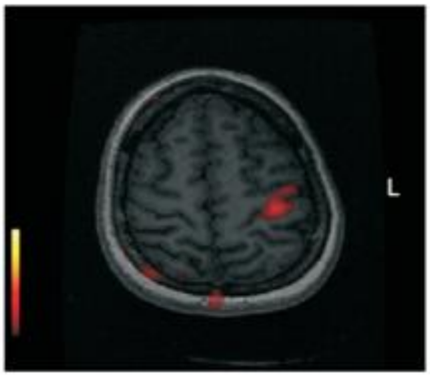


Fig 3 a

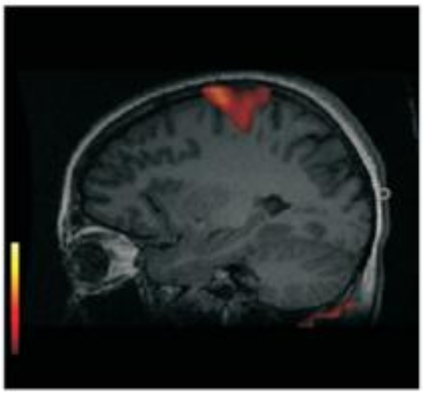
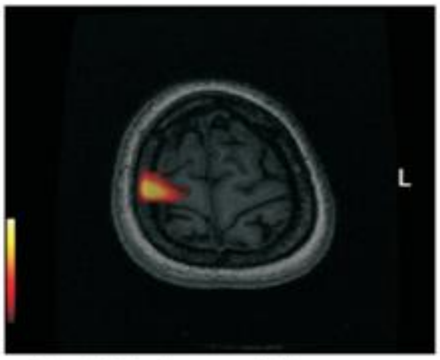


Fig 3 b

Fig 3 (a & b). Axial and sagittal MRI with BOLD showing right hand motor area in left motor cortex .



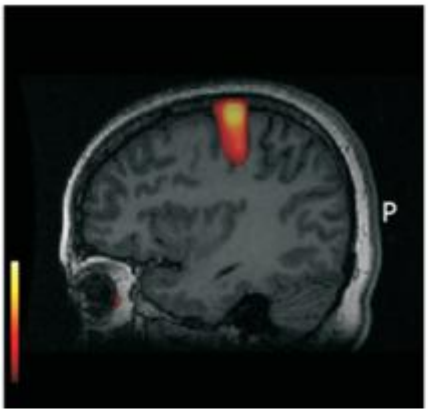


Fig 4 (a & b). Axial and sagittal MRI with BOLD showing left hand motor area in right motor cortex.

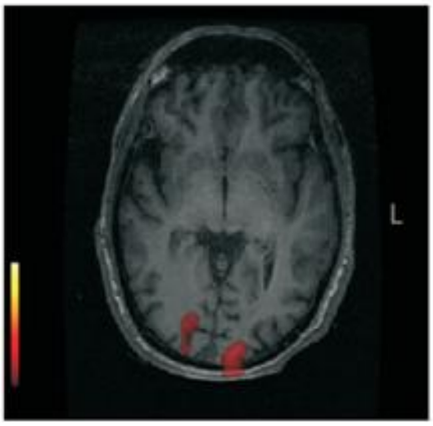


Fig 5 Axial MRI with BOLD showing visual area in bilateral occipital area

IV. DISCUSSION

Refractory epilepsy "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" [12].

Gesche et al. conducted a research in 2008 where 499 refractory epilepsy patients 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 [14]. Current research has the mean age of refractory epilepsy cases at 26.27 years with a range of 17-38 years that is the same as findings in the research of Gesche et al.

In a study by Mukherjee et al. in 2016-17 on 2153 patients, the study found that refractory epilepsy comprised 11.3% cases of epilepsy. The median age of refractory epilepsy cases in the study came out to be 12.7 years which was significantly lower than the median age found in the present study (26 years) [15].

The study also found that out of 2153 patients enrolled in the study 63% were males and 37% females. In contrast, the present study found 73.3% males and 26.7% females suffering from refractory epilepsy which emphasizes the higher proportion of males affected with refractory epilepsy. This difference was not found to be clinically significant and could be attributed to the higher proportion of males in the general population.

Hsu et al. in the year 2020 stated that trained radiologist when employ dedicated MR imaging protocols in refractory epilepsy patients, they can see structural irregularities in up to 85% of occurrences including mesial temporal lobe sclerosis (unilateral or bilateral), developmental cortical malformations (including disorders of neuronal migration, proliferation or organization) and tumors such as gangliogliomas, dysembryoblastic or neuroepithelial tumors which can be a cause for epilepsy [16]. However, the present study found focal lesions on MRI in just 40 % of the cases of refractory epilepsy which is significantly lower than what is stated by the above study.

Oertzen et al. did a study on epilepsy patients to localize focal lesions on MRI using epilepsy expert and non-expert radiologists. Focal lesions were observed in half of the standard MRI scans compared to 40% in the present study [17]. Considering this institute, a referral center for epilepsy in north India the radiologists in the institute can be addressed as experts in epilepsy MRI evaluation.

In a study by detre et al. in 1995 studied a case of partial motor seizure on fMRI. The seizures were refractory to anti-epileptic treatment. An excellent concordance was shown between the localization of the seizure focus by fMRI and infiltrative monitoring. Clinical enhancement that comes after focal resection assists the ictal onset localization [18]. Contrastingly, in this study, none of the cases showed any abnormal BOLD signal indicating epileptogenic focus.

Localizing the pertinent brain regions precisely is significant in presurgical planning because it optimizes resection and reduces postoperative neurological inadequacies. Electro-cortical stimulation (ECS) is a process where brain functions are intraoperatively plotted. It is quite dependable though there are cons such as it is used intra-operatively only. There are times when it may generate improper findings because of anesthesiological problems [15]. The major use of fMRI in epilepsy is presurgical planning to reduce post-operative neurological deficits. fMRI being a non-invasive procedure is the ideal investigation for mapping brain areas for presurgical planning.

A study done by DeYoe EA et al. [19] using the checkerboard patterns for activation of visual areas in brain. This study showed BOLD fMRI signal in visually responsive brain areas. Present study also used the checkerboard patterns for visual areas activation. BOLD fMRI signal noted in bilateral occipital regions as shown in this study. Both cases and control shows the bilateral occipital area signal change. No difference in cases and control noted regarding pattern of visual areas activation. A study done by Stathopoulos C et al [20].

showed signal changes in precentral gyrus behind central sulcus on BOLD fMRI using the finger tapping test. Present study also showed the similar activation of motor areas in precentral gyrus. Right hand motor areas activation seen left motor cortex and vice versa. fMRI with BOLD accurately map the motor and visual areas in refractory epilepsy cases. Mapping of motor and visual areas were done accurately by fMRI using task to activate these areas. Thus fMRI noninvasively map the motor and visual areas which are vital to presurgical planning in epilepsy cases. Major limitation of fMRI in patients who cannot perform the task to activate the cortical areas because of neurological deficits or neurocognitive state.

V. CONCLUSION

fMRI seems to be quite crucial while comprehending brain mechanisms, operations and patterns along with localizing motor, speech and cognitive operations. There are several pros in comparison to rest of the neuroimaging and functional plotting techniques. It does not infiltrate, radioactive isotopes are not used, it can be repeated without any risks or stakes. Presurgical mapping of motor, visual, language and memory areas has seen the most researched clinical use of fMRI in intractable epilepsy.

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