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Use of Magnetic resonance imaging and Diffusion tensor weighted imaging in intractable epilepsy

Radiology

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ABSTRACT 506 patients with intractable epilepsy were assessed using magnetic resonance imaging (MRI) and Diffusion Tensor Weighted Imaging (DTWI) to identify structural lesions. A significant proportion of patients in MRI presented with Malformation of cortical development (MCD), Mesial temporal sclerosis (MTS) and non specific lesions. DTWI could identify various white matter abnormalities in same side or in bilateral hemispheres. Though the MRI revealed structural abnormalities at one hemisphere, the DTWI revealed white matter abnormalities in same or both hemispheres. In addition patients suffering from complex partial seizure and MRI (without any abnormalities) revealed white matter abnormalities in various region of interest studied bilaterally or unilaterally. Thus the epileptic network in intractable epilepsy is extensive and stresses the need to study further.

Introduction:

Intractable epilepsy or drug resistant 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. (ILAE, 2010) (Kwan et al., 2010). One of the important causes of intractable epilepsy is MTS (Thom & Bertram, 2012). The clinical presentation of MTS is complex partial seizure of temporal lobe origin. The MRI studies in these patients reveal hippocampal sclerosis unilaterally (right or left) and bilaterally (Kuzniecky et al., 1987; Thom & Bertram, 2012). MTS is often associated with dual pathologies such as MCDs (Thom & Bertram, 2012). Magnetic resonance imaging studies in patients with intractable childhood epilepsy shows a prevalence rate of MCDs ranging from 25% to 40% (Barkovich, Guerrini, Kuzniecky, Jackson, & Dobyns, 2012; Kuzniecky et al., 1987; Leventer, Guerrini, & Dobyns, 2008). The following types of MCD are associated with MTS, such as Focal cortical dysplasia (FCD), Poly microgyria, Lissencephaly, Nodular heterotopias, dysembryonic neuroepithelial tumor and Hemimegalencephaly are reported in MRI studies in patients with intractable epilepsy(Leventer et al., 2008; Mathew, Srikanth, & Satishchandra, 2010; Sporis et al., 2008).

Diffusion Tensor Weighted Imaging (DTWI) is a recently developed MRI technique which has gained importance over time to assess abnormalities with focal epilepsy (Arfanakis et al., 2002; Diehl et al., 2005; Gross, Concha, & Beaulieu, 2006). DTWI measures the molecular motion of water in tissue at various directions in every voxel, providing information regarding the microstructure of the white matter & grey matter, cellular packing, cellular loss or regional edema in focal status epilepticus (Hagmann et al., 2006). In DTWI, Apparent Diffusion Coefficient (ADC) and Fractional Anisotropy (FA) are the commonly recorded tensors in structural MRI (Hagmann et al., 2006; Tuch, Reese, Wiegell, & Wedeen, 2003). Interictal DTWI studies are reported to be more sensitive in identifying hippocampal involvement rather than conventional MRI in TLE (Wehner et al., 2007). Interictal imaging studies in patients with medial temporal lobe epilepsy associated with hippocampal sclerosis showed diffusion abnormalities involve a pathologic hippocampaus and larger network involvement (Thivard et al., 2005). DTWI in patients with epilepsy and MCD have shown changes in tissues beyond the areas of MCDs which appeared normal on conventional MRI (Eriksson, Rugg-Gunn, Symms, Barker, & Duncan, 2001). Patients with partial seizures and normal MRI findings showed various areas with abnormal anisotropy or diffusion, which were normal in conventional MRI (Rugg-Gunn, Eriksson, Symms, Barker, & Duncan, 2001). Interictal studies in TLE patients who showed normal MRI study presented with bilateral and extratemporal lobe involvement in DTWI (Gross et al., 2006). In TLE, lateralization of the epileptogenic region using DTWI studies highly correlates with the presence of unilateral hippocampal sclerosis on conventional MRI (Assaf et al., 2003).

From the review of literature, there are ample evidences of DTWI abnormalities unilaterally or bilaterally when MRI studies of brain are normal or abnormal. Since these DTWI studies have been carried out in a small group of intractable epilepsy patients with few regions of interest (ROI), we conducted a study using MRI and DTWI to identify various structural lesions of brain in 506 patients with intractable epilepsy.

Aims:

1) To identify various structural lesions in the brain associated with intractable epilepsy using MRI and DTWI
2) To associate the side of lesion in conventional MRI and DTWI.

Material and methods:

Subjects:

A prospective study of intractable epilepsy was carried out during September 2011 to September 2014 at the epilepsy clinic, Department of Neurology, Institute of Neurology, Rajiv Gandhi Government Hospital, Chennai. A total number of 3000 patients were screened to identify patients with intractable epilepsy. Patients who fulfilled the criteria for intractable epilepsy as defined by International League Against Epilepsy (ILAE) were considered for the present study. A total of 506 patients (294 males and 212 females) found to be suffering from intractable epilepsy and were assessed using MRI and DTWI. Written Informed consent from each subject and approval by the local ethical committee of the hospital were obtained.

Conventional MRI protocol:

All the subjects underwent conventional MRI and DTWI imaging on a 1.5T, 48 channel System (Seimens Aera, Germany) using a head coil (40 element), Gradient strength of 45mT & flow rate of 200 Mt/sec. MRI protocol consisted of axial T1 weighted sequence (T_1), axial T_2 weighted sequence (T_2) and volumetric T1 weighted MRI (3D – SPGR) sequence. These images were analyzed by experienced neuroradiologists who detected the MCDs and hippocampal malformations.

DTWI Protocol:

DTWI was performed in the axial plane by using single-shot echoplanar imaging with the following parameters: TR/TE, 3500/83 ms; diffusion-gradient encoding in 20 directions ;b0, 1000 s/mm^2; FOV, 230 X 100 mm; matrix size, 128 X 128; section thickness, 5 mm; band width- 1500, EPI factor- 128 average - 3 and number of signals were acquired. Standard DWI acquires data in three orthognal planes (typically X, Y, and Z axis). Acquisition was repeated with gradients oriented in each of the 3 directions in space. With 2 acquisitions with different b-factors (typically b = 0 and 1000 s/mm2), it becomes possible to calculate the apparent diffusion coefficient (ADC) without the T2. While ADC maps reveal the tendency of the water molecules to diffuse within a voxel, directional variation is also required to image 3D anisotropic diffusion. The complex mathematical equation used to model 3D anisotropy is called tensor. Images were transferred to a separate multi modality work station (Siemens MMWP) - Neuro 3D software for post processing. Maps of FA and ADC were calculated at various region of interest especially in Frontotemporal fasciculus, fronto perital fasciculus, temporoparieto fasciculus, temporo occipital fasciculus, parieto occipital fasciculus, uncinate fasciculus, hippocampal and parahippocampal region, fornix and fimbrae, cingulated gyrus to identify various tracts or regions which are involved in maintenance of normal brain function.

Results:

MRI:

Most common abnormality (32.02%, n=162) that was observed in patients with intractable epilepsy were Mesial temporal sclerosis (MTS). Following MTS, non specific lesions that include cortical atrophy, periventricular white matter calcifications were commonly observed in 15.61% (n=79) of the population. Neoplastic and nonneoplastic lesions including gliosis, cyst, vascular malformations, Hemorrhage and infective lesions were observed in 12.06% (n=61%). Malformations of cortical development were observed in 9.88% (n=50) of patients with intractable epilepsy. Incomplete hippocampal inversion was observed in 35 patients with intractable epilepsy that constitute 6.92% of the total population studied. Commonly lesions were observed on left side (35.57%, n=180), compared to bilateral (23.52%, n=119) and right sided lesions (17.39, n=88). 119 (23.52%) patients with intractable epilepsy did not show any abnormalitlies in 1.5Tesla MRI. Various abnormalities in MRI were summarized in table 1.

Table 1: structural abnormalities in MRI

Structural abnormalities	n	%
MCD	50	9.88
MTS	162	32.02
IHI	35	6.92
Neoplastic and Non neoplastic lesions	61	12.06
Gliosis	29	5.70
Cyst	5	.98
Infarction	12	2.37
Arteriovenous malformations	6	1.18
Inflammation and Infections	5	.98
Hemorrhage	2	.39
Neoplastic	2	.39
Nonspecific lesions	79	15.61
Cortical atrophy	11	2.20
Calcifications	68	13.43

DTWI findings:

Diffusion tensor weighted images (DTWI) showed increased FA (fractional anisotropy) values and decreased ADC (apparent diffusion coefficient) values in one or several regions in the brain among the various regions interest considered for the present study. DTWI were significantly abnormal in 406 (80.23%) intractable epilepsy patients. 158 (31.23%) patients showed left sided abnormality followed by bilateral (30.24%) and right sided (17.39%) abnormality. The areas of interest considered for the present study were Frontotemporal fasciculus, frontoparietal fasciculus, temporoparietal fasciculus, temporooccipital fasciculus, parietooccipital fasciculus, uncinate fasciculus, hippocampal and parahippocampal region, thalamus, corpus callosum, fornix and fimbrae and cingulate gyrus. 217 patients especially patients with MTS showed abnormal DTWI values in hippocampal and prahippocampal regions. Also abnormal ADC and FA values were observed in higher frequencies at middle cerebellar peduncle, uncinate fasciculus, temporooccipetal fasciculus, temporoparietal fasciculus, fimbrae, fornix, thalamus and corpus callosum. Also involvement of cingulate gyrus, parito occipital fasciculus, fronto parietal fasciculus, uncinate fasciculus were less commonly observed in patient with intractable epilepsy as seen in Table 2.

Table 2: Number of patients with abnormal ADC and FA values in DTWI across various regions of interest

Regions of interest	**No. of patients (N=506)**
Hippocampal and parahippocampal region	**217**
Middle cerebellar peduncle	**134**
Uncinate fasciculus	**110**
Frontotemporal fasciculus	**10**
Frontoparietal fasciculus	**4**
Temporoparietal fasciculus	**30**
Temporooccipital fasciculus	**46**
Paritooccipital fasciculus	**13**
Fornix	**48**
Fimbrae	**59**
Cingulate gyrus	**9**
Thalamus	**27**
Corpus callosum	**28**

Association of side of lesion on MRI and DTWI

Chi square test was applied to find association between DTWI and MRI side of lesion. We observed a significant proportion of patients who have normal MRI showed significant DTWI abnormalities (left and bilateral hemispheres of brain). Also a significant proportion of patient with right hemisphere MRI lesions showed right and bilateral hemispheric abnormalities in DTWI. Similarly a significant proportion of patients with left hemispheric lesions in MRI showed left or bilateral hemispheric lesions. Also significant proportion of patients who showed bilateral lesions in MRI showed bilateral abnormalities in DTWI as seen in table 3.

Table 3: Association of side of lesion in MRI with DTWI

Side of lesion - MRI		Side of lesion – DTWI				Total
		Normal	Right	Left	Bilateral	
Normal	Count	46	16	29	28	119
	Row %	38.7*	13.4	24.4*	23.5*	100.0
Right	Count	11	54	5	18	88
	Row %	12.5	61.4*	5.7	20.5*	100.0
Left	Count	24	14	103*	39*	180
	Row %	13.3	7.8	57.2*	21.7*	100.0
Bilateral	Count	19	11	21	68	119
	Row %	16.0	9.2	17.6	57.1*	100.0
Total	Count	100	95	158	153	506
	Row %	19.8	18.8	31.2	30.2	100.0
Pearson's Chi-Square Test: Value: 236.226; Sig.: 0.000						

Note: * level of significance $P<0.05$

Discussion:

From the present study it was observed that MCD and MTS were common among patients with intractable epilepsy (Cascino et al., 1991; Kuzniecky et al., 1987; Thom & Bertram, 2012). DTWI could identify various white matter structural abnormalities in one or bilateral hemispheres (Gross et al., 2006; Rugg-Gunn et al., 2001). Though the MRI revealed structural abnormalities one hemisphere, the DTWI revealed white matter abnormalities in same or opposite side hemispheres (Assaf et al., 2003; Gross et al., 2006; Rugg-Gunn et al., 2001). The abnormalities in DTWI indicate, cellular packing, cellular loss or regional edema in focal status epilepticus In addition, patients suffering from complex partial seizure and MRI (without any abnormalities) revealed white matter abnormalities in various region of interest studied bilaterally or unilaterally. Thus the epileptic network in intractable epilepsy is extensive (Thivard et al., 2005; Wehner et al., 2007) as reported earlier.

Conclusion:

We conclude that MRI and DTWI are very important imaging tools to assess the intractable epileptic patients to identify macro and micro structural abnormalities (white matter) of brain. DTWI is helpful in identifying epileptic network especially when MRI does not localize any abnormalities.

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