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Functional MRI in epilepsy – Comparison of Lateralization index and language scoring

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Abstract

Aims: To evaluate the role of functional magnetic resonance imaging (fMRI) in epilepsy management and to ascertain whether laterality index (LI) derived from fMRI data, using routinely utilized paradigms, can serve as an adjunct to/or replace preoperative neuropsychological testing for evaluation of language lateralization and impairment. **Materials and Methods:** This was a prospective study which included 20 consecutive patients with a clinical diagnosis of temporal lobe epilepsy over a period of 1 year. Neuropsychological assessment included oral word association test and animal names test. The scores of both tests were compared with normographic data provided in the NIMHANS neuropsychology battery. Three fMRI paradigms were used, namely, picture naming, word generation, and sentence completion. Processing and statistical analysis were performed subsequently. **Results and Conclusion:** Right temporal lobe epilepsy (RTLE) was seen in 12 patients and left temporal lobe epilepsy (LTLE) in 8 patients. All patients were right handed. The activation pattern was predominantly left lateralized. Language lateralization varied with the type of paradigm. The overall percentage of patients showing left lateralization ranged from 44.00% for the picture naming task to 75% for the sentence completion. Reduced left lateralization was noted in both LTLE and RTLE patients. A negative correlation was observed in LTLE patients between performance in the verbal fluency and the lateralization index in the temporal and parietal regions of interest (ROI) in the word generation paradigm, suggesting that increased left lateralization was associated with a poorer score on neuropsychological tests. In RTLE patients, however, there was no significant correlation between performance in neuropsychological tests and LI. In conclusion, language lateralization using LI can serve as an adjunct during preoperative evaluation. However, it cannot replace neuropsychological testing.

Key words: Epilepsy; functional magnetic resonance imaging; language; lateralization

Introduction

Epilepsy is a common neurological disease that affects approximately 50 million people worldwide; 80% of these patients live in the developing world.[1] It has been estimated that about 10 million people have epilepsy in India. The disease affects an estimated 1% of our population.[2] The prevalence of epilepsy is more in the rural as compared with the urban population (1.9% vs. 0.6%, respectively).[2] In the

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Bangalore Urban--Rural Neuroepidemiological survey, a prevalence rate of 8.8 per 1,000 was observed. The prevalence in rural communities is double the prevalence rate of urban areas.[3] The burden of epilepsy, when evaluated using disability-adjusted life years, is approximately 1% of the total worldwide disease burden.[2] There are significant disparities in the availability of epilepsy treatment globally. The treatment gap, for active epilepsy, ranges from 75% to 50% for lower- and middle-income countries. High-income countries, on the other hand, have less than 10% treatment gap. The treatment gap in India varies between 40%and 90% in rural areas and from 22% to 50% in mixed, urban, and suburban populations.[4] Upto 20--40% of freshly diagnosed epilepsy patients become refractory to treatment.[5] Many of these patients may benefit from surgical management.[6]

Hippocampal sclerosis is a distinct pathological condition that leads to temporal lobe epilepsy. It is characterized by neuronal cell loss and gliosis involving the Cornu Ammonis 1 and endothelium.[7] Anterior temporal lobectomy is a useful mode of treatment in patients suffering from drug refractory seizures. It may be beneficial in upto 60--80% of these cases. However, the anterior and middle temporal lobes are involved in language processing, particularly naming. A decline in naming capability may be seen in about 30% of left temporal lobe epilepsy (LTLE) patients after anterior temporal lobectomy.[8]

Similarly, a reduction in verbal fluency has been described in 12--17% of LTLE patients.The risk of postoperative decline in language capability is proportional to the degree of left lateralization in LTLE.[8] Language defects have also been reported in right temporal lobe epilepsy (RTLE). Wada test is the gold standard for evaluating language lateralization; however, it is invasive. Functional magnetic resonance imaging (fMRI) provides a more straightforward and noninvasive technique to assess the language lateralization. fMRI studies show good correlation with Wada test.[9]

We aimed to evaluate the role of fMRI in epilepsy management and to ascertain whether laterality index (LI) derived from fMRI data, using routinely utilized paradigms, can serve as an adjunct to/or replace preoperative neuropsychological testing for evaluation of language lateralization and language impairment. This is the first study evaluating the relationship between LI and neuropsychological testing in the Indian population.

Materials and Method

Participants

This was a prospective study which included 20 consecutive patients with a clinical diagnosis of epilepsy over a period of 1 year. Patients more than 12 years of age who were suffering from complex partial seizures because of temporal lobe epilepsy that was localized on MRI/ electroencephalography (EEG)/video EEG or positron emission tomography (PET) were included in this study. Also, adequate vision and hearing for neuropsychological testing were prerequisites for participation in the study. All subjects and study informants signed a written consent. Patients suffering from CNS infection, malignant neoplasm, medical disease, or any psychiatric disorders that could interfere with study participation were excluded from the study.Patients with pacemakers/incompatible heart valves/ metallic prosthesis/implants were also not included in the study.

A detailed clinical history was taken and physical, neurological examination was performed by the neurologist. Handedness was decided using the Edinburg handedness inventory.[10]

Neuropsychological assessment was performed by a neuropsychologist. Two tests were performed, namely, oral word association test and animal names test. In the oral word association test, the patients were asked to generate words beginning with a consonant provided by the neuropsychologist. The consonants used in our study were "Ka,""Pa," and "Ma." The subjects generated words for 1 min for each consonant and were instructed not to repeat words or to use the names of people/places while doing the test. The total number of accepted new words was calculated for each trial. The average of new words generated over three trials formed the score. During the animal names test, the patients were asked to create the names of land-based animals excluding fishes, snakes, or birds. The total number of new words generated in 1 min formed the score. The scores of both tests were compared with normographic data provided in the NIMHANS neuropsychology battery and were converted into percentile based on the age, gender, and educational status of the patients.[11] The percentile data was then further used to evaluate the correlation with the LI.

Imaging protocol

MRI was performed on GE 750 W Discovery (3Tesla) using a 32 channel head coil. The patient was placed in supine position, and the structural MRI was performed. T1 (FSPGR 3D), and FLAIR axial sections were obtained. Subsequently, for fMRI, the images for the fMRI paradigms were projected on an MR compatible widescreen monitor placed behind the magnet. A mirror was attached to the coil and adjusted such that the patient while lying in a supine position within the gantry was able to see a reflection of the screen in the mirror. The images were suitably inverted and flipped before projection so that they appeared straight to the patient. Patients with myopia were provided with MR compatible spectacles for the duration of the study. A box car design was used. During the active phase, the images were projected on the screen in the MRI which was seen by the patient via a two-mirror system placed on the head coil. During the rest of the phase, a cross was projected on the screen, and the patient was asked to lie quietly with eyes open, looking at the cross. Three paradigms were used, namely, picture naming, word generation, and sentence completion. The local language (i.e. Hindi) was used during word generation and sentence completion paradigms. The three paradigms were performed in all patients. The protocol was as follows: TR: 4000ms; TE: 35, flip angle: 90°; no of slices: 36; slice thickness: 4mm; slice order: interleaved bottom up; no of samples: 80; total scan time: 5 min 40 s; dummy samples: 5; control: 10 samples; stimulus: 10 samples; initial state: control.

Data processing

The raw DICOM data was processed, and statistical analysis was performed using SPM 8 as follows:

The DICOM data was imported. Correction of position, reorientation, and slice timing were performed. The anatomical and fMRI data were realigned, followed by coregistration and segmentation for T1-weighted anatomical data. Subsequently, normalization (for fMRI, T1-weighted anatomical data) and smoothening (for fMRI data) were done. For voxel-wise comparisons, the data was smoothed with an 8×8×8 mm^3 Gaussian kernel and first, second level analysis was performed.

LI was calculated using the LI tool box created by Wilke *et al*.[12] A bootstrap approach was used which yields a robust and specific lateralization index and also sensitively detects outliers and allow to assess the underlying data quality.[13] This approach avoids the issue of using a fixed threshold, which has been recognized as one of the main drawbacks when assessing laterality, by applying the concept of threshold-dependent laterality curve.[12]

Lateralization index was calculated as follows:[12]

$$LI = \{(L-R)/(L+R)\}$$

Where L indicates the number of voxels activated in the left hemisphere,

R indicates the number of voxels activated in the right hemisphere.

Regions of interest (ROI) from the frontal region, parietal region, and temporal region were included, disregarding 5 mm left and right of the interhemispheric fissure. LIbased on the mean value computed for each of the three ROIs was calculated.[3]

Positive values represented mainly left-hemisphere lateralization, and negative values represented lateralization to the righthemisphere. Left-hemisphere dominance was presumed when LI >0.2. Bilateral lateralization was assumed at LI −0.2 to 0.2. The subject was considered to be right dominant if the LI <−0.2. Also, language lateralization was considered to be as left dominant if two of the three ROIs showed left-sided lateralization, right-sided dominant if two of the three ROIs were right lateralized. Language dominance was considered as bilateral if two of the three ROIs were bilateral or if right, left, and bilateral dominance was found in the three ROIs.

Statistical analysis

First, the data was visually evaluated, with a focus on the quality of the imaging as regards to motion artifact. Generation of a general linear matrix was performed for each patient using first level analysis in SPM 8 after the preprocessing steps enumerated earlier. Subsequently, voxel-wise group analysis was done. The first level analysis was performed based on reference functions consisting of deconvolution of the task boxcars convolved with the canonical hemodynamic response function. For the second-level group analysis, individual contrast images were entered into a one-sample *t*-test to examine the effects across each group (LTLE patients and RTLE patients), and activations were reported at a significance level of $P < 0.001$, with an additional extent threshold of 10 voxels. Only voxels where the brain tissues probability exceeded 0.5 were tested in the statistical analyses.

ROIs for frontal, parietal, and temporal regions were extracted from the partial volume corrected, spatially and intensity normalized functional activation maps, and a LI was calculated for all three ROIs. The relationship between LIs and gender/site of TLE was scrutinized using the nonparametric Mann--Whitney U test. The relationship between neuropsychological tests and gender/site of TLE was also analyzed using the nonparametric Mann--Whitney U test.

A linear regression analysis, using Statistical Product and Service Solutions software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp, was performed to assess relationships between the LI for each ROI and the neuropsychological testing scores. A Pearson correlation was calculated. Values close to 1 with a two-tailed significance value <0.05 were considered significant.

Results

Data of all 20 patients was evaluated. Eleven patients were in the 21--30 years age group (55%). Seven patients (35%) were in the 31--40 years age group. Two patients were in the 12--20 age group.Eleven were females and nine males. RTLE was seen in 12 patients (60%) and LTLE in 8 patients (40%); 50% were school educated (up till 12 standard) and 50% were college educated (graduates). All patients were righthanded.

Neuropsychological tests

The mean number of new words spoken by college-educated patients during the oral words association test was 7.53, whereas the mean number of new words spoken by school-educated patients during the same trial was 7.49. A significant difference was noted between the performance of the college-educated population and the mean population as described in the neuropsychology battery (*P* value: 0.01). No difference was found in neuropsychological performance between patients with LTLE and patients with RTLE. Also, there were no significant gender-based differences.

During the animal names test, the mean number of new words spoken by college and school educated patients was 8.9. A significant difference was noted between the test population mean and the control population mean as given in the neuropsychology battery (*P* values: 0.01 and 0.02, respectively).

fMRI activation results

The activation pattern was predominantly left lateralized for all paradigms [Table 1].

All three tasks revealed activations predominantly in the temporal, inferior frontal, and peri-insular regions. When differences between tasks were evaluated, the sentence completion task revealed increased activation in both frontal and temporal regions as compared with the picture naming and word generation tasks [Figures 1 and 2].

Language lateralization in fMRI

Language lateralization in LTLE and RTLE varied with the type of paradigm used. The overall percentage of right-handed patients showing left lateralization ranged from 44.00% for the picture naming task, 56.2% for word generation paradigm to 75% for the sentence completion.

LTLE

In the picture naming paradigm, 50% of the patients showed left lateralization, 37.5% showed right lateralization, and 12.5% showed bilateral lateralization. For word generation paradigm, 62.5% of the patients showed left lateralization, 12.5% showed right lateralization, and 25% showed bilateral lateralization. For sentence completion paradigm, 37.5% of the patients showed left lateralization, 12.5% showed right lateralization, and 50% showed bilateral lateralization.

RTLE

In the picture naming paradigm, 33.33% of the patients showed left lateralization, 8.33% showed right lateralization, and 58% showed bilateral lateralization. During the word generation paradigm 58% of the patients showed left lateralization, 8.33% showed right lateralization, and 33% showed bilateral lateralization. For sentence completion paradigm, 83.3% of the patients showed left lateralization, 8.33% showed right lateralization, and 8.33% showed bilateral lateralization.

No gender-specific differences were noted. There was no difference in mean LI between patients with LTLE and patients with RTLE. Minimum mean left lateralization in both RTLE and LTLE patients was noted in the picture naming paradigm in the temporal lobe.

Group analysis within paradigms

Group analysis for all three paradigms was also performed for left and RTLE patients separately.

LTLE

In the picture naming task in LTLE patients, significant activations were noted in the parahippocampal gyrus, inferior parietal lobule, inferior prefrontal gyrus, precentral

Table 1: Mean laterality index

Variable	LTLE		RTLE	
	Mean	Std Dev	Mean	Std Dev
PN FR	0.08	0.29	0.12	0.23
PN PAR	0.06	0.48	0.24	0.24
PN TEM	-0.24	0.28	0.05	0.34
WG FR	0.19	0.45	0.23	0.32
WG PAR	0.31	0.42	0.37	0.25
WG TEM	0.20	0.34	0.12	0.29
SC FR	0.16	0.35	0.32	0.28
SC PAR	0.27	0.30	0.33	0.31
SC TEM	0.02	0.36	0.33	0.31

PN - picture naming, SC - sentence completion, WG - word generation, FR - frontal lobe, TEM - temporal lobe, PAR - parietal lobe, LTLE – left temporal lobe epilepsy, RTLE – right temporal lobe epilepsy

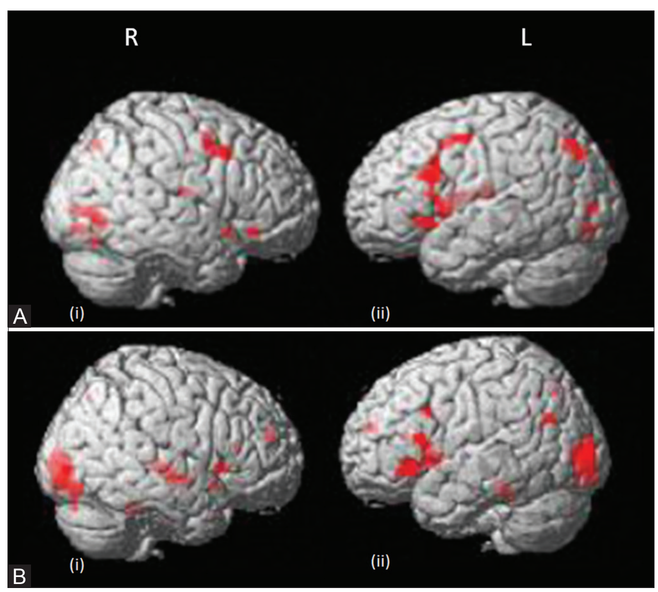

Figure 1 (A and B): In LTLE, group comparison of sentence completion with picture naming (A i, ii) revealed significant activation ($P < 0.001$) in Brodmann areas 6, 18, 9, 19, 44, 47 on left and 6, 19 and 47 on right. On comparison with word generation (B i, ii) Brodmann areas 17, 18, 9, 44, 45, 39, 7, 24 on left and areas 9, 18 on right were activated ($P < 0.001$). Higher activation was noted on the left

gyrus, and lingual gyrus on the left and fusiform gyrus, inferior frontal gyrus on the right [Figure 3A].

During the sentence completion paradigm in LTLE patients, activation was noted in the left insula, left inferior frontal, lingual, medial frontal middle temporal, and parahippocampal gyri. On the right, activation was noted in the middle frontal, inferior frontal, superior frontal, and middle occipital gyri [Figure 3B].

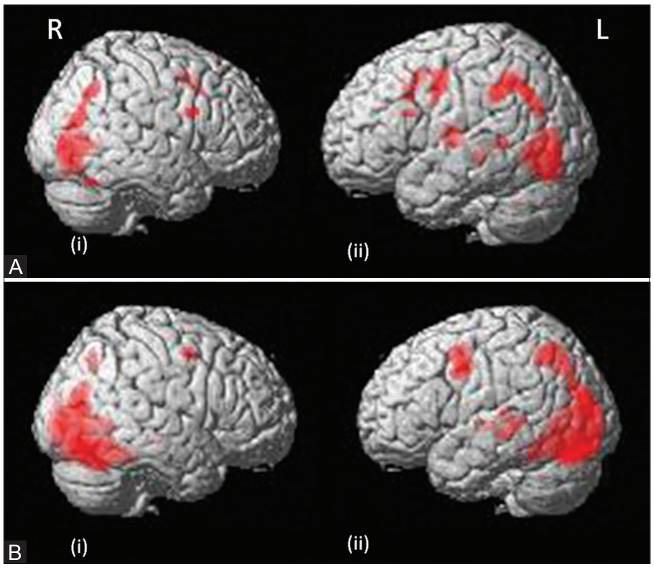

Figure 2 (A and B): In RTLE, group comparison of sentence completion with picture naming (A i, ii) showed significant activation in Brodmann 18, 7, 6, 22, 9, 32 on left and 18, 30, 7, 9 on right ($P < 0.001$). On comparison with word generation (B i, ii) activation was seen in left Brodmann areas 18, 6, 27, 22 and right 6, 7 ($P < 0.001$). Higher activation was noted on the left

During the word generation task, activation was observed in precentral gyrus, fusiform gyrus, and inferior frontal gyrus on the left. On the right side, the precentral gyrus, inferior occipital gyrus, and the fusiform gyrus showed activation [Figure 3C].

RTLE

In RTLE patients during the picture naming task, the medial frontal, precentral, cingulate, and fusiform gyri and the insula showed activation in the left hemisphere. Fusiform, cingulate, parahippocampal, and precentral gyri also showed activation on the right side [Figure 4A].

In the sentence completion paradigm, significant activation was noted in the right inferior frontal and superior frontal gyri. Bilateral precentral, middle frontal gyri, and left inferior parietal lobule also showed activation [Figure 4B].

Group analysis of RTLE patients who performed the word generation test revealed activation in the right cingulate gyrus, right parahippocampal gyrus, bilateral fusiform, inferior frontal, middle frontal and precentral gyri, left medial frontal, and supramarginal gyrus [Figure 4C].

Relationship between LI and neuropsychological tests

LTLE

No significant correlation was noted between the oral word association test and lateralization index in LTLE patients. On the other hand, a significant negative correlation was observed between the performance in the animal names test and the lateralization index in the temporal (P value = –0.81, sig [2 tailed] =0.02) ROI in the word generation paradigm [Figure 5]. A negative correlation was

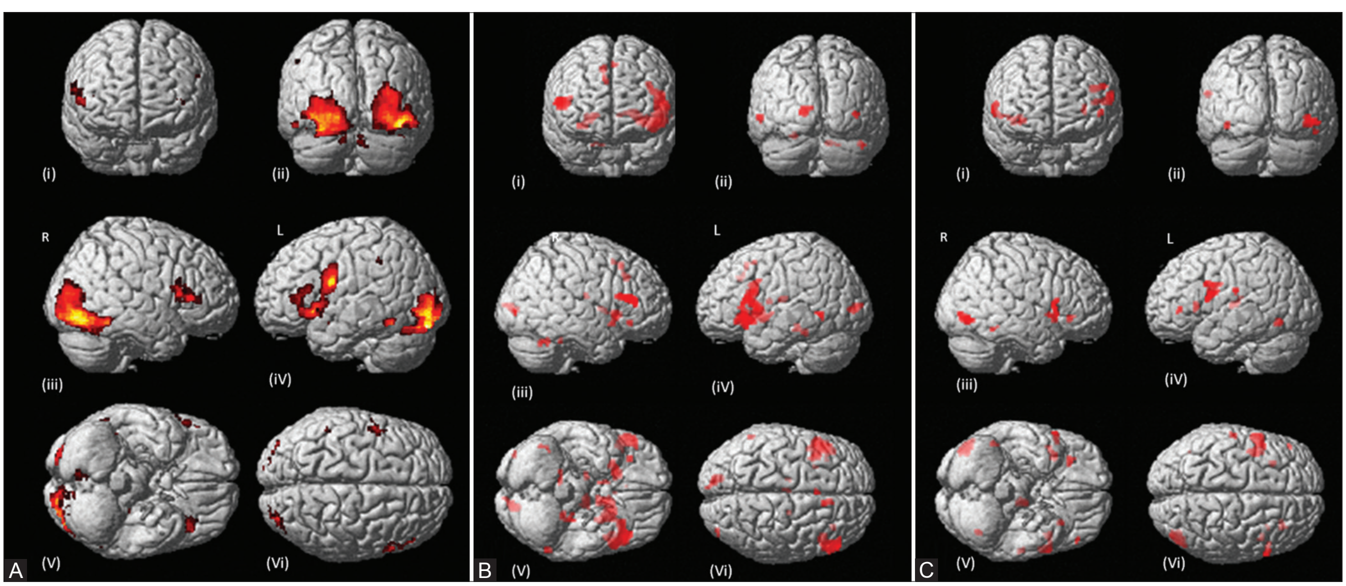

Figure 3 (A-C): Group analysis of activation during picture naming (A i-vi), sentence completion (B i-vi) and word generation paradigms (C i-vi) respectively in LTLE patients ($P < 0.001$). For picture naming activation is seen in Brodmann areas 46, 19, 37, 13 on the right and Brodmann areas 40, 47, 35, 6 and 18 on left. For sentence completion activation is seen in Brodmann areas 46, 47, 18, 32, 9 on the right and Brodmann areas 47, 35, 17, 13, 21 and 6 on left. During word generation activation is seen in Brodmann areas 44, 19, 13, 37 on the right and Brodmann areas 6, 9, 13, 37, 46, 40, on left

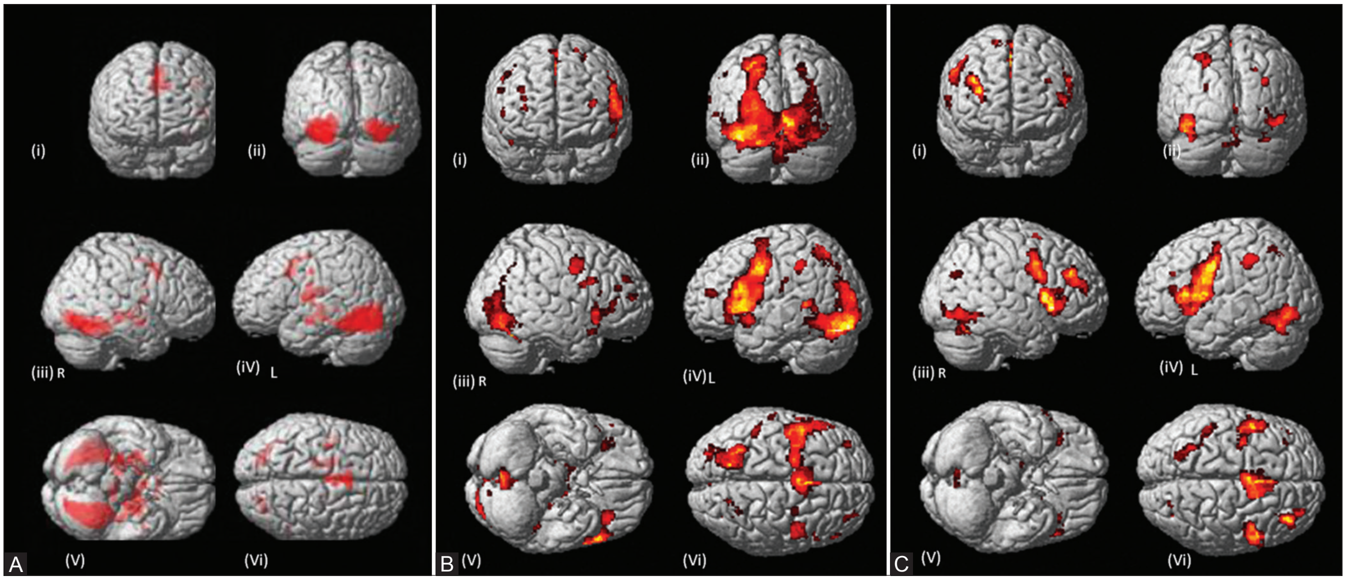

Figure 4 (A-C): Group analysis of activation during picture naming (A i- vi), sentence completion (B i-vi) and word generation (C i-vi) paradigms in RTLE patients; $P < 0.001$. During picture naming activation was seen in Brodmann areas 37, 24, 6 on the right and Brodmann areas 37, 24, 6, 13 on left. In sentence completion activation was noted in Brodmann areas 13, 6, 47, 9, 10 on the right and Brodmann areas 40, 10, 24, 6, 7 on left. Analysis of word generation revealed activation in Brodmann areas 6, 7, 9, 13, 24, 30, 31, 37 on the right and Brodmann areas 6, 7, 9, 13, 18, 31, 37, 40, 45 on left

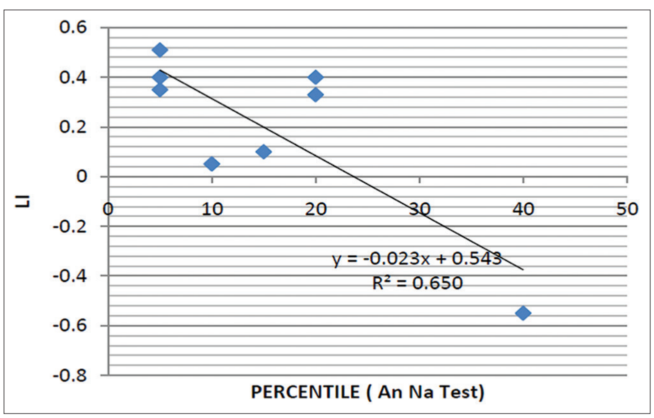

Figure 5: Scatter plot with linear regression showing the negative correlation between animal names test and the LI in the temporal ROI in the word generation paradigm in LTLE

also seen between the performance in the animal names test and the lateralization index in the parietal (P value = –65, sig [2 tailed] = 0.08) ROI in the word generation paradigm.

RTLE

No significant correlation was noted between performance, of patients suffering from RTLE, in either oral word association or animal names tests and lateralization index in any of the paradigms. When only school-educated patients were assessed separately, significant correlations were noted between the percentiles obtained in the oral word association test and the lateralization indices for the parietal region in the word generation paradigm (P value = 0.88, sig [2 tailed] =0.02) [Figure 6]. A moderate correlation was also seen in performance in the oral word association test and the LI in the frontal region in the sentence completion paradigm (P value = 0.78, sig [2 tailed] =0.07) in school-educated patients.

Discussion

The present study aimed to evaluate the fMRI language activation patterns in LTLE or RTLE and to investigate further whether lateralization as derived from various paradigms, which are routinely used in clinical practice, is related to preoperative neuropsychological verbal fluency scores.

Language lateralization using fMRI is an acceptable alternative to the Wada procedure. Multiple studies have shown that the results obtained using fMRI are concordant with the Wada procedure.[14] Usually, the left hemisphere dominates during language processing. The more critical areas are the temporal, frontal, and parietal left perisylvian regions which contribute towards networks that support components of language processing, including word recognition, syntax, and semantics.[15] In an older study,[16] it has been shown that 96% of subjects who were righthanded had fMRI signal lateralized to the left hemisphere, whereas 4% had bilateral fMRI activation.

In contrast, left lateralization was noted in 76% of left-handed subjects, bilateral activation in 14%, and right lateralization in 10% of subjects. In another study by Knecht *et al.*, right hemisphere dominance was found in 7.5% of healthy right-handed patients.[17] In the present study, the overall percentage of right-handed patients showing left lateralization varied from 44.00% for the picture naming task

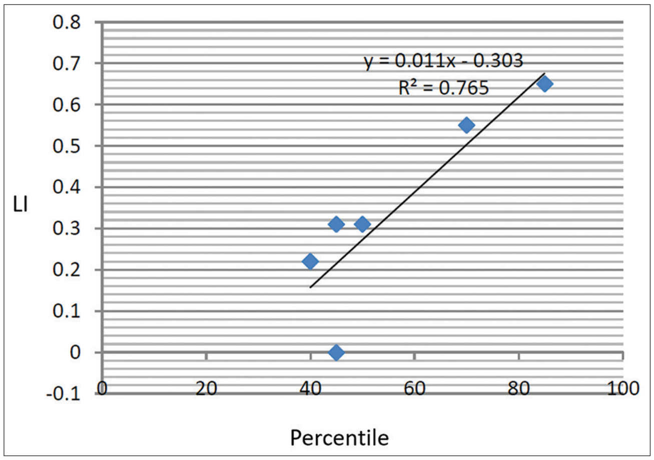

Figure 6: Scatter plot with linear regression showing correlations between oral word association test and the LI for the parietal region in the word generation paradigm in RTLE

to 75% for the sentence completion. The relative reduction in the proportion of patients showing left lateralization is likely because the populations studied in the research mentioned above consisted of normal people. Atypical language representation was found in 19% of TLE patients by Thivard *et al*.[18] As TLE is a chronic condition, it leads to structural and functional abnormalities that are progressive over time. Such epileptic activity allows the language function to either shift from right to left or to reroute the pathways to other non-traditional areas within the ipsilateral hemisphere.[19]

Powell *et al*. demonstrated that LTLE patients showed more symmetrical language activations, along with reduced left hemisphere and increased right hemisphere structural connection.[20] Janszky *et al*. also established that the incidence of atypical language lateralization was higher in LTLE patients as compared withRTLE patients while using a covert word generation task.[19] Similar results were obtained for the sentence completion paradigm in the present study. Rosazza *et al*. reported that the naming and verb generation tasks performed in their study revealed a decline in left lateralization in temporal and frontal regions in patients suffering from LTLE as compared with normal controls. In their research, RTLE patients also showed diminished left lateralization during the verb generation task.[8] The present study also revealed increased right or bilateral lateralization in both RTLE and LTLE patients.Minimum mean left lateralization was seen in the picture naming task in the temporal ROI in both right and LTLE patients as compared withother ROIs. Also, the temporal lobes had relatively reduced mean left lateralization as compared withfrontal and parietal lobes in all paradigms [Table 1].

In contrast to LTLE, atypical language dominance in RTLE is suggestive of higher risk of postsurgical language deficits. In RTLE patients, the incidence of atypical language dominance when compared with normal subjects has been reported to range from 7% to 30%.[21] Our study revealed atypical lateralization in 66.3% to 16% of the patients depending upon the paradigm used. Thus, it is essential to evaluate language lateralization in both right and LTLE.

Everts *et al*. reported that there was no significant difference in language lateralization between RTLE and LTLE.[22] Miró *et al*. evaluated atypical language organization in temporal lobe epilepsy using a passive semantic paradigm. They also reported no significant differences were found between the mean LI of LTLE and RTLE patients.[23] Our observations agree with this result.

The more critical areas involved in language processing are the left perisylvian regions in the frontal, temporal, and parietal lobes which contribute to networks supporting many components of language processing, including word recognition, syntax, and semantics.[15] We performed simple picture naming, word generation, and sentence completion tasks as it was determined that these are easier to implement in the routine clinical setting and as half of our study population consisted of only school-educated patients who might not have been able to follow more complex tasks. Mbwana *et al*. evaluated the difference between the areas showing activation in patients who have left hemispheric epilepsy and normal control patients. The primary purpose of their study was to assess the interhemispheric and intrahemispheric reorganization that occurs in patients suffering from left-sided lesions. They divided their patients into multiple subgroups, based on the areas that were activated. Their results revealed that the regions of activation were displaced to the left superior temporal sulcus in group 1a, suggesting intrahemispheric reorganization. In group 1b, there were no significant differences in comparison with the control group. Groups 2a and 2b had right-sided activation predominantly. Significant loci of activation were seen in the right inferior frontal gyrus, superior frontal gyrus, middle frontal gyrus, middle temporal gyrus, left cerebellum, and right cingulate in group 2a.

On the other hand, group 2b had predominant activation in the right inferior, middle, superior frontal gyri, right angular gyrus, and left cerebellum. This recruitment of the right cerebral hemisphere was interpreted as interhemispheric reorganization.[24] A similar interhemispheric reorganization was noted in LTLE patients in our series also. They had increased activation in the right fusiform gyrus as compared withthe left side during picture naming. Bilateral precentral and fusiform gyri were activated during the word generation task. During sentence completion, the right frontal region revealed increased activation.

Everts *et al*. showed a strong association between verbal memory performance in neuropsychological tests and lateralization of language in patients with left-sided epilepsy using a word generation task.[22] In a large study by Rosazza *et al*. it was seen that in LTLE, decreased left frontal lateralization during the verbal fluency task in the frontal ROI was associated with better verbal fluency performance in neuropsychological tests.[8] In our study also, a negative correlation was noted in LTLE patients between performance in the verbal fluency test (animal names test) and the lateralization index in the temporal and parietal ROI in the word generation paradigm, suggesting that increased left lateralization was associated with a poorer score on neuropsychological tests. For RTLE patients, Rosazza *et al*. showed that in the naming task, LI in the frontal ROI correlated positively with the Boston naming score, as well as in the fluency task, the temporal ROI correlated positively with the Boston naming score.[8] In our RTLE patients, there was no significant correlation between performance in neuropsychological tests and LI. However, when only school-educated patients were evaluated, then significant correlations were noted between the verbal fluency test (oral word association test) and the LI for parietal, frontal regions in the word generation and sentence completion paradigms, respectively. This atypical result in RTLE patients must be viewed with caution as it may be secondary to the small sample size.

Limitations

The present study is only a pilot study in the North Indian population, and a more extensive study with more patients necessary to validate the findings of our research. Another limitation of our study was the absence of normative data for neuropsychological tests for the local population, as the north Indian community has a different socio-cultural makeup as compared with a south Indian subset. Normative data for internationally used verbal fluency scoring systems like the Boston naming test are also not available for India. Also, more refined paradigms that result in activation of the medial temporal lobes may be necessary.

In conclusion, lateralization correlates partially with language performance on verbal fluency tests. A significant negative correlation was noted between the performance in the animal names test and the lateralization index in the temporal and parietal ROIs in the word generation paradigm for LTLE. fMRI complements neuropsychological tests in the evaluation of TLE patients and has become an essential part of the presurgical evaluation. Language lateralization using a LI may be useful in the preoperative assessment and can serve as an adjunct during the preoperative evaluation. However, it cannot replace neuropsychological testing. Further research with a larger data sample is required.

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Conflicts of interest

There are no conflicts of interest

References

1. Leonardi M, Ustun TB. The global burden of epilepsy. Epilepsia 2002;43:21-5.
2. Tripathi M, Jain DC, Devi MG, Jain S, Saxena V, Chandra PS, *et al.* Need for a national epilepsy control program. Ann Indian Acad Neurol 2012;15:89-93.
3. Gourie-Devi M, Gururaj G, Satishchandra P, Subbakrishna DK. Prevalence of neurological disorders in Bangalore, India: A community-based study with a comparison between urban and rural areas. Neuroepidemiology 2004;23:261-8.
4. Meyer A-C, Dua T, Ma J, Saxena S, Birbeck G. Global disparities in the epilepsy treatment gap: A systematic review. Bull World Health Organ 2010;88:260-6.
5. French JA. Refractory epilepsy: A clinical overview. Epilepsia 2007;48(Suppl 1):3-7.
6. Perry MS, Duchowny M. Surgical versus medical treatment for refractory epilepsy: Outcomes beyond seizure control. Epilepsia 2013;54:2060-70.
7. Thom M. Review: Hippocampal sclerosis in epilepsy: A neuropathology review. Neuropathol Appl Neurobiol 2014;40:520-43.
8. Rosazza C, Ghielmetti F, Minati L, Vitali P, Giovagnoli AR, Deleo F, *et al.* Preoperative language lateralization in temporal lobe epilepsy (TLE) predicts peri-ictal, pre- and post-operative language performance: An fMRI study. NeuroImage Clin 2013;3:73-83.
9. Woermann FG, Jokeit H, Luerding R, Freitag H, Schulz R, Guertler S, *et al.* Language lateralization by Wada test and fMRI in 100 patients with epilepsy. Neurology 2003;61:699-701.
10. Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. Neuropsychologia 1971;9:97-113.
11. Rao S.L, Subbakrishna D.K, Gopukumar K. NIMHANS neuropsychology battery-2004, manual. 1st ed. Bangalore Natl. Inst. Ment. Health Neurosci; 2004. 267 p.
12. Wilke M, Lidzba K. LI-tool: A new toolbox to assess lateralization in functional MR-data. J Neurosci Methods 2007;163:128-36.
13. Wilke M, Schmithorst VJ. A combined bootstrap/histogram analysis approach for computing a lateralization index from neuroimaging data. NeuroImage 2006;33:522-30.
14. Arora J, Pugh K, Westerveld M, Spencer S, Spencer DD, Todd Constable R. Language lateralization in epilepsy patients: fMRI validated with the Wada procedure. Epilepsia 2009;50:2225-41.
15. Gupta S. fMRI for mapping language networks in neurosurgical cases. Indian J Radiol Imaging 2014;24:37.
16. Pujol J, Deus J, Losilla JM, Capdevila A. Cerebral lateralization of language in normal left-handed people studied by functional MRI. Neurology 1999;52:1038-43.
17. Knecht S, Deppe M, Dräger B, Bobe L, Lohmann H, Ringelstein EB, *et al*. Language lateralization in healthy right-handers. Brain 2000;123:74-81.
18. Thivard L, Hombrouck J, Tézenas du Montcel S, Delmaire C, Cohen L, Samson S, *et al.* Productive and perceptive language reorganization in temporal lobe epilepsy. NeuroImage 2005;24:841-51.
19. Janszky J, Mertens M, Janszky I, Ebner A, Woermann FG. Left-sided interictal epileptic activity induces shift of language lateralization in temporal lobe epilepsy: An fMRI study. Epilepsia [Internet] 2006;47:921-7.
20. Powell HWR, Parker GJM, Alexander DC, Symms MR,

Boulby PA, Wheeler-Kingshott CAM, *et al*. Abnormalities of language networks in temporal lobe epilepsy. NeuroImage 2007;36:209-21.

21. Weber B, Wellmer J, Schür S, Dinkelacker V, Ruhlmann J, Mormann F, *et al*. Presurgical language fMRI in patients with drug-resistant epilepsy: Effects of task performance. Epilepsia 2006;47:880-6.
22. Everts R, Simon Harvey A, Lillywhite L, Wrennall J, Abbott DF, Gonzalez L, *et al*. Language lateralization correlates with verbal memory performance in children with focal epilepsy. Epilepsia 2010;51:627-38.
23. Miró J, Ripollés P, López-Barroso D, Vilà-Balló A, Juncadella M, de Diego-Balaguer R, *et al*. Atypical language organization in temporal lobe epilepsy revealed by a passive semantic paradigm. BMC Neurol 2014;14:98.
24. Mbwana J, Berl MM, Ritzl EK, Rosenberger L, Mayo J, Weinstein S, *et al*. Limitations to the plasticity of language network reorganization in localization related epilepsy. Brain 2009;132:347-56.