Cortical and subcortical brain language mapping: correlation of fMRI and 3D-tractography with intraoperative cortical and subcortical stimulation of brain tumors located in eloquent areas

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Purpose

Surgical treatment is the election of the majority focal brain tumors, specially glial tumors. The goal is to obtain the maximum degree of tumor resection while preserving the patient’s quality of life.

Advances in neurosurgery of previous unaccessible lesions due to the proximity to eloquent areas, are based in the development of new surgical techniques as intraoperative cortical and subcortical stimulation.

The benefit to risk ratio of surgery has also improved thanks to the preoperative functional neuroimaging.

Functional MR imaging has become a viable clinical technique for presurgical planning in patients with brain lesions. The combination of BOLD imaging (f-MRI) and diffusion tensor imaging (DTI) are indispensable components in the surgical approach to lesions located in eloquent areas.

Functional MR imaging has also contributed to the evolution of the knowledge regarding language processing and overall cortical and subcortical language representation in the human brain.

Several authors have emphasized the good correlation between intraoperative cortical mapping and motor fMRI findings. Other authors compared preoperative DTI motor results with those of awake intraoperative subcortical stimulations.

On the other hand, language brain organization is not yet fully understood and the classic model of Broca-Wernicke areas has been recently replaced for a more complex and expansive language cortical and subcortical network.

Language f-MRI studies need more sophisticated methodology to be performed and the paradigms are more difficult to reproduce among patients, so there is a few number of publications comparing language fMRI and brain cortical mapping. The more used and correlated paradigms are "verb generation" and "passive listening" to evidence the "motor and receptive language cortical areas", respectively.

In the last years intraoperative electrical subcortical mapping of the white matter, has detected the subcortical structures crucial to language function acting as resection limits in the eloquent areas.

New DTI sequences provide a valid information about the disposition of the fines white matter tracts and has been integrated in clinical practice, as BOLD imaging for delineation of eloquent cortex, because surgical severing of the tracts can produce similar postoperative neurologic deficits.
In our study, we are correlating eloquents language cortical and subcortical areas resulting from the preoperative data of both f-MRI and DTI studies with cortical and subcortical intraoperative mapping in awake patients.

Methods and Materials

In our study we selected fifteen patients (6 women and 9 men) ranging in age from 20 to 65 years who underwent surgery with intraoperative electrical mapping for hemisphere lesions located in eloquent areas. The lesions include focal dysplasias, a complicated neuroepithelial cyst, cavernomas, a pleomorphic xantoastrocitoma, oligoastrocitomas and low and high grade glial tumors. All lesions were left hemispheres lesions with two exceptions: one, in the right precentral gyrus, near the facial motor cortex and the second in the right calcarine cisure. Presenting symptoms included none, parestesias, seizures, horizontal nystagmus, homonym hemianopsia and mild languages disorders. All these patients were right handed assessed by Edinburgh inventory. Our protocol in all patients included:

1. Pre and postoperatively neurological examination.
2. Preoperative 3T MRI morphological study with MRI-spectroscopy and MRI-perfusion studies.
3. Preoperative motor and language 3T f-MRI and 3D -DTI studies.
4. Cortical and subcortical intraoperative brain mapping and resection
5. Postoperative MRI control before 48 hours.

We describe our protocol for f-MRI and DTI studies.

Routinely we obtaine motor f-MRI sequences before language f-MRI studies because sensorimotor mapping is always performed first to identify central sulcus and to confirm the patient response. Motor paradigms commonly used are the classic movements of "right-left" and "up-down" of the tongue and foot, and the "finger tapping" of the digits of the hands to evidence eloquent motor areas in a craneocaudal and in a medial to lateral sense in the ascendent frontal gyrus or precentral gyrus. Activated areas are also seen in supplementary motor area located in the medial portion of the precental sulcus, specifically in the paracentral gyrus, and the posterior portion of the superior frontal gyrus.

Four paradigms are used in the language f-MRI studies:

1. "Verb generation" (Find verbs in relation to the presented objects. During the rest periods the patients were asked to count)
2. "Passive listening" (Listen to a text. Rest periods: invert text)
3. "Reading a text" (Reading a text. Rest periods: illegible text)
4. “Symbols identification” (Recognize significance of the symbols. Rest periods: count)

The first paradigm is used to evidence activated frontal "expressive or motor language areas", the second paradigm is used to evidence posterior receptive language area and the last two paradigms are used to elicit the "visual word form areas".

3T-MRI PROTOCOL gradient echo-planar (TE:35ms; TR:3000ms; flip angle 90°; matrix 64x64; 1nex; FOV:24; slice thickness:4.0 mm; spacing:0.0. During the procedure the patient alternate periods of rest and periods of activation. Each period (rest or activation) lasted 30 seconds for the three first paradigms and 15 seconds for the last one. Postprocessing : 3D Brainwave program.

3D - DTI studies are obtained in the same radiologic session. We used a diffusion SE-echo-planar with 25 -45 directions in axial, sagittal and coronal planes (TE:minimum; TR:6000ms; matrix128x128;1 nex; FOV:24; thickness: 4 mm; spacing:1,5 mm; maximum value of B:1000). Postprocessing: 3D Fiber Tracking program (Functool)

The different subcortical white matter tracts routinely searched are inferior frontooccipital fasciculus, arcuate fasciculus, subcallosal fasciculus, frontooccipital loop and inferior longitudinal fasciculus. Indeed, corticospinal tract and optic radiations are always obtained.

Intraoperative mapping

The patients underwent surgery under local anaesthesia so that functional cortical and subcortical mapping could be carried out using direct brain stimulations. Briefly, a bipolar electrode with 5 mm spaced tips delivering a biphasic current (pulse frequency 60 Hz; single pulse phase duration 1 ms; amplitude 2 to 8 mA) was applied on the brain of conscious patients. Neuronavigation system was sometimes used, but the neurosurgeons preferred to use a real time ultrasonographic system so as not only to delineate the tumour ( steril tag with the letters A,B,C,D) before its removal but also to identify residual tumour along the resection plane. In a first stage, cortical mapping was carried out before any resection, in order to avoid damage to eloquent areas. Sensorimotor mapping was done first, to confirm a positive response—for example, the induction of movement or paraesthesiae in the contralateral hemibody when the primary sensorimotor areas were stimulated in a patient at rest. The patient was then asked to count (in order from 1 to10, and so on), to read a text and to identify symbols and pictures (preceded by "this is a..."), so as to map the cortical language sites known to be inhibited by electrical stimulation. The patient was never informed when the brain was stimulated. The duration of each stimulation was four seconds. At least one picture presentation without stimulation separated each stimulation, and no site was stimulated twice in succession, to avoid seizures. Each cortical site was tested three times..
type of language disturbance was defined by a speech therapist who was present in the operative room during the functional mapping. Each eloquent area was marked using a sterile number tag on the brain surface, and its location was correlated with the anatomical landmarks (sulci, gyri, tumour boundaries) previously identified by ultrasonography. During a second surgical stage, the tumour was removed, with alternating resection and subcortical stimulation. The functional pathways were followed progressively from the cortical eloquent sites already mapped to the full depth of the resection. The patient was asked to continue to carry out both motor tasks (repeated opening and closing of the non-dominant hand) and language tasks (picture naming, reading) when the resection approached the subcortical language structures (white fibers and grey nuclei). These were identified by speech inhibition during stimulation in the same way as at the cortical level. To achieve the optimum tumour removal consistent with preservation of functional areas, all resections were continued until eloquent structures were encountered around the surgical cavity, and were then terminated along functional boundaries. In all patients were performed a postoperative control before 48 hours, at 3 months and then every 6 months after surgery.

Results

Morphogical MRI showed focal lesions near eloquent areas. 13 lesions were left hemispheres and 2, right hemispheres tumors.

f-MRI RESULTS CORRELATED WITH RESULTS FROM CORTICAL BRAIN MAPPING

The f-MRI areas obtained in our patients corresponded to the areas identified in the cortical intraoperative stimulation. Only in two cases where the lesions were near motor primary languages areas, the correlation was not fully complete. The correlation with frontal and parietal language areas was completed in terms of gyrus location and spatial relation to the lesions.

The verb generation paradigm evidenced activated frontal language areas implicated in the planning and execution of speech. These areas were (fig.1 on page 8):

- **frontal inferior gyrus, triangular and opercular pars** (the speech disorder when stimulated was anomia)

- **premotor cortex** (the disorder was anarthria)

- **facial motor cortex** (movement disorder in facial muscles and tongue when electrical cortical mapping was performed)
- **supplementary motor area** (disorders in the initiation and preparation of the speech)

The second paradigm or passive listening activated posterior receptive language area, located in (fig.2 on page 8):- **left posterior temporal cortex izquierdo:** posterior portion of the superior temporal sulcus and superior and medial temporal gyrus (the cortical stimulation induced semantic paraphasias).

- **Left inferior parietal gyrus: angular and supramarginal gyrus** (the language disorder was anomia)

The last two paradigms elicited the "visual word or objects form areas". These were located in (fig.2 on page 8):

- **Occipitotemporal basal cortex:** inferior temporal and fusiform gyrus (when stimulated produced difficulties in reading and symbols identification).

**DTI RESULTS CORRELATED WITH RESULTS FROM SUBCORTICAL BRAIN MAPPING.**

The correlation of the 3D - DTI maps of the white matter tracts implicated in the network language was complete with the data obtained from the brain subcortical mapping. These fascicles were:

- **Arcuate fasciculus (fig.3 on page 9)** medial part of the superior longitudinal fasciculus that connects the lateral frontal cortex with the lateral parietotemporal cortex, through the extreme and external capsule. Its stimulation induced a phonemic paraphasia or conduction aphasia (disorder in the phonological form of the word)

- **Frontoparietal loop (fig.3): on page** lateral part of the superior longitudinal fasciculus, that connects Broca's area with inferior parietal lobe. The cortical stimulation induced apraxia.

- **Inferior frontooccipital fasciculus (fig.4 on page 10)** connects prefrontal zones with medial occipitotemporal areas. It pass through the anterior third of the temporal stem, posterior to uncinate fasciculus, cranial to the roof of the temporal horn and to the optic radiations. Its occipito-temporal segment is located lateral to the occipital horn and join the sagittal stratum. The occipital radiations terminate in the inferior temporal gyrus, fusiform and lingual gyrus. Its stimulation induced a semantic paraphasia (disorders in the significance of the word)

- **Subcallosal fasciculus (fig.5 on page 11)** this fascicle surround the frontal horn and connects the supplementary motor area and the cingulate gyrus to the caudate nucleus. Its stimulation induced transient cortical motor aphasia with initiation disorders.
- **Inferior longitudinal fasciculus (fig.6 on page 12)**: recently implicated in the network language, specially its temporooccipital portion. Its stimulation induced transitory reading disorder and disorders in visual identification of words, objects and symbols.

Other fascicles commonly searched are:

- **Uncinate fasciculus (fig.4 on page 10)** connects frontotemporal anterior cortex, recently implicated in visual memory of famous faces. It was always identified as point of reference of the origin of the Meyer loop and the optic radiations (fig.7 on page 13) (its stimulation induced phosphenos).

- **Corticoespinal tract (fig.8 on page 14)** with parestesias or movements of the first finger, hand, elbow or face during cortical brain mapping.

We are showing some of our most representative cases:

**Case 1.** Left low grade insular oligoastrocytoma (fig.9 on page 15)

**Case 2.** Left posterior temporal glioblastoma (fig.10 on page 16)

**Case 3.** Left frontal recurrence of pleomorphic xantroastrocytoma (fig.11 on page 17)

**Case 4.** Left low grade insular oligodendroglioma (fig.12 on page 18)

**Case 5.** Left temporal pole low grade astrocytoma (fig.13 on page 19)

**Case 6.** Left occipitotemporal basal dysplasia. (fig.14 on page 20)

**Case 7.** Right frontal low grade glioma (fig.15 on page 21).

**Case 8.** Right occipital cavernoma (fig.16 on page 22). We are showing this case because we routinely expose optic radiations in all our studies; although is a right lesion the good correlation is very illustrative.

Postoperative control within the 24 hours show complete or partial resection, with a residual volume inferior to 10cc, except or a gyant anaplastic temporal oligodendroglioma and one anaplastic cyngular glioma.

All patients were evaluated pre and postoperatively by a neuropsychologist, achieving absent language déficits in asymptomatic patients and the same preoperative language disorders in the rest of the subjects.
Images for this section:

Fig. 1
Fig. 3
Fig. 4
Fig. 5
Fig. 8
Fig. 13
Fig. 14
Fig. 15
Conclusion

Surgical treatment is the election (when is possible) in brain tumors. Maximal tumor removal is the goal of neurosurgery while preserving brain functions. Indeed, anaplastic transformation is reduced in low grade gliomas < 10 cc. and is noted that radiochemotherapy treatment are more effective in low residual volumes.

For this reason intraoperative cortical and subcortical brain mapping is becoming a common surgical procedure in lesions involved eloquent areas, as also the combination of BOLD imaging (f-MRI) and diffusion tensor imaging (DTI) are indispensible components in this surgical approach.

The development of new equipments, coils, programs and software has contributed to improve the diagnostic potential for structural and vascular MR scans, functional activation imaging and tractography studies.

BOLD technique for f-MRI studies in 3T magnet is clearly improved, because the changes of BOLD effect are more linked to cortical activity and less closely linked to venous drainage, thus with a more "real activation". Indeed the same task produces changes of a greater extent and in larger areas than in 1.5T and reproducibility of functional imaging has better results in 3T.

3T - DTI studies are clearly superior in spatial (each slice can collected 45 non collinear directions) and temporal resolution (sequences < 4 minutes) defining the fines white matter tracts and their relations with the brain lesions.

In our study the correlation of our f-MRI and DTI data with cortical and subcortical mapping was nearly completed, as we have showed in our results.

There were only two exceptions of this good correlation: two patients with lesions near of the motor language cortex, one with false positive cortical activated areas, probably secondary to venous flow contamination and the second, with false negative data due to infiltration.

The correlation with the subcortical areas (white matter tracts) was complete.

The good results are also reinforced for the absent pooperative language deficits and for the great resection in the majority of the cases.

We propose two directions to continue this study: one, to extent the correlation to a great number of patients (we acknowledge that our series is small), to confirm these results and to validate the data of functional MRI studies. The second one, according to the new neurosurgical strategies for slow grow tumors with a multistage approach of
residual lesions, the utility of a multistage f-MRI and DTI studies to visualize the cerebral reorganization aiding to plannify a possible re-intervention.

References


Personal Information