Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/pjnns

ELSEVIER

NEUROLOGIA I NEUROCHIRURGIA POLSKA
POLISH JOURNAL OF NEUROLOGY AND NEUROSURGERY

Original research article

Reorganization of language centers in patients with brain tumors located in eloquent speech areas – A pre- and postoperative preliminary fMRI study

Katarzyna Gębska-Kośla[a,*], *Bartosz Bryszewski*[b], *Dariusz J. Jaskólski*[b], *Jan Fortuniak*[b], *Maciej Niewodniczy*[c], *Ludomir Stefańczyk*[d], *Agata Majos*[a]

[a] *Department of Radiological and Isotopic Diagnosis and Therapy, Medical University of Lodz, Central Clinical Hospital, Czechoslowacka 8/10, 92-216 Lodz, Poland*
[b] *Department of Neurosurgery, Medical University of Łódź, Kopcińskiego 22, 90-153 Łódź, Poland*
[c] *Institute of Health Sciences, University of Social Sciences, Gdańska 121, 90-508 Łódź, Poland*
[d] *Department of Radiology and Diagnostic Imaging, Medical University of Łódź, Kopcińskiego 22, 90-153 Łódź, Poland*

ARTICLE INFO

Article history:
Received 2 August 2016
Accepted 6 July 2017
Available online 29 July 2017

Keywords:
Language
Functional magnetic resonance imaging
Brain mapping

ABSTRACT

Introduction: The aim of this study was to determine in pre- and postsurgical fMRI studies the rearrangement of the Broca's and Wernicke's areas and the lateralization index for these areas in patients with brain tumors located near speech centers. Impact of the surgical treatment on the brain plasticity was evaluated.

Materials and methods: Pre- and postoperative fMRI examinations were performed in 10 patients with low grade glial, left-sided brain tumors located close to the Broca's (5 patients) or Wernicke's area (5 patients). BOLD signal was recorded in regions of interest: Broca's and Wernicke's areas, and their anatomic right-sided homologues.

Results: In the preoperative fMRI study the left Broca's area was activated in all cases. The right Broca's area was activated in all the patients with no speech disorders. In the postoperative fMRI the activation of both Broca's areas increased in two cases. In other two cases activation of one of the Broca's area increased along with the decrease in the contralateral hemisphere.

In all patients with temporal lobe tumors, the right Wernicke's area was activated in the pre- and postsurgical fMRI. After the operation, in two patients with speech disorder, the activation of both Broca's areas decreased and the activation of one of the Wernicke's areas increased.

Conclusions: In the cases of tumors localized near the left Broca's area, a transfer of the function to the healthy hemisphere seems to take place. Resection of tumors located near Broca's or Wernicke's areas may lead to relocation of the brain language centers.

* *Corresponding author.*
E-mail addresses: katarzyna_kosla@wp.pl (K. Gębska-Kośla), bartoszbryszewski@gmail.com (B. Bryszewski), dariusz.jaskolski@umed.lodz.pl (D.J. Jaskólski), jfort@tlen.pl (J. Fortuniak), maciekn@orange.pl (M. Niewodniczy), stefanczyk_l@wp.pl (L. Stefańczyk), agata.majos@umed.lodz.pl (A. Majos).

http://dx.doi.org/10.1016/j.pjnns.2017.07.010

1. Introduction

Treatment of the brain tumors localized near language areas remains a real challenge. Surgical excision of these tumors frequently leads to the irreversible speech impairment. The electrical cortical mapping (ECM) is still accepted as a gold standard of intraoperative localization the language centers. However, it is invasive and time-consuming [1–4]. Moreover, some behavioral responses triggered during surgery do not provide relation between electrical stimulation and the function of the stimulated area [5].

In an attempt to overcome these limitations, functional magnetic resonance (fMRI) becomes a tool of increasing importance enabling safe presurgical determination of both speech centers' position and language lateralization. It can answer the question whether and how speech areas are displaced due to the presence of a tumor. FMRI studies provide better understanding of brain plasticity and may predict clinical and functional outcome of the surgery. Nevertheless, the quoted sensitivity and specificity of fMRI compared to electrical stimulation is 66% and 90% respectively. That is why fMRI protocols are not yet used alone to make critical surgical decisions [6–9].

The present study was undertaken in right-handed patients with low grade glial tumors, in an attempt to determine by means of fMRI examinations the functional reorganization of Broca's and Wernicke's areas before and after surgery

2. Materials and methods

2.1. *Patients*

The study protocol was approved by the local Commission of Bioethics: Decision no. RNN/123/09/KE. Ten patients with primary brain tumors were enrolled into the study – 5 men and 5 women, aged 22–55 years (median 35.5) according to the following criteria: (1) tumor located near the Broca's or Wernicke's area of the left hemisphere (2) right handedness of patients (3) neuropsychological status of patients allowing for planned, standardized procedures of fMRI. The right-handedness was defined on the base of the inventory test.

The patients were divided into two groups – one group consisted of 5 patients with tumors located in the frontal lobe and the other group of 5 patients with temporal lobe tumors. The distance between the eloquent brain areas and the tumor border was measured on the morphological, three-dimensional T1-weighted sequences with a mask based on functional activation. In all cases the distance was less than 2 cm.

The patients were operated on at the Department of Neurosurgery in 2010–2014 with intraoperative brain mapping performed in all the cases. All the patients underwent total or subtotal resection of the tumors. Histopathology showed 4 high grade gliomas, HGG: (three WHO IV and one WHO III) and 6 low-grade gliomas, LGG (5 WHO II and one WHO I). In each patient speech was assessed twice by the clinical neuropsychologist – before the preoperative and before postoperative fMRI. The patients data are summarized in Table 1.

Each patient had a preoperative and a postoperative fMRI performed at least 3 months after the operation.

2.2. *FMRI study*

2.2.1. *MRI scanner*

fMRI study was performed in all the patients using a 1.5 T scanner (Siemens, Avanto). Morphological, three-dimensional T1-weighted sequences were obtained according to the following protocol: FOV = 256 × 256 mm, matrix = 512 × 512, TR = 8.8 ms, TE = 4.8 ms, TA = 5′07. Each volume acquired contained 160 slices of 1 mm thick. The functional examination included echoplanar imaging (EPI) sequences: TR = 3000 ms, TE = 50 ms, FOV = 1680 × 1680 mm, matrix 64 × 64, TA = 5′11, thirty-eight 3 mm thick slices.

2.2.2. *Data analysis*

The analysis of the data was conducted using the statistical program SPM 2, running in MATLAB (http://www.fil.ion.ucl.ac.uk/spm/). Data were analyzed for $p = 0.05$.

All the patients had been informed about the exact course of the study 30 min in advance before it started. The used paradigm was word generation (WG). The study was divided into five blocks, each containing 10 acquisitions. Pattern of stimulation proceeded in ABABABABAB block diagram, where A was the rest (control), and B represented stimuli. The patients were ordered to pronounce in periods of stimulation non-repetitive male and female names, for example: Kate,

Table 1 – Characterization of the patients group including gender, age and tumor localization, size, histopathological type of the tumor and WHO grade.

Patient	Gender	Age (years)	Tumor localization	Tumor size (cm^3)	Histopatological type of the tumor	WHO grade
KwJ	F	36	Frontal lobe	2.63	Astrocytoma pilocyticum	L
SzK	M	22	Frontal lobe	10.95	Astrocytoma pilocyticum	L
DeB	F	23	Frontal lobe	66.78	Ependymoma	L
SiA	F	32	Frontal lobe	16.63	Astrocytoma fibrillare	L
KaM	F	31	Frontal lobe	23.8	Astrocytoma fibrillare	L
KwS	M	55	Temporal-parietal border	37.42	Glioblastoma	H
BlK	M	38	Temporal lobe	23.21	Oligodendroglioma	L
MiK	M	44	Temporal lobe	24.68	Glioblastoma	H
NiS	M	47	Temporal-occipital border	21.77	Glioblastoma	H
RoM	F	35	Temporal lobe	6.8	Glioma mixtum anaplasticum	H

John. The signals for stimulation and rest were shown to the patient, respectively the text: ''NAME'' and the sign ''X''.

Using radiological anatomy atlases four regions of interest (ROIs) responsible for language functions were designated:

a. Broca's area in the left inferior frontal gyrus (Brodmann area, BA) – BA 44, BA 45),
b. the anatomically corresponding area in the right hemisphere,
c. Wernicke's area in the left superior temporal gyrus (BA 22) and adjacent: superior temporal sulcus, middle temporal gyrus (BA 21), angular gyrus (BA 39) and supramarginal gyrus (BA 40),
d. the anatomically corresponding area in the right hemisphere [2].

The lateralization index (LI) was calculated according to the literature, i.e. on the basis of the number of activated voxels in the four defined areas [10,11]. It enabled to avoid analysis of non-specific activity or activity of non-linguistic areas, activated as a consequence of sensory or motor stimuli (10). Lateralization index was calculated according to the formula: $LI = (L - R)/(L + R)$, separately for the Broca's and Wernicke's area and their right-sided homologous regions [12]. The obtained results were in the range from −1 to 1. Positive value of LI was synonymous with left-sided laterality. Negative value of the LI meant right-sided lateralization. The values from −0.25 to 0.25 were considered to be symmetrical activation [13].

3. Results

3.1. *Tumors located in the left frontal lobe*

3.1.1. *Preoperative study*

In all the patients with tumors located in the left frontal lobe, the left Broca's area was active in the preoperative fMRI study. In 3 patients with no speech disorders, the right area corresponding to Broca's center was also active. The lateralization index was in one case right-sided, in one case symmetrical and in one case left-sided. In 2 of 3 patients with speech disorders there was no activation of the right-sided area corresponding to Broca's center. In the preoperative fMRI the lateralization index for the Wernicke's area was strong left-sided in three cases and in one case symmetrical.

3.1.2. *Postoperative study*

In the postoperative fMRI, the activation of both Broca's areas increased in two cases. One of them was a patient who recovered from speech disorder after surgery. It was also the only case of the postsurgical increased activation of the right Wernicke's area. In two cases activation increased in one of the Broca's area whereas the activation decreased in the contralateral hemisphere. The lateralization index was in two cases right-sided and in three cases left-sided. In four patients the activation in the left Wernicke area decreased after surgery and in one patient it increased. Summary of speech disorders with the calculated LI for Broca's and Wernicke's area is summarized in Table 2. A detailed list of results is shown in Tables 3 and 4.

3.2. *Tumors located in the left temporal lobe*

3.2.1. *Preoperative study*

In patients with temporal lobe tumors, the lateralization index for the Broca's area was left-sided in 4 patients in the preoperative fMRI among them 3 had aphasia. In two of them the right Broca's area was active. The right-sided Wernicke's area was active in all patients with temporal lobe tumors, and the left-sided Wernicke's area was activated in one patient with speech disorder and one patient without speech impairment.

3.2.2. *Postoperative study*

After the operation in two patients with speech disorders, the activation of both-sided Broca's areas decreased while the activation of one of the Wernicke's areas increased. In one patient with no speech impairment, both Wernicke's areas activation decreased after the operation, while the left Broca's area activation increased. In one case the activation of right-sided Broca's and right-sided Wernicke's area increased. The left-sided lateralization index for the Wernicke's area became greater in two cases. A summary of the speech disorders with the calculated LI for Broca's and Wernicke's area is given in Table 5. A detailed list of the results is shown in Tables 6 and 7.

4. Discussion

Language is a complex brain function that involves two primary language regions – Broca's and Wernicke's areas.

Table 2 – Pre- and postoperative impairment of language ability in patients with brain tumors located in the left frontal lobe compared with calculated laterality index (LI) for Broca's and Wernicke's areas separately.

Patient	Postoperative fMRI (months)	Speech disorders		LI Broca's area		LI Wernicke's area	
		Pre-operative	Post-operative	Pre-operative	Post-operative	Pre-operative	Post-operative
KwJ	3	Transient motor aphasia after epi	Transient motor aphasia after epi	1	1	1	1
SzK	3	2 episodes of dysphasia	no speech disorders observed	1	0.26	0.86	−0.84
DeB	3	No speech disorders observed	No speech disorders observed	0.24	−0.59	0.18	−0.03
SiA	5	No speech disorders observed	No speech disorders observed	−0.65	−1	1	–
KaM	3	No speech disorders observed	No speech disorders observed	0.65	0.83	–	1

Table 3 – Value of *t*-statistics (*T*) and number of activated voxels within each cluster (ke) in patients with left frontal lobe tumors: pre- and postoperative for both Broca's areas; ↑, higher number of voxel activation in postoperative fMRI; ↓, lower number of voxel activation in postoperative fMRI.

Patient	Broca's area									
	Left hemisphere					Right hemisphere				
	Preoperative		Postoperative			Preoperative		Postoperative		
	T	ke	T	ke	Δke	T	ke	T	ke	Δke
KwJ	4.83	53	3.66	7	↓	–	–	–	–	–
SzK	5.08	31	6.83	128	↑	–	–	5.44	75	↑
DeB	4.45	26	4.23	28	↑	4.24	16	6.14	108	↑
SiA	3.00	19	–	–	↓	4.00	114	6.78	263	↑
KaM	6.31	117	9.28	222	↑	3.79	24	3.69	21	↓

Table 4 – Value of *t*-statistics (*T*) and number of activated voxels within each cluster (ke) in patients with left frontal lobe tumors: pre- and postoperative for both Wernicke's areas; ↑, higher number of voxel activation in postoperative fMRI; ↓, lower number of voxel activation in postoperative fMRI.

Patient	Wernicke's area									
	Left hemisphere					Right hemisphere				
	Preoperative		Postoperative			Preoperative		Postoperative		
	T	ke	T	ke	Δke	T	ke	T	ke	Δke
KwJ	4.39	66	4.73	22	↓	–	–	–	–	–
SzK	5.58	43	6.81	8	↓	5.12	3	5.73	91	↑
DeB	6.06	143	5.66	75	↓	7.29	107	5.54	80	↓
SiA	6.92	386	–	–	↓	–	–	–	–	–
KaM	–	–	4.13	23	↑	–	–	–	–	–

Table 5 – Pre- and postoperative speech impairment in patients with brain tumors located in the temporal lobe compared with calculated laterality index (LI) for Broca's and Wernicke's areas separately.

Patient	Postoperative fMRI (months)	Speech disorders		LI Broca's area		LI Wernicke's area	
		Pre operative	Post operative	Pre operative	Post operative	Pre-operative	Post-operative
KwS	3	Mixed aphasia	Dysphasia	1	1	−1	–
BlK	3	Transient motor aphasia	Transient motor aphasia	0.21	0.69	−1	−1
MiK	5	Mixed aphasia	Dysphasia	0.28	1	0.02	0.86
NiS	3	No speech disorders observed	No speech disorders observed	–	−1	−1	−1
RoM	3	No speech disorders observed	No speech disorders observed	1	1	0.18	0.2

Table 6 – Value of *t*-statistics (*T*) and number of activated voxels within each cluster (ke) in patients with left temporal lobe tumors: pre- and postoperative for both Broca's areas; ↑, higher number of voxel activation in postoperative fMRI; ↓, lower number of voxel activation in postoperative fMRI.

Patient	Broca's area									
	Left hemisphere					Right hemisphere				
	Preoperative		Postoperative			Preoperative		Postoperative		
	T	ke	T	ke	Δ ke	T	ke	T	ke	Δ ke
KwS	3.44	2	4.83	61	↑	–	–	–	–	–
BlK	6.13	413	6.38	33	↓	6.10	269	5.62	6	↓
MiK	5.04	29	3.77	19	↓	3.51	4	–	–	↓
NiS	–	–	–	–	–	–	–	4.14	3	↑
RoM	3.97	9	5.58	111	↑	–	–	–	–	–

Table 7 – Value of t-statistics (T) and number of activated voxels within each cluster (ke) in patients with left temporal lobe tumors: pre- and postoperative for both Wernicke's areas; ↑, higher number of voxel activation in postoperative fMRI; ↓, lower number of voxel activation in postoperative fMRI.

Patient	Wernicke's area									
	Left hemisphere					Right hemisphere				
	Preoperative		Postoperative			Preoperative		Postoperative		
	T	ke	T	ke	Δke	T	ke	T	ke	Δke
KwS	–	–	–	–	–	5.14	33	–	–	↓
BlK	–	–	–	–	–	8.25	166	8.32	201	↑
MiK	4.86	43	3.26	48	↑	4.79	57	3.72	9	↓
NiS	–	–	–	–	–	4.42	15	4.90	48	↑
RoM	5.32	145	5.37	126	↓	4.52	122	5.31	60	↓

According to different studies of healthy individuals, 92.5–97% of right-handed people show a left-sided lateralization for language functions [14,15]. Therefore, pathological processes that involve the left frontal and temporal lobes frequently cause speech disorders in right-handed patients as they affect the above-mentioned speech centers.

In our study all the patients with left frontal lobe tumors had low grade gliomas. Two of 3 patients who had tumors located in the frontal lobe and suffered from speech disorders, had activation only in the left Broca's area. It is possible that because of the small volume of these two lesions, and possibly shorter duration of their growth, the full acquisition of language function by right-sided areas had not yet taken place, thus not helping their speech disorders. All 3 patients without speech deficits had activation in the right-sided Broca's area, which may suggest that the process of the functional rearrangement of the speech centers had occurred. Out of the patients with the frontal lobe tumors, the preoperative fMRI studies displayed activity in the Wernicke's area in 4 cases, the LI was left-sided in 3 cases whereas symmetrical in one case. We suppose that in this group of patients, this area plays a minor role in the tumor-induced reorganization. After the operation, speech difficulties decreased in one patient. Here, the activation of both Broca's areas increased in the postoperative fMRI study. It is possible that both – the recovery and functional reorganization of the speech centers occurred both in this case. Activation of the left Broca's area also increased in the postoperative fMRI in two patients with no speech disorders, what may also prove postoperative recovery of this center (Figs. 1 and 2). Speech disorders remained unchanged after the operation in one patient. In this case, a lower voxel activation in the left Broca's region was noted along with no activation in the right hemisphere. The left-sided Broca's area activation decreased after the operation also in another patient without pre- and postoperative speech deficits, but in this case the activation of the right-sided Broca's region increased. After left frontal lobe tumor operation 4 out of 5 patients had lower voxel activity of the left-sided Wernicke's area. We have not confirmed that the tumor resection in these cases shifted the activation from frontal toward temporal lobe as it was recently suggested [16]. We think that with the postoperative increase of Broca's region activity, the role of Wernicke's area in the process of maintaining speech decreases. In patients with tumors in the left hemisphere the functional network can adapt to the lesion. Dislocation of areas activated during language tasks is observed, either to ipsilateral regions, not involved in the pathological process, or to contralateral homotopic areas. This patterns of intrahemispheric as well as interhemispheric compensation are explained by reduction of collateral inhibition of specific centers on other structures within the language network. This shift can be reversed after surgical resection of a tumor leading to improved speech performance [17,18].

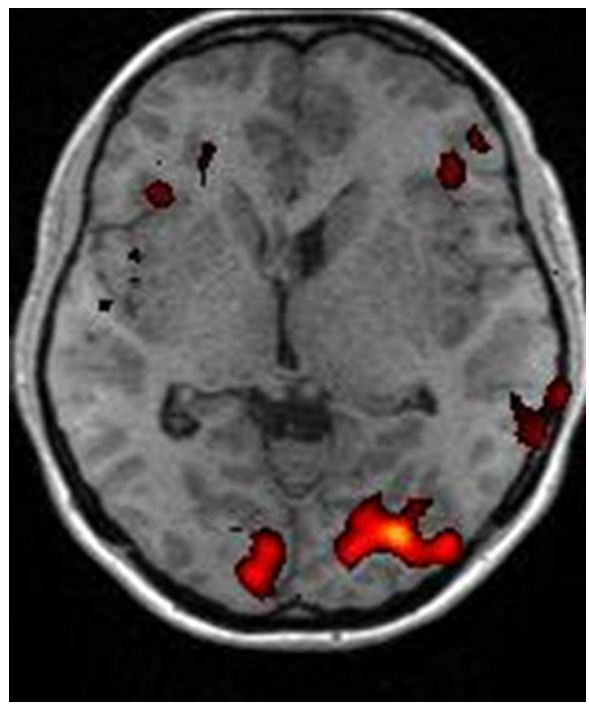

Fig. 1 – Patient with left frontal lobe tumor (DeB). Broca's and Wernicke's region activation in preoperative fMRI examination.

From the group of the patients with the temporal lobe tumors four had HGG and one LGG. In preoperative fMRI study the lateralization index for Wernicke's area was in 3 cases strong right-sided and in 2 cases symmetrical. Despite the activation of the right Wernicke's area, 3 patients had speech disorders. In all these cases the speech impairment decreased after the operation. In postoperative fMRI of the patient with LGG the activation in the right Wernicke's area increased,

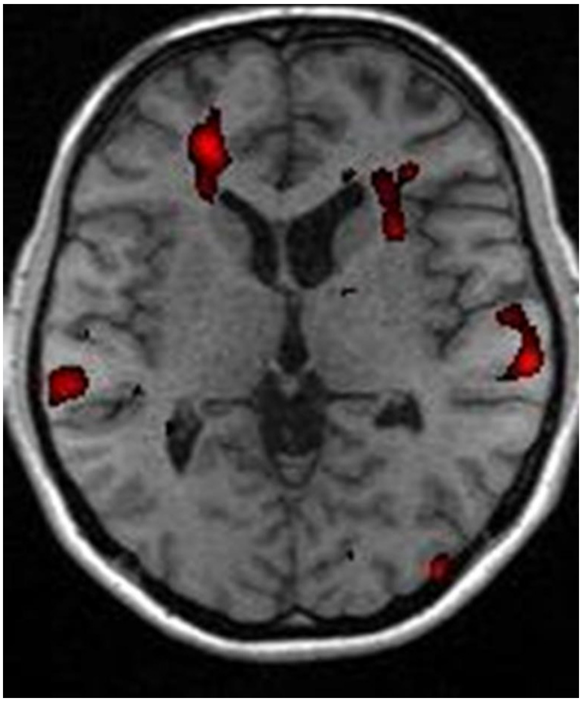

Fig. 2 – Patient with left frontal lobe tumor (DeB). Broca's and Wernicke's region activation in postoperative fMRI examination. Notice the increase of Broca activation.

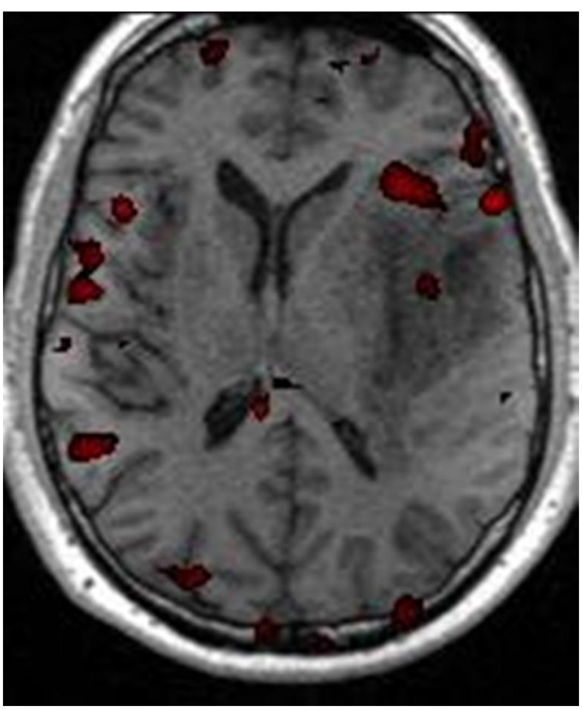

Fig. 3 – Patient with left temporal lobe tumor (BlK). Broca's and Wernicke's regions activation in preoperative fMRI examination.

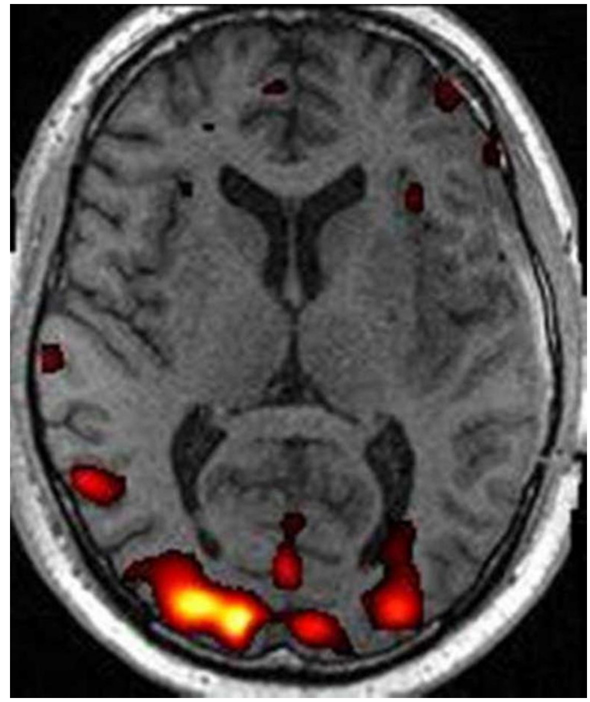

Fig. 4 – Patient with left temporal lobe tumor (BlK). Broca's and Wernicke's regions activation in postoperative fMRI examination. Notice the increase of right-sided We amination. Notice the increase of right-sided Wernicke's area activation.

while there was still no activation of the left-sided area corresponding to the Wernicke center (Figs. 3 and 4). It is likely that a permanent reorganization of the speech centers had occurred there. A recent study suggests that involvement of the basal ganglia (as it was in this case) is significantly correlated with co-dominant language function and better functional outcome [19]. In one of the patients with HGG the activation in the left-sided Wernicke's region increased while the BOLD signal in the right Wernicke's area decreased. Probably the removal of the pathological mass led in this case to the recovery of the left Wernicke's area [18,19]. In a patient with the biggest HGG tumor volume in the temporo-parietal area, we obtained no BOLD signal in the Wernicke's areas after the operation, but the signal in the left Broca's area significantly increased. It is possible that the edema caused by the tumor could affect the BOLD signal in the left Broca's area, which recovered after the operation. In one of the patients without speech disorder, we obtained eloquent areas activation only in the right hemisphere, which additionally increased after the operation. Reorganization of both speech centers seems to be unlikely. It might be a case of a right-handed patient with right-sided lateralization of the speech centers [15]. In another patient without speech difficulties, the lateralization index did not change significantly after the operation, although the activation of both Wernicke's areas decreased.

In our study we noticed an increased activation of the right-sided region corresponding to Broca center in the group of patients with left frontal lobe tumors and in the right-sided region corresponding to Wernicke center in the group of left temporal lobe tumors. The patient groups were small, but a reorganization process in cases of LGG was noticeable. Our results confirm the observations of other researchers, that the slow growing LGG may lead to functional reorganization of eloquent areas [20–25]. High grade and low grade gliomas have different pathophysiology and natural history so the fMRI studies results in those two groups cannot be compared. Some pathophysiological changes associated with fast and aggressively growing HGG lead to structural and functional neural networks changes in the brain. BOLD fMRI study enables mapping of the language areas but the evaluation of remodeling of central nervous system might be ambiguous. The pathological mass can alter blood flow or induce neovascularization and affect the BOLD signal which is based on cerebrovascular hemodynamics and therefore can influence fMRI results [24,26]. In our study the group of patients with HGG was quite heterogenous, so no conclusions can be drawn.

Abnormal language areas activation pattern is not necessarily related to recovery. Activation in the right-sided region corresponding to Wernicke center does not guarantee absence of speech disorders in patient with temporal lobe tumors, but it might be one of the factors in the complex process of brain functional rearrangement.

Our results proved the possibility of performing language fMRI in patients with brain tumors and determining language lateralization by calculation of the LI for Broca and Wernicke regions. We also confirmed that the Word Generation paradigm was effective to define lateralization [27,28]. A combination of fMRI results and intraoperative brain mapping improve the sensitivity of each technique and reduce the time of surgery [4,29,30].

Comparative pre- and postoperative fMRI studies in evaluation of rearrangement process of language areas in patient with brain tumors are of important value [31]. The fMRI has become a mainstream neuroimaging in patients with brain tumors, the task failures are relatively low and are reduced by paradigm repetition [32,33]. FMRI is a useful tool for predicting postoperative outcome in patients with a single brain tumor [34,35]. Some authors suggest that activation of the speech centers in the right hemisphere may afford a behavioral advantage to patients with left-hemispheric tumors. However, the precise trigger for functional reorganization of the language centers in brain tumor patients remains unknown [19].

However the present study has a number of limitations. The groups of patients were admittedly uniform in lesion location, but rather small. Further analysis on larger groups is needed to estimate the functional rearrangement of language areas. The evaluation of pre- and postoperative neuropsychological status of patients is crucial to prove the clinical importance of fMRI observations.

5. Conclusion

Our fMRI studies conducted on the right-handed patients with brain tumors located in the left frontal or temporal lobes have suggested that in the cases of LGG tumors localized near the left Broca's area there is a transfer of function to the right-sided region corresponding to Broca center. Furthermore, these studies showed that resection of tumor located near Broca's or Wernicke's areas may lead to restoration of function of the brain language centers in the affected hemisphere and/or promote their functional reorganization.

Conflict of interest

None declared.

Acknowledgement and financial support

This work was supported by the Medical University of Łódź, research task No. 502-03/1-136-01/502-14-171.

references

[1] Bizzi A, Blasi V, Falini A, Ferroli P, Cadioli M, Danesi U, et al. Presurgical functional MR imaging of language and motor functions: validation with intraoperative electrocortical mapping. Radiology 2008;248:579–89.

[2] 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.

[3] 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;66:3–20.

[4] Brennan NP1, Peck KK, Holodny A. Language mapping using fMRI and direct cortical stimulation for brain tumor surgery: the good, the bad, and the questionable. Top Magn Reson Imaging 2016;25(1):1–10.

[5] Borchers S, Himmelbach M, Logethetis N, Karnath HO. Direct electrical stimulation of human cortex – the gold standard for mapping brain functions? Nat Rev Neurosci 2011;13:63–70.

[6] Cao Y, Vikingstad EM, George KP, Johnson AF, Welch KM. Cortical language activation in stroke patients recovering from aphasia with functional MRI. Stroke 1999;30(11):2331–40.

[7] Thulborn KR, Carpenter PA, Just MA. Plasticity of language-related brain function during recovery from stroke. Stroke 1999;30(4):749–54.

[8] Calvert GA, Brammer MJ, Morris RG, Williams SCR, King N, Matthews PM. Using fMRI to study recovery from acquired dysphasia. Brain Lang 2000;71(3):391–9.

[9] Rosen HJ, Petersen SE, Linenweber MR, Snyder AZ, White DA, Chapman L, et al. Neural correlates of recovery from aphasia after damage to left inferior frontal cortex. Neurology 2000;55(12):1883–94.

[10] Rutten GJ, Ramsey NF, van Rijen PC, Alpherts W, van Veelen C. Reproducibility of fMRI-determined language lateralization in individual subjects. Brain Lang 2002;80(3):421–37.

[11] Benson RR, FitzGerald DB, LeSueur LL, Kennedy DN, Kwong KK, Buchbinder BR, et al. Language dominance determined by whole brain functional MRI in patients with brain lesions. Neurology 1999;52(4):798–809.

[12] Stippich C, Rapps N, Dreyhaupt J, Durst A, Kress B, Nennig E, et al. Localizing and lateralizing language in patients with brain tumors: feasibility of routine preoperative functional MR imaging in 81 consecutive patients. Radiology 2007;243(3):828–36.

[13] Lehéricy S, Cohen L, Bazin B, Samson S, Giacomini E, Rougetet R, et al. Functional MR evaluation of temporal and frontal language dominance compared with the Wada test. Neurology 2000;54(8):1625–33.
[14] Knecht S, Deppe M, Drager B, Bobe L, Lohmann. Language lateralization in healthy right-handers. Brain 2000;123 (1):74–81.
[15] Partovi S, Jacobi B, Rapps N, Zipp L, Karimi S, Rengier F, et al. Clinical standardized fMRI reveals altered language lateralization in brain tumor patients. Am J Neuroradiol 2012;33(11):2151–7.
[16] Avramescu-Murphy M, Hattingen E, Forster MT, Oszvald A, Anti S, Frisch S, et al. Post-surgical language reorganization occurs in tumors of the dominant and non-dominant hemisphere. Clin Neuroradiol 2016 [Epub ahead of print].
[17] Belin P, Van Eeckhout P, Zilbovicius M, Remy P, François C, Guillaume S, et al. Recovery from nonfluent aphasia after melodic intonation therapy: a PET study. Neurology 1996;47:1504–11.
[18] Heiss WD, Thiel A, Kessler J, Herholz K. Language activation in ischemic stroke and brain tumor: a PET study. Zentralbl Neurochir 2002;63(4):133–40.
[19] Shaw K, Brennan N, Woo K, Zhang Z, Young R, Peck K, et al. Infiltration of the basal ganglia by brain tumors is associated with the development of co-dominant language function on fMRI. Brain Lang 2016;155–156:44–8.
[20] Desmurget M, Bonnetblanc F, Duffau H. Contrasting acute and slow-growing lesions: a new door to brain plasticity. Brain 2007;130:898–914.
[21] Duffau H. Brain plasticity: from pathophysiological mechanisms to therapeutic applications. J Clin Neurosci 2006;13(9):885–97.
[22] 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(6):941–3.
[23] Pillai JJ. Insights into adult postlesional language cortical plasticity provided by cerebral blood oxygen level-dependent functional MR imaging. Am J Neuroradiol 2010;31:990–6.
[24] Robles SG, Gatignol P, Lehericy S, Duffau H. Long-term brain plasticity allowing a multistage surgical approach to World Health Organization Grade II gliomas in eloquent areas. J Neurosurg 2008;109(4):615–24.
[25] Thiel A, Habedank B, Winhuisen L, Herholz K, Kessler J, 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.
[26] Ulmer JL, Hacein-Bey L, Mathews VP, Mueller WM, DeYoe EA, Prost RW, et al. Lesion-induced pseudo-dominance at functional magnetic resonance imaging: implications for preoperative assessments. Neurosurgery 2004;55:569–81.
[27] Zacà D, Nickerson JP, Deib G, Pillai JJ. Effectiveness of four different clinical fMRI paradigms for preoperative regional determination of language lateralization in patients with brain tumors. Neuroradiology 2012;54:1015–25.
[28] Dong JW, Brennan NM, Izzo G, Peck KK, Holodny AI. fMRI activation in the middle frontal gyrus as an indicator of hemispheric dominance for language in brain tumor patients: a comparison with Broca's area. Neuroradiology 2016;58(May (5)):513–20.
[29] D'Andrea G, Trillo' G, Picotti V, Raco A. Functional Magnetic Resonance Imaging (fMRI), pre-intraoperative tractography in neurosurgery: the experience of Sant' Andrea Rome University Hospital. Acta Neurochir Suppl 2017;124:241–50.
[30] Alimohamadi M, Shirani M, Shariat Moharari R, Pour-Rashidi A, Ketabchi M, Khajavi M, et al. Application of awake craniotomy and intraoperative brain mapping for surgical resection of insular gliomas of the dominant hemisphere. World Neurosurg 2016;92(August):151–8.
[31] Dreher JC, Tremblay L, editors. Brain mapping. New York: Elsevier; 2011 [chapter 12].
[32] Barras CD, Asadi H, Baldeweg T, Mancini L, Yousry TA, Bisdas S. Functional magnetic resonance imaging in clinical practice: State of the art and science. Aust Fam Phys 2016;45 (11):798–803.
[33] Tyndall AJ, Reinhardt J, Tronnier V, Mariani L, Stippich C. Presurgical motor, somatosensory and language fMRI: Technical feasibility and limitations in 491 patients over 13 years. Eur Radiol 2017;27(January (1)):267–78.
[34] Bryszewski B, Tybor K, Ormezowska EA, Jaskólski DJ, Majos A. Rearrangement of motor centers and its relationship to the neurological status of low-grade glioma examined on pre- and postoperative fMRI. Clin Neurol Neurosurg 2013;115(12):2464–70.
[35] 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(4):E6.