Original article

Functional Evaluation of the Human Language

Estudo Neurofuncional da Linguagem Humana

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Received and accepted during the first semester of 2005

ABSTRACT

A new scientific horizon has been opened on the understanding of human language with the use of functional magnetic resonance imaging (fMRI).

The authors review the neuroscience historical landmarks on this subject, the advances made since the introduction of fMRI, its present limitations and its potential role as a tool on the evaluation of neurosurgical patients.

Key words : Language, Functional MRI, Neurosurgery.

RESUMO

O estudo da linguagem através da imagem de ressonância funcional (RMf) abre uma nova perspectiva na compreensão desse processo, característico da espécie humana.

Os autores analisam os marcos referenciais no estudo da linguagem até o presente, os avanços realizados com o uso dessa técnica, suas limitações atuais e seu papel como ferramenta na avaliação pré-operatória de pacientes neurocirúrgicos.

Palavras-Chave: Linguagem, Ressonância Funcional, Neurocirurgia.

LANGUAGE: CONCEPT AND TRADITIONAL METHODS OF INQUIRY

The language is the way through which it is possible to transmit complex information from a person to another. The understanding of the complex cerebral process which results in the human language has been the focus of study for several decades.

One of the first methods to study the acquisition, development and use of language consisted of animal experimentation. The study of language using animals, with the aim to understand, by comparison, the development and cerebral processing of language in the human species have been marked though, by unsatisfactory results. The studies carried using non-primates have demonstrated that, although there are evidences of communication between animals of these species; the use of language is stereotyped and lack the characteristics of interpersonal relation. In a similar way, the studies of language using inferior primates, demonstrated that, although these individuals possess a relatively larger capacity for acquisition and use of language, including the ability to associate a causal nexus, limitations as the anatomical incapacity of vocalization, reduced capacity to acquire new terms and to use them in a creative manner, added to the limitation of development of grammar and other basic characteristics that distinguish the human language, made this model clearly inferior, even when compared to human babies. These evidences point to the fact that language is an essentially human characteristic and any observational study of human language using animal models is limited.

Looking at the human evolution through this prism - of language - and considering the findings of anthropological studies, it is possible to imagine that evolution of the human species has been marked for selection of individuals whose brains were anatomically more apt to develop language, since specific regions of the brain, fundamental for this function, seem to have developed early. In addition, when one considers the motor development of man up to the biped position and the gestalt and vocal theories, it is indeed possible that one of these two theories, or even a combination of them, has been the way that allowed the gradual improvement of the language capacity [3]. It is possible, therefore, to consider human language as the result of a combination of innate and learned characteristics. Innate are the dominance of the left temporal lobe, the newborn intrinsic ability to distinguish a large variety of sounds, the constant landmarks of language development present in every growing human child and the existence of a critical period for the development of this capacity. On the other hand, evidences of the acquired characteristics in human language are the practical learning of grammar, the appropriate use of circumstantial intonation and pronunciation.

Another study object, classically used to understand how human language is formed, stored and processed, consists of observation of patients with brain lesions or the study of aphasias. Aphasia is the impairment of the language capacity, including understanding, production or both, and it needs to be differentiated of pure motor disability to produce the speech, which basically involves a deficiency in controlling the muscles of the vocal device. One of the most popular models used for understanding language and its distortions in illness resulted from study of the aphasias: the model of Wernicke-Geshwind. This model organizes the functional language into three basic areas: 1) the angular gyrus, on the inferior parietal lobule, the center for processing the visual, auditory and tactile stimuli, 2) Wernicke´s area, on the superior surface of the superior temporal gyrus, involved in the understanding of sensorial inputs and 3) Broca´s area, on the anterior portion of the inferior frontal gyrus, involved with articulation of speech. In this circuit, the arcuate fasciculus connects these centers. From the Wernicke-Geshwind model, three basic forms of dysfunction can be distinguished: 1) Wernicke´s aphasia, caused by an injury of the area of same name and in which the fundamental problem comprises the understanding of language; 2) Broca´s aphasia, which involves a problem with production of speech with relatively preserved comprehension and 3) conduction aphasia, a truly sensitive-motor disconnection, caused by injury of the arcuate fasciculus. These basic and simplistic categories, hold a didactic and referential value for those initiating in the study of language, however, it is important to grasp that their scope is limited as not all the language problems are restricted to lesions involving these areas.

LANGUAGE AND FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI)

In this scenario, the study of language using functional magnetic resonance imaging (fMRI) opens a new perspective for understanding the process. The fMRI is based on the intrinsic contrast effect produced by local metabolites that act as paramagnetic particles. Changes in concentration of these metabolites result into an alteration of the signal in T2* images. The method of fMRI most used, and that has dominated the field since its beginning, depends on the level of blood oxygenation (BOLD). fMRI BOLD uses the hemoglobin as the endogenous contrast agent, and is based on the difference of magnetization between oxi and deoxihemoglobin for creation of signal [1]. The temporal course of the BOLD effect is characterized for a triphasic response (Fig. 1) which is initiated with a negative curve, followed by a positive change of signal and a recurrent fall. Under physiological conditions, the initial negative curve seems to represent the increase of deoxihemoglobin due to a temporary imbalance between blood flow and local metabolism.

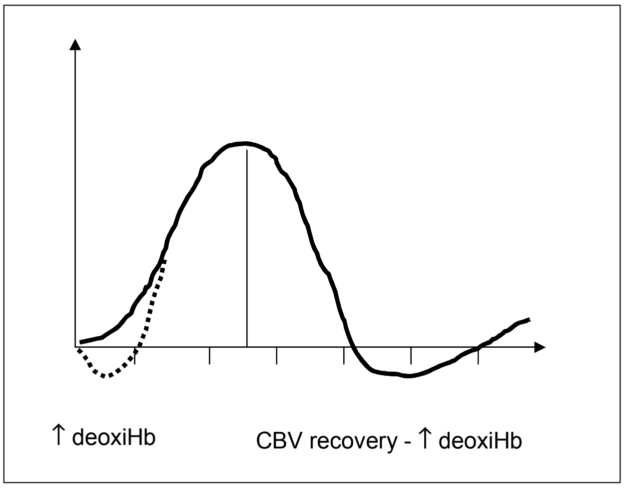

FIG. 1. Hemodynamic response. To be measurable by MR, the increase in blood flow must last at least 2s. The peak is 5-7s after the electrical event.

In other words, the BOLD effect seems to result from a relative imbalance between local blood flow and a simultaneous, but rather smaller, increase on the O2 metabolism, that causes a transitory fall in the deoxihemoglobina:hemoglobina ratio [7]. Thus, the physiological basis of BOLD image rests on the principle that neuronal activity is closely connected to an increase in blood flow and local energy metabolism.

However, BOLD images could be measuring only hemodynamic changes as blood volume or intravascular magnetic susceptibility; to clarify this matter, and therefore result in a clearer understanding of the nature of the local phenomenon and its temporal course, there was a need of simultaneous measurement of the neuronal activity [5]. Logothetis and cols (2001) were the pioneers in simultaneous acquisition of electric data and fMRI in primates [5]. These authors registered brain electric activity through micro-electrodes – a classic method in the neurophysiologic research - and adapted it to a simultaneous capture of functional images, making possible the comparison of studies using humans, with a massive body of evidences derived from animal experimentation collected over the last 50 years. The results of this seminal study demonstrated the existence of a linear relation between the magnitudes of neural activity and the BOLD effect, supporting the theory that the BOLD effect directly reflects the neural response elicited by a stimulus.

Many questions await answers though, and many unfoldings of the BOLD technique need to be understood. For example, although it is reasonable to consider that the resultant activity correlates with neurotransmitter release and sprouting of pre and post-synaptic events; in the instances where the input in an specific area has a modulating effect, fMRI experiments can disclose activation of areas in which no electric activity has been recorded in physiological experiments. Furthermore, as the BOLD effect is dependent on many physiological and biophysical parameters that can vary between species, these comparisons must be considered semi-quantitative [1]. Amongst the many experimental parameters that can affect the amount of BOLD signal in a specific device are: the power of the magnetic field, the time of echo and technique used to record the image. The BOLD effect is also susceptible to several potential artifacts as movement of the head, ghosts and magnetic field imbalances. Physiological factors that can add to the changes on measured concentration of the deoxihemoglobin and influence, therefore, the final BOLD effect are: the blood volume, the vascular geometry, hematocrit, and initial oxygen saturation [1, 7].

Once all these considerations have been made, it is important to point out that BOLD images have generated interest, not only as a tool to map brain activation alone, but also as a method to study the neural nets, as functional images can be studied under variations of space and time [5].

FMRI AND PREOPERATIVE EVALUATION OF LANGUAGE AREAS

Another use for fMRI is in preop localization of eloquent brain areas. The golden method for intra-operative identification of essential motor, sensory and language areas has been the intra-operative cortical mapping, using cortical stimulation and monitoring of evoked potentials. These techniques, however, are complex and invasive and require for their application, the trans-operative awakening of the patient - called technique of conscious surgery - which demands from the patient a high degree of understanding and collaboration that, *per si* is an exclusion factor for many. Moreover, the intra-operative monitoring does not provide information for pre-op planning and usually requires large craniotomies, which can increase the chance of postop complications [9].

Theoretically, fMRI offers a structural and functional model of each patient's brain by combining detailed anatomical information and hemodynamic changes derived from cognitive activity (Fig. 2).

Functional images can be used in the pre-op to discuss risks and to plan the best approach to allow maximum preservation of essential cortex. By allowing a reduction of significant morbidity while maximizing the chances of achieving the surgical goal (resection of tumor or epileptogenic area), fMRI can be considered an instrument of minimally invasive neurosurgery [4].

Many studies have analyzed the use of fMRI as a pre-op tool for localization of language, sensory, primary and supplementary motor areas. To fMRI become useful in neurosurgical practice up to surpass trans-op mapping, it is necessary that it precisely detects language areas and that, when no area of activation is seen on fMRI, no point of positive cortical stimulation could be elicited by cortical mapping. However, recent evidence points to fMRI low sensitivity when compared to trans-op stimulation during evaluation of language areas [8].

Many confounding factors exist in this analysis. The first is the intrinsic differences between the methods: while trans-op stimulation theoretically demonstrates essential areas to complete the function, being also able to evaluate the function of sub cortical circuitry, the fMRI offers information on cortical areas involved in function and not necessarily the crucial ones for performance.

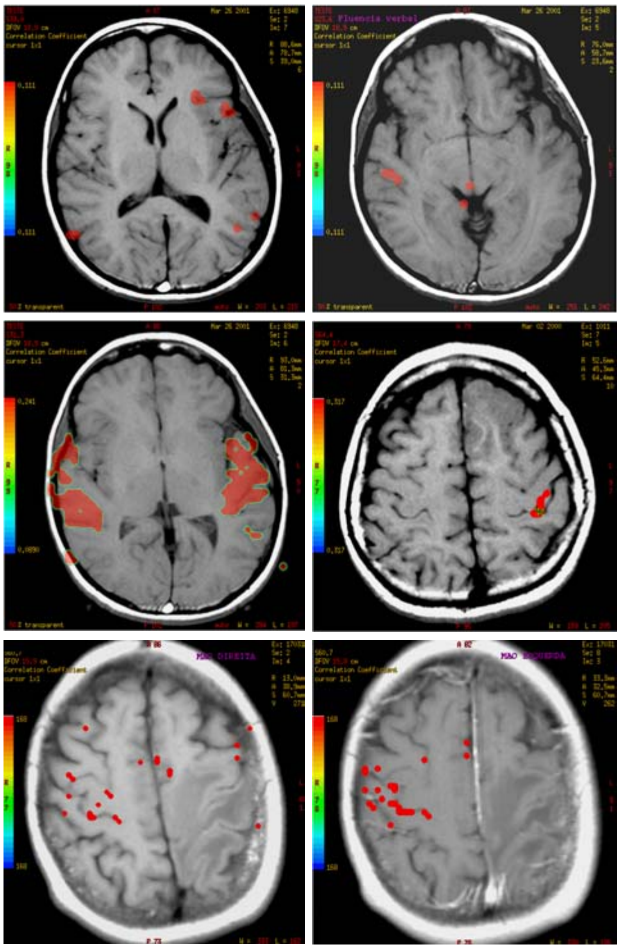

FIG. 2. A-C: Language experiment. 25-year-old, female, healthy volunteer A. Naming task locates Broca´s area on the dominant hemisphere (left) B. Silent generation of words locates Wernicke´s area on the non-dominant hemisphere (right) C. Passive listening activates the Heschl´s gyrus on both hemispheres. D-F. Pre-op mapping of motor cortex. 28-year-old, female, left frontal tumor (oligodendroglioma). D. Motor task right hand. The left motor cortex is activated on the posterior portion of precentral gyrus and anterior surface of postcentral gyrus. E-F: Unsolved issues. Motor task successfully performed with right (E) and left (F) hands. Both tasks activate the right precentral gyrus. The supplementary motor area has also been activated in E and F. Changes induced by the tumor have not allowed detection of BOLD effect on the left? Was there a detour of activation to the right? In such situation it is not possible to affirm, based only on the fMRI that there is no activity on the left sensory-motor cortex.

On the other hand, while fMRI can test the whole cortical surface, including the depth of the gyri, the trans-op stimulation can test only the area exposed by the craniotomy and is further limited, usually, to the top of the gyri. There is also the difficulty in finding a task that is effective for use with both methods. Naming objects exemplifies this difficulty: although this task is classically used during trans-op monitoring of language, for fMRI this task generates small signals [2, 8, 9]. Add to this the need of a paradigm that limits the interference caused by movement during image capture and that results in the purest possible activation of language areas.

Other factors to be considered are the inherent error associated with coupling the functional images to anatomical images; the choice of recording threshold for the BOLD signal and the effect of lesion on the BOLD effect. This latter aspect - the influence of brain injuries on BOLD effect - has assumed importance in the scientific discussion at this time. The first problem, which concerns specifically infiltrative lesions, is the inclusion of functional tissue by some tumors, a fact recognized by the neurosurgeons, for years [6]. Other factors are: the presence of susceptibility artifacts (which particularly affect eco planar images), the effect of tissue compression by the lesion and the changes of activation in this interface, as well as the effect of cerebral plasticity, ipsi and contra lateral to the lesion [9]. A tool that will assist in the understanding of how expansive lesions affect the BOLD effect is the comparison between the pre and postop functional images [8].

At this point, it is possible to identify the uses of fMRI in the preop evaluation of language at three levels: 1) evaluating the viability of resection, 2) in planning the surgical procedure and 3) as a guide during intra-op monitoring, potentially reducing the stimulation time and, consequently, the surgical time [9].

CONCLUSION

The language, its components, creative use and learning - peculiar characteristics of the human brain - are the landmark of selective and specialized evolution of the specie. Its study and understanding today, more than ever, require joined efforts and challenge the diverse areas neurosciences.

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