THE IMPORTANCE OF FUNCTIONAL MRI (FMRI) IN THE NEUROSURGICAL STRATEGY IN BRAIN TUMORS

PANAGIOTIS D. TOULAS M.D.

Neuroradiologist, Institute Euromedica-Encephalos, Athens, Greece

Functional MRI (fMRI) is an indirect depiction of the functionality of brain neurons using local changes of circulation. The continuous evolution of MRI led to pulse sequences which could display the circulation of the brain at rest, with or without exogenous contrast agents. fMRI seems capable of determining the dominant hemisphere and the language centers. This is important for the pre-operational evaluation of patients with lesions in the frontal or temporal lobes (tumors or epilepsy resistive to medication), which might have extended centers in these lobes.

Keywords: epilepsy ,functional MRI, brain tumors

INTRODUCTION

Functional MRI (fMRI) is an indirect depiction of the functionality of brain neurons using local changes of circulation. Historically, the first observations of brain circulation and its changes upon brain activity were made by many investigators during the last decades of the 19th Century. In 1890 Roy and Sherrington published experimental observations that correlated increase of blood circulation in the brain with metabolism and consequently, established the close relationship between neuronal activity and circulation-metabolism of the brain (1). The functional mapping of the human brain was studied during the last few decades with Positron Emission Tomography (PET), Single Photon Emission Tomography (SPET), imaging methods that use radioisotopes as markers, and Magnetoencephalography (MEG), a method which measures small variations of magnetic fields in the brain.

PET in particular is considered the reference method (Gold Standard) and measures small local variations in the circulation of the brain during a known task. The method can utilize radioisotopes of oxygen (15O) or FDG (2). This method is not readily available in most Laboratories because of the high cost of the equipment and operation of the method. Furthermore, technical complications and the relatively high radiation involved in the process limit the method for children.

The evolution of MRI the 80's was especially spectacular in Neuroradiology, and the use of multiple sequences, acquisition of images in all planes, easy availability, relatively low cost and the steadily increasing number of MR imagers worldwide made MRI the method of choice for examining the central nervous system.

The continuous evolution of MRI led to pulse sequences which could display the circulation of the brain at rest, with or without exogenous contrast agents. The discovery of the Blood Oxygenation Level Dependent (BOLD) contrast of the brain in the early 90's gave birth to Functional MRI, a method which found remarkable applications in the last few years.

EXPLANATION OF FUNCTIONAL MRI (FMRI)

As was previously stated, fMRI is an indirect depiction of neuronal activity. Such neuronal activity causes local increase of brain metabolism, therefore increased oxygen consumption. This in turn requires an automatic increase of microcirculation locally, with fresh arterial blood rich in oxyhemoglobin, which can provide the required oxygen. The removal of oxygen from oxyhemoglobin leads to de-oxyhemoglobin, a molecule with paramagnetic properties. All in all, during the process, the accumulation of deoxyhemoglobin, prior to its removal through the venous pathways, acts as a local contrast agent, enhancing signal intensity locally by paramagnetic relaxation. This way a natural contrast agent is acted upon the area responsible for a task and this can be depicted by fMRI.

TECHNIQUE

Variations of the signal intensity in fMRI depend on the static magnetic field Bo, they are rather low in magnitude and they require a high signal to noise ratio (SNR) in order to be “visible”. The BOLD phenomenon increases with magnetic field strength and the variation in signal intensity are of the order of 2-5% for usual high field clinical MR imagers (1.5 Tesla) but they can reach 20% for higher strength magnets (3-4 Tesla). Practically such high strength magnets (3-8 Tesla) are ideal for specific uses in neurosciences, although their availability is very low worldwide. Most studies nowadays are conducted in commercial MR imagers of 1.5 and 2 Tesla.

The ideal acquisition technique is Echo Planar Imaging, which has several advantages over traditional gradient echo methods (FLASH, SPGR, etc.) in regard to temporal resolution. The same method is also used in DWI and Perfusion imaging, acquiring slices covering the entire brain in 3-5 sec. The higher the gradient strength (>20 mT/m) the more effective EPI can be. Typically T2*-weighted EPI images with TE>60 msec are acquired in fMRI.

Classical sequences such as spin echo, FLASH, SPGR, etc, can also be utilized for known areas of brain activity, such as motor center areas of the limbs, vision etc.

fMRI in general has limitations because of artifacts due either to the patient (motion artifacts) or to magnetic susceptibility, flow, and natural physiological noise. EPI is particularly sensitive to magnetic susceptibility variations amongst tissues and with air, which are more visible in the skull base and in areas with prior surgery (eg., biopsy).

EXAMINATION PROTOCOL

The data are acquired usually with the conventional brain coil. Initially some sagittal images are acquired (SE or SPGR) which are used for localization. Subsequently axial and/or coronal T1-weighted are acquired, although a 3D set of thin slices covering the entire brain is preferable so that 3D reconstruction can be used for the superposition of the fMRI data.

From this point on the “actual” fMRI starts with the acquisition of EPI-GRE T2*-weighted images at the proper brain level. All paradigms involve the activation of one specific area (e.g., motion of one hand), or other specific paradigm (e.g., verbal), for the determination of word centers. At our Center we use 5-stage paradigms in which two activation periods of 30 sec each are alternated with 3 periods of brain rest (rest-activation-rest-activation-rest), for a total time of 2 ½ minutes. The images are acquired continuously, under the guidance of the fMRI specialist, who gives the instructions to the patient for activation and rest during the entire acquisition.Activation is inspected in real time,using<<Brain Weave>>, before the patient is out of the magnet so that additional acquisitions can be added in case of artifacts or failure of the patient to perform properly. For the determination of each major center (e.g. motor center, language, memory, etc.) at least 3-4 paradigms are used, thus a typical fMRI examination is 15-20 minutes. Typically 500 or more images are acquired for each paradigm used.

Extended data analysis takes place at a separate workstation using apropriete soft-weare (functool). Paradigms with significant artifacts which cannot be removed with the proper statistical analysis are rejected in the Pre-Treatment stage.

The paradigms that pass the first stage of quality control are then analyzed extensively and the activation maps are being formed. There is no consensus yet for the statistical tests and the sensitivity threshold to be used. There are many methods as well as programs for analyzing the fMRI data and removal of motion artifacts. Once the statistical analysis is finished the fMRI color data are superimposed on high resolution images acquired prior to the fMRI acquisition, or to depict the x,y,z coordinates of each activated area in stereotactic maps or atlases (e.g., Talairach), which allow a better depiction of the activation areas. It is also possible superimposition with tractography (fusion) that correlate activation areas with mains neuronal tracts(e.g. corticospinal tract). There are possibilities of graphing signal intensity variations versus time for each voxel.

CLINICAL APPLICATIONS

For the depiction of the motor center of the upper limbs the most common paradigm involves the motion of each finger against the thumb (finger-tapping). In special cases there are other types of motion that can be used, such as opening-closing of the hand successively, turning the hand in prone and supine positions successively, etc.

For the feet, the most commonly used motion is that of extension-bending of the toes, because motion of the entire foot is being accompanied by motion of the entire trunk/head, increasing the motion artifacts. If sensory paradigms are required light “brushing” of the hands with a brush can be used. Keeping in mind that sensory centers coincide with motor centers in the brain this method can be an alternative for patients that are not capable to perform specific tasks (muscular paralysis, coma, etc.).

Practically, for patients with a hemispheric tumor in the proximity of the sulcus of Rolando two paradigms of the corresponding limbs are enough for the mapping of the primitive motor-sensory areas in relation to the tumor. This requires less than 10 minutes of examination time and 15-30 minutes at the workstation for statistical analysis.

Pre-operational fMRI provides useful information for surgical planning, helping the neurosurgeon avoid critical areas in the proximity of or in the tumor (in cases of infiltrating tumors with some functionality). With neuro-navigational techniques available nowadays neurosurgical planning is even more precise and functional information in relationship to the tumor is very important.

The determination of the dominant hemisphere and the depiction of the language centers are being accomplished with special verbal paradigms during which words with a special relationship are being utilized (for example words that start with the same letter, conjugation of a verb, thinking of opposite words, spelling, etc.). In order to minimize motion artifacts all paradigms are acquired silently, with the eyes closed. Prior to acquisition of images the whole procedure is explained to the patient and it is certain that it has been understood.

For the determination of the language centers we routinely use three paradigms in succession (verb conjugation, opposite word formation, rhyming) and some times we also use recitation in addition, which also adds some memory centers. Two paradigms, word and concept formation are enough to determine language centers.

fMRI seems capable of determining the dominant hemisphere and the language centers. This is important for the pre-operational evaluation of patients with lesions in the frontal or temporal lobes (tumors or epilepsy resistive to medication), which might have extended centers in these lobes. The reference examination up to date has been the Wada test, in which the patient receives intra-arterial amobarbital, successively in the two carotids during an angiographic examination and checking the corresponding hemisphere with the patient awake.

fMRI is risk-free compared to angiography and the Wada test and of course repeatable without any limitations in case of failure and the results are comparable to the Wada test in the adults as well as in children.

OTHER APPLICATIONS-PROSPECTS

In addition to the aforementioned “practical” applications in pre-operational evaluation of the patient there are more prospects. One of the more used applications is the evaluation of brain plasticity, i.e., the gradual functional rehabilitation after an ischemic or traumatic lesion.

Being a painless examination and having a relatively low cost allows frequent examinations to be performed in order to evaluate the effects of therapy or the degree of rehabilitation. The evaluation of an epileptogenic focus can also be made with fMRI. There is also promise for patients with basal ganglia lesions, dystonia, myotonia, chorea, athetosis, etc.

Numerous are the newest applications in the diagnosis of neurological and psychiatric diseases and also in the evaluation of the effects of certain drugs.

Finally, fMRI in children is an excellent way of determining the evolution of brain. Functional organization of the cortex in various diseases, dysplasias, tumors, or malfunctions such as dyslexia, etc., can hopefully be studied and understood, with the ultimate goal being to reach the proper therapy.

CONCLUSIONS

fMRI is a new, revolutionary, non-invasive method to study and map the functions of the brain.

Pre-operational fMRI provides important functional information for neurosurgical planning, helping the neurosurgeon avoid critical areas. Its use is not limited to pre- and/or post operated patients but also to other groups of patients and also of healthy volunteers, including children.

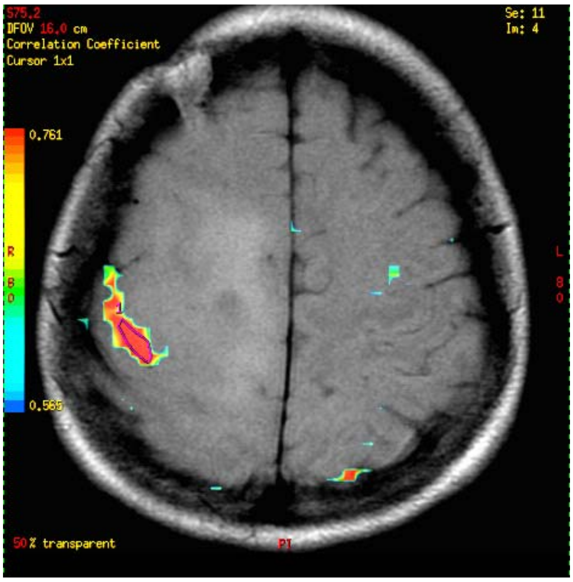

FIG. 1 Left hand finger-tapping of a patient with an infiltrating tumor (low grade glioma)

Putting aside the initial enthusiasm for the ten-year initial results of the method, the rapid development and the multiplicity of the clinical applications of the method, we must not forget that additional work is still required to make the method more reliable, simpler in standardization and analysis.

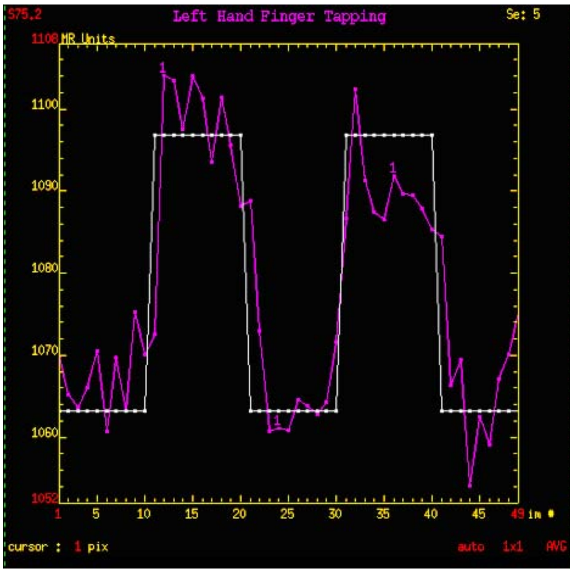

FIG. 2 Signal Intensity temporal dependence (off-on-off-on-off, in 30 second activation-inactivation intervals)

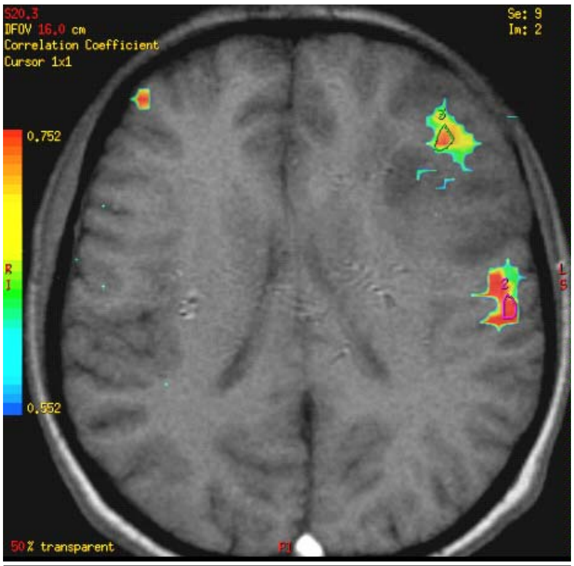

FIG. 3 Verb conjugation paradigm, of 36 year old female patient with low grade glioma

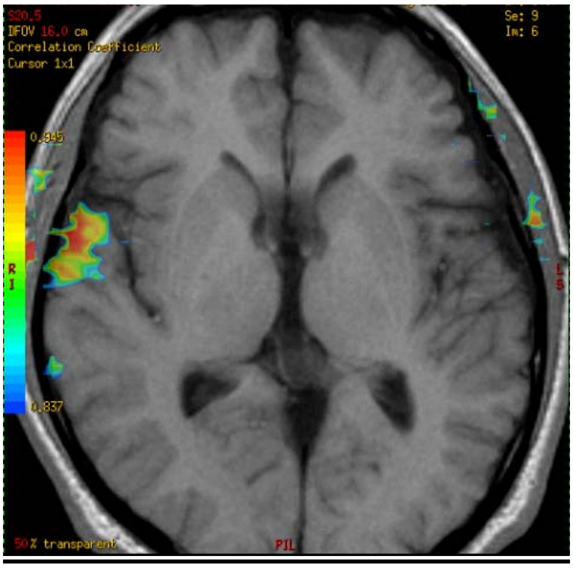

FIG. 4 Verb conjugation of a 52 year old dyslexic right-handed patient. Notice the right hemisphere dominancy

REFERENCES

1.1.D'Elia A, Melone GA, Brogna C, Formichella A, Santoro A, Salvati M. Radio-induced low-grade glioma: report of two cases and review of the literature.Neurol Sci. 2009 ;30(2):137-41.

2.2.Douglas-Akinwande AC, Payner TD, Hattab EM. Medulloblastoma mimicking Lhermitte-Duclos disease on MRI and CT. Clin Neurol Neurosurg. 2009 ;111(6):536-9.

3.3.Foroglou N, Zamani A, Black P. Intra-operative MRI (iop-MR) for brain tumour surgery. Br J Neurosurg. 2009 Feb;23(1):14-22.

4.4.Sharma MC, Jain D, Gupta A, Sarkar C, Suri V, Garg A, Gaikwad SB, Chandra PS. Dysembryoplastic neuroepithelial tumor: a clinicopathological study of 32 cases. Neurosurg Rev. 2009;32(2):161-9

5.Song J, Li C, Wu L, Liu M, Lv Y, Xie G, Li L, Blanco Sequeiros R. MRI-guided brain tumor cryoablation in a rabbit model. J Magn Reson Imaging. 2009 ;29(3):545-51.