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Original Article

Preoperative functional magnetic resonance imaging in patients undergoing surgery for tumors around left (dominant) inferior frontal gyrus region

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Abstract

Background: Preoperative functional magnetic resonance imaging (fMRI) helps to preserve neurological function and ensure maximal tumor tissue excision. We studied the lateralization and localization of speech centers in select cases of tumors around the left (dominant) inferior frontal gyrus (IFG).

Methods: Twenty-three right-handed patients, harboring tumors involving the left (dominant) IFG or causing mass effect or edema extending onto the left IFG, were recruited over 17 months. Preoperatively, all patients underwent language and speech assessment followed by MRI and fMRI with paradigm (picture naming). Normative data for language fMRI was taken from the institute's imaging data bank.

Results: The study included 23 patients [mean age: 38.9 (±11.9) years; M: F = 16:7; 9 – normal speech, 14 – abnormal speech]. Group analysis of controls showed significant activation in the region of interest (ROI) – left Brodmann's areas (BAs) 44,45. Group analysis of patients with normal speech showed no activation in the left BAs 44,45; however, activation was noted in the immediate adjacent areas, left BAs 13,47 and contralateral prefrontal cortex. Group analysis of patients with impaired speech showed no activation in BAs 44,45 or in the immediate adjacent areas.

Conclusions: Neuroplasticity in the brain may enable functional language areas to shift to adjoining or distant regions in the brain when the primary areas are involved by intrinsic tumors. This phenomenon is more likely in slow-growing compared to fast-growing tumors. Preoperative language fMRI may help us in identifying and protecting these areas during surgery.

Key Words: Cerebral re-organization, functional MRI, glioma surgery, left (dominant) inferior frontal gyrus, neuro-plasticity mechanisms, surgery for tumors involving the left inferior frontal gyrus

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INTRODUCTION

Tumors located in eloquent cortical areas of the brain pose significant risks of neurological deficits during surgical extirpation. Current strategy of maximal safe resection is aimed at preserving neurological function to the fullest.[5] In addition to the motor and sensory functions, language is of utmost importance in maintaining the quality of life. Tumors located around the left (dominant) inferior frontal gyrus (IFG) may involve Broca's area, which sub-serves important language functions. Tumors arising within or adjacent to this region can affect certain aspects of language function. Recent advances in functional imaging have shown that cerebral plasticity plays an important role in functional re-organization of the cerebral cortex involved by progressively infiltrating lesions such as gliomas.[5]

In addition to the effects caused by the tumor itself, surgical intervention for tumor excision can cause additional deficits in these patients from either swelling or stroke or disruption of fiber tracts; these effects may be transient or permanent. Intraoperative cortical and subcortical stimulation is considered a high yield method for localizing language areas during neurosurgical procedures.[15,20] However, there are limitations which preclude its use in all patients. Functional magnetic resonance imaging (fMRI), because of its noninvasive nature and increasing availability, can also be a very useful tool in determining language lateralization and localization of speech areas.[14]

Several studies have recognized the good spatial correlation between physiological intraoperative cortical mapping and anatomical localization of motor fMRI findings based on blood oxygenation level derived (BOLD) imaging.[6,20,26] Accordingly, recent interest has been towards understanding whether fMRI—in particular, the BOLD signal—can be used to aid the presurgical planning of lesion resections involving language areas to minimize disruption of speech and ensure maximal tumor removal. There is relatively scant literature pertaining to the fMRI findings for language function in patients harboring tumors in language-eloquent areas.[14,15,20]

Our study aimed at studying the effects of tumors involving the left (dominant) IFG (commonly designated as the Broca's area) on the lateralization and localization of speech centers. It is an effort to understand the "functional reshaping" that occurs in tumors around the left (dominant) IFG and its effect on the language function in affected patients.

PATIENTS AND METHODS

A prospective study was conducted and patients were recruited over a period of 17 months from August 2012 to December 2013. Clearance from the institutional ethics committee was taken before commencement of the study. A written informed consent was obtained from the patients or relatives before recruitment for the study.

Inclusion criteria

- Lesions involving the left IFG (gliomas, extension of insular glioma, mass effect, or edema involving the left IFG)
- Both genders
- Right-handed individuals
- Age 15–65 years
- Ability and willingness to participate in a follow-up fMRI study
- With normal/corrected hearing and vision.

Exclusion criteria

- Neuropsychiatric conditions – major depressive disorder, schizophrenia, etc.
- Alcohol or drug dependence
- Chronic neurological illnesses
- Any contraindication to MRI
- Left-handed individuals
- Unwillingness to participate in the study or refusal of consent.

Assessment of speech and language

Patients underwent language and speech assessment at the department of speech pathology and audiology of our institution by a certified speech pathologist using Western Aphasia Battery (Indian version by Karanth *et al.*).[12] In addition to this, all patients underwent speech and language assessment as a part of NIMHANS neuropsychological battery by a neuropsychologist.[2]

Functional magnetic resonance imaging protocol

All patients underwent preoperative MRI and fMRI with paradigms designed at our institute.[1,17] Images were obtained on a 3.0-Tesla Siemens Skyra MR scanner with a 20-channel coil. The T1 sequences on the Siemens Skyra scanner console were acquired using the following protocol: TR = 1900 ms, TE = 2.44 ms, matrix = 256 × 256, slice thickness = 1 mm, voxel size = 1 × 1 × 1 mm, and number of slices = 192.

Functional magnetic resonance imaging paradigm

Picture naming: A block design was used. There were four blocks of "active condition" alternating with four blocks of "rest." During the "active" condition, individual pictures were presented once every 4 seconds and the patient was asked to silently generate the name of the picture in his/her native language. During the rest condition, the patient would view a cross hair in the centre of the screen. The imaging protocol was as follows: TR = 4000 ms, TE = 30 ms, matrix = 64 × 64, number of dynamics = 85, slice thickness = 4 mm.

Clinical data collection

The nature and duration of symptoms including speech disturbances, behavioral symptoms, motor, or sensory symptoms were documented. Clinical examination included neurological assessment of higher mental functions (MMSE), bedside speech assessment, and assessment of cranial nerves, motor, sensory, and cerebellar system.

Preoperative radiological investigations

- MRI of the brain and/or CT scan of head
- Functional BOLD MRI of the brain with the abovementioned paradigms.

Functional magnetic resonance imaging data analysis and visualization

Anatomical and functional images were processed using Statistical Parametric Mapping 8 (SPM8) software (Wellcome Trust Centre for Neuroimaging, London, UK). Preprocessing involved re-orientation of functional and structural images to anterior commissure-posterior commissure plane followed by realignment of images. When a dataset exhibited more than a 2-mm translation in the x, y, or z plane during the imaging procedure, it was not used for analysis. Normalization with the Montreal Neurological Institute (MNI) template was done for both structural and functional data such that processed data was superimposed on the structural images and inter-subject comparison could be done.[11] Second-degree B- Spline was used for interpolation. Smoothing was done with full width at half maxima Gaussian kernel of 8 mm. Each stimulus onset was modelled as a Box car design encoded in condition-specific "stick-functions" with an inter-stimulus interval of 4 seconds with onsets and duration of the stimuli per block. The resulting stimulus functions were convolved with a canonical hemodynamic response function to form regressors for the linear model.[26] This also included six covariates of no interest representing the head motion parameters. Parameter estimates (beta images) were assessed with least square regression analysis, and the contrast images (con images) were computed for the effect of each task at hand. The individual analysis of controls was carried out with a $P < 0.05$ ([FWE (family-wise error rate) corrected]) where the region of interest (ROI) was activated consistently across the group. Group analysis was done with $P < 0.001$ (uncorrected). In the patient group, the thresholds were lowered as they did not show significant activations in the ROI. The individual analysis in patients was done with $P < 0.001$ (uncorrected) at which the ROIs were activated. For group analysis, $P < 0.005$ with cluster threshold of 10 was chosen, because at this threshold, the ROIs were activated in the patient group. Finally, functional volumes were registered to the anatomic images, as described by the Talairach client atlas, and the corresponding Brodmann areas were generated.[16,17]

Laterality index

Laterality index (LI) as a measure of hemispheric dominance was measured for all controls and all patients preoperatively using picture naming task. LI was measured for the whole hemisphere (excluding cerebellum) as well as for the specific ROI. ROI was determined as the frontal lobes bilaterally with other areas masked using a pre-formed mask.

LI was measured using the formula $LI = t_l - t_r/t_l + t_r$,

where t_l and t_r are a sum of all t values in left and right hemisphere above a predefined individual threshold "T" which is mean of the 5% most activated voxels within each hemisphere or ROI. Sum of all the t values of all voxels above 50% of this mean was considered to be t_l and t_r for left and right, respectively.

RESULTS

The study was conducted from August 2012 to December 2013 over a duration of 17 months accrual time. Twenty-three patients, who fulfilled the inclusion criteria and were willing to participate in the study, were recruited. These included 16 males (~69%) and 7 females (~31%). The patients' age ranged from 15 to 65 years (mean = 38.9 ± 11.9 years). Normative data for language fMRI was taken from the institute's data bank for imaging in healthy controls. The control group consisted of 9 males and 1 female. Age ranged from 26 to 51 years (mean = 33 years). Their minimum qualification was high school graduation, with 8 being college graduates.

Both the patient group as well as the control group gave no history of prior neurological illness and did not have any contraindications for MRI. The clinical and radiological profile of the study group is presented in Table 1. The patient data of the study group (including speech disturbances in the patients, radiological location of the tumors, surgical intervention performed, and histopathological diagnosis of the tumors) is detailed in Table 2.

Clinical presentation

Patients presented with symptoms including headache, seizures, speech disturbances, weakness of limbs, or memory disturbances [Table 1]. The duration of presurgical symptoms ranged from 1 month to 72 months with a mean of 8.7 months.

Speech and language assessment

All 23 patients underwent formal clinical speech-language assessment by a trained speech pathologist. The test included Western Aphasia Battery.[12] In addition, all patients were also evaluated for speech and language as a part of the NIMHANS neuropsychological battery.[2] Of the 23 patients, 9 patients had normal results on speech

Table 1: Clinical and radiological profile of study group

Patient characteristics	Number (%)
Age	
Mean	38.9 (±11.9) years
Range	15 to 65 years
Sex	
M:F	16:7
Clinical Symptoms	
Headache	8 (34.7)
Seizures	18 (78.2)
Speech disturbances	14 (60.8)
Weakness of limbs	4 (17.4)
Behavioral changes and memory disturbances	1 (4.3)
Speech function	
Normal	9 (39.1)
Abnormal	14 (60.9)
Radiological characteristics	
Left insular gliomas	4 (17.4)
Left insular glioma with frontal or temporal opercular involvement	4 (17.4)
Left frontal tumors involving IFG or edema extending to IFG	14 (60.8)
Left pterional meningioma (extra-axial tumor)	1 (4.3)

assessment. The rest had some form of speech/language abnormality, ranging from dysarthria to aphasia.

Radiological evaluation

All patients underwent routine CT scan and MRI of the brain as part of routine preoperative assessment. All, but one patient, had an intra-axial tumor. This single patient (P11) had an extra-axial tumor in the left pterional region. Among intra-axial tumors, four tumors were located exclusively in the insula, four tumors were predominantly insular with surrounding extension to either frontal or temporal lobes, and the remaining 14 were situated around the IFG, with edema extending to the IFG or with mass effect on the IFG.

Functional magnetic resonance imaging analysis of controls

Group analysis of controls shows significant activation in the ROI (Brodmann areas 44,45). Significant activation was also noted in Brodmann area 6 in the precentral gyrus and Brodmann area 46 in the middle frontal gyrus of the left hemisphere [Figure 1].

Functional magnetic resonance imaging analysis of patients

The patients were divided into two groups. The first group did not display any speech deficits on testing. The second group had an identifiable speech/language deficit. fMRI results were analyzed for each group separately.

Group I (patients with normal speech and language): Group analysis of patients in this group showed no activation in Brodmann areas 44 and 45 on the left frontal lobe. Significant activations were found in left BA 13 and 47 which are in the areas immediately adjacent to Brodmann areas 44 and 45. Activations were also noted in the contralateral IFG (BA 9) [Figure 2].

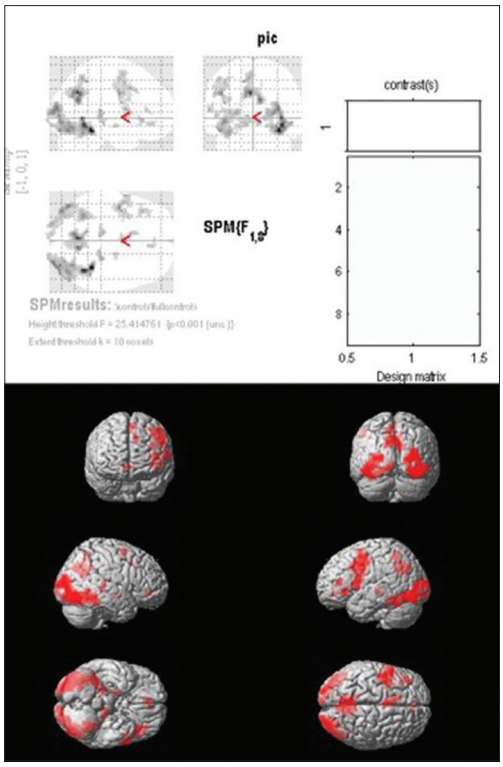

Figure 1: Photograph of group analysis in controls ($P < 0.001$ uncorrected) showing activity in the left inferior frontal gyrus. Functional images are superimposed on pre-available templates on SPM8 for better visualization

Group II (patients with impaired speech/language): Group analysis of patients in this group showed no activation in left BA 44 and 45, i.e., the Broca's area. There was no significant activation even in the adjacent areas of the left IFG. Significant activation was noted in BA 6, i.e. the supplementary cortex [Figure 3].

The areas activated in the two groups, i.e. groups I and II, and the corresponding voxels of activation showed that Broca's area (BA 44 and 45) was not activated in either group [Figures 2 and 3]. Of note, other BAs in the IFG were only activated in the group with preserved speech but not in patients with speech/language deficits.

Laterality index

LI was calculated in both patients as well as controls for picture naming task with a *P* value of 0.001 for the whole hemisphere (excluding cerebellum) as well as for the ROI, as described above. Normality of data was tested before further analysis.

The mean hemispheric LI value for the controls was 0.22 ± 0.23, and the mean ROI LI was 0.36 ± 0.33.

Table 2: Patient-wise clinical, radiological, surgical, and histopathological data of the patient study group

No.	Age (in years)	Sex	Speech and language evaluation	Location of tumor	Edema or mass effect in IFG	Surgical intervention	Histopathological diagnosis (WHO Grade)
P1	35	Female	Normal	IFG and insula	NA	Craniotomy + STR	Anaplastic oligodendroglioma (III)
P2	38	Female	Flaccid dysarthria	SFG and MFG	Yes	Craniotomy + GTR	Anaplastic oligodendroglioma (III)
P3	43	Female	Anomic aphasia	Insula and temporal	Yes	Craniotomy + STR	Anaplastic oligodendroglioma (III)
P4	18	Male	Transcortical motor aphasia	Insula	Yes	Craniotomy + PDC	Anaplastic oligodendroglioma (III)
P5	39	Male	Normal	Insula	Yes	Craniotomy + STR	Anaplastic oligoastrocytoma (III)
P6	15	Female	Normal	MFG	Yes	Craniotomy + PDC	Low-grade astrocytoma (II)
P7	56	Male	Spastic dysarthria	IFG	NA	Craniotomy + PDC	Glioblastoma multiforme (IV)
P8	42	Male	Spastic dysarthria	IFG and PCG	NA	Craniotomy + PDC	Anaplastic gemistocytic astrocytoma (III)
P9	38	Male	Transcortical sensory aphasia	Insula	Yes	Craniotomy + STR	Primitive neuroectodermal tumor (IV)
P10	28	Male	Normal	MFG	Yes	Craniotomy + GTR	Anaplastic oligodendroglioma (III)
P11	42	Male	Dysarthria	Pterional	Yes	Craniotomy + GTR	Transitional meningioma (I)
P12	37	Male	Normal	Insula and temporal	Yes	Craniotomy + PDC	Anaplastic mixed oligoastrocytoma (III)
P13	35	Female	Dysarthria	Insula and IFG	NA	No surgical intervention	NA
P14	55	Male	Transcortical sensory aphasia	MFG	Yes	Craniotomy + STR	Glioblastoma multiforme (IV)
P15	32	Male	Anomia	MFG	Yes	Craniotomy + STR	Oligoastrocytoma (II)
P16	36	Male	Normal	IFG and orbital	NA	Craniotomy + GTR	Anaplastic glioma (III)
P17	65	Male	Broca's aphasia	IFG	NA	Craniotomy + PDC	Glioblastoma multiforme (IV)
P18	32	Male	Normal	SFG and MFG	Yes	Craniotomy + PDC	Anaplastic oligodendroglioma (III)
P19	48	Female	Normal	Insula	Yes	Craniotomy + PDC	Oligodendroglioma (II)
P20	56	Male	Transcortical sensory aphasia	IFG and MFG	NA	Craniotomy + PDC	Anaplastic oligodendroglioma (III)
P21	21	Female	Normal	IFG	NA	Craniotomy + GTR	Anaplastic astrocytoma (III)
P22	45	Male	Broca's aphasia	PCG	Yes	No surgical intervention	NA
P23	38	Male	Transcortical sensory aphasia	IFG, MFG and corpus callosum	Yes	Craniotomy + PDC	Anaplastic oligodendroglioma (III)

IFG: Inferior frontal gyrus, MFG: Middle frontal gyrus, SFG: Superior frontal gyrus, PCG: Pre-central gyrus, NA: Not applicable, STR: Subtotal resection (90 to 99%), GTR: Gross total resection (>99%), PDC: Partial decompression (>60%), WHO: World Health Organization

The mean hemispheric LI across the patient group was 0.19 ± 0.18, and mean ROI LI across patient group was 0.29 ± 0.38.

The preoperative LI values of controls were compared to the patient group using independent-sample *t*-test. There was no statistical significance between LI values of the two groups in either the hemispheric or ROI LIs. The LIs were compared across controls and patients using analysis of variance (ANOVA) test, with the patient group divided into those who had normal speech and those who had speech/language deficits. This analysis showed that there was no significant difference in LI values (both hemispheric and ROI) among patients who did not have speech deficits, those who had speech deficits, and controls.

Surgical intervention and histopathological diagnoses

Of the 23 patients included in the patient group, 21 underwent open surgical intervention. Two patients refused surgical intervention. Out of 21 surgical interventions, only six patients had a gross total resection of the tumor, five patients had subtotal resection, and ten patients underwent decompression of the tumor. The histopathological diagnosis was grade III astrocytoma in 13 patients, grade II astrocytoma in 3 patients, grade IV astrocytoma (glioblastoma multiforme) in 3 patients, primitive neuroectodermal tumor (PNET) in 1 patient, and transitional meningioma (grade I) in 1 patient. Patient-specific data is presented in Table 2.

DISCUSSION

The canonical view that the brain has a fixed functional organization that is similar in all individuals has been challenged by recent advances in functional brain imaging that have demonstrated large interindividual variability in the functional organization of the brain.[25] This concept has also highlighted the existence of plasticity in adult central nervous system, which accounts for

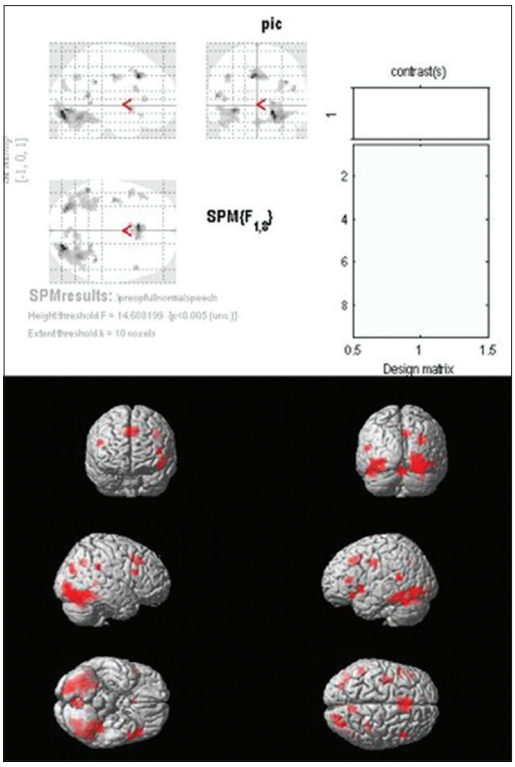

Figure 2: Photograph of group analysis in patients with normal speech (*P* < 0.005 uncorrected) showing decreased activity in the left inferior frontal gyrus compared to controls. Functional images are superimposed on pre-available templates on SPM8 for better visualization

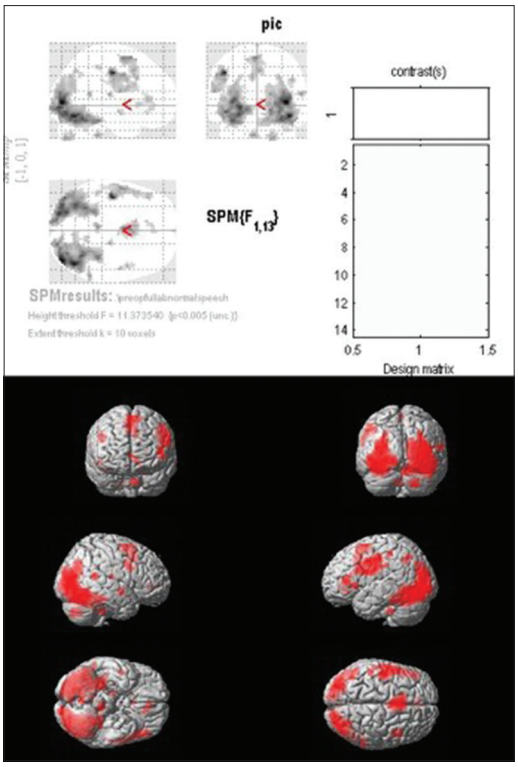

Figure 3: Photograph of group analysis in patients with abnormal speech (*P* < 0.005 uncorrected). Functional images are superimposed on pre-available templates on SPM8 for better visualization

the "functional reshaping" that can be seen in select cases of progressive intra-axial tumors such as low-grade gliomas (LGG).[5] Cerebral plasticity is a continuous process allowing short-term, middle-term, and long-term remodeling of the connectivity maps in an effort to optimize the functioning of networks.[4,5] The mechanisms of this complex process are still not fully understood though various theories have been proposed.[4]

When an intracranial lesion infiltrates or impinges on an eloquent region/cortex of the human brain, plasticity is postulated as the mechanism by which the brain re-organizes connectivity for functional areas and possibly shifts the function from one initially eloquent (functional) area to another noneloquent (nonfunctional) area of the brain. With the help of preoperative fMRI studies, we wanted to study cases of intracranial tumors involving or compressing the predominant motor language area, i.e. the left (dominant) IFG region and we also wanted to assess the areas of functional language cortex in this setting.

Our normative data showed significant activation in the region of interest (ROI), i.e., the BAs 44 and 45 on the left side. In addition to this, significant activation was also noted in BA 6 in the precentral gyrus and BA 46 in the middle frontal gyrus of the left hemisphere. This substantiates the previously established concept, that in normal individuals, the motor speech areas are located in the BAs 44 and 45 on the left side.

In patients harboring a tumor in this locale but with clinically preserved speech and language function (n = 9), group analysis showed that there was no residual activation in BAs 44 and 45 of the left frontal lobe. However, significant activations were found in the immediate adjacent areas – left BAs 13 and 47. Activations were also noted in the right IFG (BA 9). In tumor patients with impaired/absent speech and language function (n = 14), group analysis showed that in addition to the absence of activation in the left BA 44 and 45, there was no such activation in the adjacent cortex of BA 13 and 47. However, there was significant activation noted in the supplementary cortex (BA 6).

In the present study, the LI measured for the whole hemisphere ranged from −0.04 to 0.33 in patients who had normal speech with a mean of 0.23. This implies that the majority of patients with intact speech had left-sided lateralization. Two patients with intact speech had LI in the range of −0.1 to 0.1, indicating bilateral representation of speech areas.

It has been stated that slow-growing lesions permit the induction progressive functional reshaping of brain networks.[3,7] Theoretically, preoperative functional redistribution in patients with lesions in eloquent cortical areas is possible in three different ways. First, function

can persist within the tumor-occupying part of the brain. Second, eloquent areas can be redistributed to areas around the tumor (adjacent plasticity).[27] Third, preoperative compensation for loss of primary function may occur with the redistribution of that function to some remote area(s) within the same hemisphere or in parts of the contralateral hemisphere, which are homologous to the invaded structures (remote plasticity).[10,21,23]

Our study shows that in the group of patients harboring tumors in and around the left IFG (BA 44 and 45), with preserved speech and language function, the activation had shifted from BAs 44 and 45 to the adjacent BAs 13 and 47, and even to the contralateral IFG (BA 9). Significant activity was noted in the adjacent perilesional areas including BA 47, 9, and 13 in patients who had intact speech/language compared to patients who had speech/language deficits. These findings are in line with the theories of functional redistribution mentioned above.

Furthermore, bilateral dominance, as observed in the LI studies in two patients, indicates recruitment of homologous structures in the right hemisphere, which may account for preserved speech/language in a subgroup of patients.

Yousry *et al*. demonstrated shifting of hand-motor cortex to perilesional areas in a case of a tumor affecting the hand area of the motor cortex.[28] Meyer *et al*. demonstrated that in nonaphasic patients harboring a glioma within the Broca's area, speech-related activations were noted in the left inferior frontal cortex adjacent to the tumor.[18] These cases corroborate the theory of "adjacent plasticity."

"Remote plasticity" has also been described in patients harboring intracerebral gliomas within the language system. fMRI revealed speech-related activations were (i) in the left superior temporal gyrus following tumor invasions of Broca's area[9,18] and (ii) in Broca's area following tumor invasions of the left temporo-parietal region.[18] Here, the activation is "within" the language system. In some patients with slowly evolving gliomas affecting language functions, there appears to be recruitment of "nontypical" language areas in the left frontolateral regions, including Brodmann areas (BA) 46 and 47, and the SMA.[13,18,23,24] In these cases, the activation was "outside" the language system.

Kośla *et al*. showed that in patients with LGGs located in the left frontal lobe near the frontal operculum of insula, 75% of the patients showed activation of Broca's area in the right hemisphere with half of the LGG tumors showing a strong right-sided lateralization (LI = −1), whereas in the other half the LI was left-sided (strong: LI = 1 and weak: LI = 0.28).[14] This indicates recruitment of homologous structures in the opposite hemisphere in patients showing right-sided lateralization. Petrovich *et al*. reported translocation of Wernicke's area to the right hemisphere in a patient with left temporoparietal glioma.[19] Holodny *et al*. reported a similar translocation of Broca's area to the right hemisphere in a patient with left inferior frontal tumor.[10]

The fMRI findings in the set of 9 patients with intact speech/language function demonstrate that a multitude of plasticity mechanisms work synchronously to reorganize functional brain networks and shift foci to adjacent as well as remote cortical areas within the brain to maintain language function.

The findings in our cohort subset of 14 study participants with impaired speech/language function demonstrate that plasticity mechanisms have not been able to compensate for the loss of function. This may be attributable to rapid progression of the lesions (outpacing the plasticity mechanisms) or the eventual involvement of the adjacent areas (to which the language function had shifted) by the tumor.[22]

Roux *et al*. analyzed the utility of preoperative fMRI for identifying functional language areas in patients with brain tumors.[20] They correlated preoperative fMRI data with intraoperative direct cortical stimulation in 14 patients and concluded that language fMRI could not be used to make critical surgical decisions in the absence of direct brain mapping. The reasons for this could be errors in registration that occurs during surgery or the choice of experiment used to assess the language function. However, our study, considering these findings, highlights the fact that preoperative language fMRI studies may very well have a role in understanding the compensatory changes occurring due to tumor growth (in the setting of gliomas). This information may be considered as an adjunct while evaluating patients harboring tumors around the left IFG and should be supplemented by intraoperative cortical mapping.

Giussani *et al*. reviewed the pertinent literature (nine language brain mapping studies) studying the reliability of preoperative language fMRI in patients operated on for brain tumors by comparing language fMRI with direct cortical stimulation (DCS).[8] They concluded that language fMRI could not be considered an alternative tool to DCS in tumors involving the language area of the brain; however, they also noted that language fMRI conducted with high field magnets held promise as a brain mapping tool in the future.

Limitations of our study

The paradigms designed and administered in the present study included only picture naming as majority of the patients could not perform other tasks to test other domains of language. This partly depends on the educational status of the participant as well as the intellectual level and partly

on the complexity of tasks. Hence, short and effective paradigms with high sensitivity and specificity which can be easily performed are better suited in such patients.

Because the performance of tasks was limited in the patient group, uncorrected group results ($P < 0.005$) with a cluster size of 10 was used for group analysis as this was the least threshold at which we could observe any changes. Thus, our results might contain a higher percentage of false positives. As similar thresholds were applied for both groups (control and patient) and we did not get any significant difference between the groups, this might not affect the results between the two patient groups. Other techniques such as seed to voxel connectivity or resting state fMRI could be used to improve this analysis.[17] Correlation of the results with neuropsychological and aphasia batteries could have further supported the current findings.

Further, as demonstrated in Table 2, the histopathological spectrum in our study group ranged from WHO grade II gliomas to WHO grade IV gliomas. Slow-growing tumors are more likely to allow for ongoing plasticity than rapidly growing lesions, which may explain the findings seen in Group II patients (patients with impaired speech or language).[20] A homogenous group in terms of histopathological grade of tumors (especially grade II gliomas) would have better elucidated the plasticity mechanisms in such a study.

Our study, conducted with a 3.0-Tesla MR scanner is a purely preoperative study. The fact that these preoperative language fMRI results were not validated by further intraoperative DCS and were not compared with postoperative language fMRI results in the same patient group is another limitation of our study.

CONCLUSION

Preoperative fMRI should be considered in the work-up of patients with intra-axial or extra-axial lesions in the vicinity of functional language areas in the human brain for surgical planning and counseling. Due to plasticity mechanisms, select functional areas may have migrated to adjacent or distant regions in the brain, as shown in our study. fMRI with evaluation of language function may help us to identify and protect these areas during surgery. In this aspect, fMRI may act as an adjunct to other "function-preserving" modalities such as intraoperative cortical and subcortical stimulation and mapping.[5,20] Our study shows that plasticity must have occurred in the re-organization of functional cortices. This process likely starts early in the genesis of intracerebral tumors, especially gliomas, and continues during further growth of the lesion and even during treatment. Further studies with postoperative fMRI correlation will be needed to completely understand the impact of plasticity in such cases.

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Ethical approval: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Bharath RD. Functional MRI: Genesis, state of the art and the sequel. Indian J Radiol Imaging 2014;24:6-12.
2. Dalal PK, Sivakumar T. Cognitive psychiatry in India. Indian J Psychiatry 2010;52(Suppl 1):S128-35.
3. DeAngelis LM. Brain tumors. N Engl J Med 2001;344:114-23.
4. Duffau H. Brain plasticity: From pathophysiological mechanisms to therapeutic applications. J Clin Neurosci 2006;13:885-97.
5. Duffau H. Lessons from brain mapping in surgery for low-grade glioma: Insights into associations between tumour and brain plasticity. Lancet Neurol 2005;4:476-86.
6. Dym RJ, Burns J, Freeman K, Lipton ML. Is functional MR imaging assessment of hemispheric language dominance as good as the Wada test?: A meta-analysis. Radiology 2011;261:446-55.
7. Fandino J, Kollias SS, Wieser HG, Valavanis A, Yonekawa Y. Intraoperative validation of functional magnetic resonance imaging and cortical reorganization patterns in patients with brain tumors involving the primary motor cortex. J Neurosurg 1999;91:238-50.
8. Giussani C, Roux FE, Ojemann J, Sganzerla EP, Pirillo D, Papagno C. Is preoperative functional magnetic resonance imaging reliable for language areas mapping in brain tumor surgery? Review of language functional magnetic resonance imaging and direct cortical stimulation correlation studies. Neurosurgery 2010;66:113-20.
9. Heiss WD, Thiel A, Kessler J, Herholz K. Disturbance and recovery of language function: Correlates in PET activation studies. Neuroimage 2003;20(Suppl 1):S42-9.
10. Holodny AI, Schulder M, Ybasco A, Liu WC. Translocation of Broca's area to the contralateral hemisphere as the result of the growth of a left inferior frontal glioma. J Comput Assist Tomogr 2002;26:941-3.
11. Huang CM, Lee SH, Hsiao IT, Kuan WC, Wai YY, Ko HJ, *et al.* Study-specific EPI template improves group analysis in functional MRI of young and older adults. J Neurosci Methods 2010;189:257-66.
12. Karanth *P* ND, Pandit R, Shivashankar N. Cross cultural studies of aphasia. In: Chopra J, editor. Modern Trends in Neurology: Churchill Livingstone; 1995. pp 95-105.
13. Karbe H, Thiel A, Weber-Luxenburger G, Herholz K, Kessler J, Heiss WD.

Brain plasticity in poststroke aphasia: What is the contribution of the right hemisphere? Brain Lang 1998;64:215-30.
14. Kosla K, Pfajfer L, Bryszewski B, Jaskolski D, Stefanczyk L, Majos A. Functional rearrangement of language areas in patients with tumors of the central nervous system using functional magnetic resonance imaging. Pol J Radiol 2012;77:39-45.
15. Kundu B, Penwarden A, Wood JM, Gallagher TA, Andreoli MJ, Voss J, *et al*. Association of functional magnetic resonance imaging indices with postoperative language outcomes in patients with primary brain tumors. Neurosurg Focus 2013;34:E6.
16. Levesque MF, Wilson CL, Behnke EJ, Zhang J ×. Accuracy of MR-guided stereotactic electrode implantation. 1. Preimplantation correlation with the Talairach system. Stereotact Funct Neurosurg 1990;54-55:51-5.
17. Manglore S, Bharath RD, Panda R, George L, Thamodharan A, Gupta AK. Utility of resting fMRI and connectivity in patients with brain tumor. Neurol India 2013;61:144-51.
18. Meyer PT, Sturz L, Schreckenberger M, Spetzger U, Meyer GF, Setani KS, *et al*. Preoperative mapping of cortical language areas in adult brain tumour patients using PET and individual non-normalised SPM analyses. Eur J Nucl Med Mol Imaging 2003;30:951-60.
19. Petrovich NM, Holodny AI, Brennan CW, Gutin PH. Isolated translocation of Wernicke's area to the right hemisphere in a 62-year-man with a temporo-parietal glioma. AJNR Am J Neuroradiol 2004;25:130-3.
20. Roux FE, Boulanouar K, Lotterie JA, Mejdoubi M, LeSage JP, Berry I. Language functional magnetic resonance imaging in preoperative assessment of language areas: correlation with direct cortical stimulation. Neurosurgery 2003;52:1335-45; discussion 1345-1337.
21. Taniguchi M, Kato A, Ninomiya H, Hirata M, Cheyne D, Robinson SE, *et al*. Cerebral motor control in patients with gliomas around the central sulcus studied with spatially filtered magnetoencephalography. J Neurol Neurosurg Psychiatry 2004;75:466-71.
22. Thiel A, Habedank B, Herholz K, Kessler J, Winhuisen L, Haupt WF, *et al*. From the left to the right: How the brain compensates progressive loss of language function. Brain Lang 2006;98:57-65.
23. Thiel A, Herholz K, Koyuncu A, Ghaemi M, Kracht LW, Habedank B, *et al*. Plasticity of language networks in patients with brain tumors: A positron emission tomography activation study. Ann Neurol 2001;50:620-9.
24. Thiel A, Herholz K, von Stockhausen HM, van Leyen-Pilgram K, Pietrzyk U, Kessler J, *et al*. Localization of language-related cortex with 15O-labeled water PET in patients with gliomas. Neuroimage 1998;7 (4 Pt 1):284-95.
25. Tzourio-Mazoyer N, Josse G, Crivello F, Mazoyer B. Interindividual variability in the hemispheric organization for speech. Neuroimage 2004;21:422-35.
26. Weng HH, Noll KR, Johnson JM, Prabhu SS, Tsai YH, Chang SW, *et al*. Accuracy of presurgical functional MR imaging for language mapping of brain tumors: A systematic review and meta-analysis. Radiology 2018;286:512-23.
27. Wunderlich G, Knorr U, Herzog H, Kiwit JC, Freund HJ, Seitz RJ. Precentral glioma location determines the displacement of cortical hand representation. Neurosurgery 1998;42:18-26; discussion 26-17.
28. Yousry TA, Schmid UD, Jassoy AG, Schmidt D, Eisner WE, Reulen HJ, *et al*. Topography of the cortical motor hand area: Prospective study with functional MR imaging and direct motor mapping at surgery. Radiology 1995;195:23-9.