

Method of least square for the linear model to extract the neuronal activity of IRMf

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Abstract-- *Our project entitled: "Method of least square for the linear model to extract the neuronal activity of IRMf ". The goal of this theme is to study and to explore the theory of technique BOLD (Blood Oxygenation Level Dependent) of IRMf type, this technique is the most used for the detection's variations of oxygenation and blood flow bound to the activity neuronal in vivo. The functional magnetic imaging IRM (IRMf) is used by the Neurologists, Physicists and Mathematicians who work on the brain activation card. For the treatment of the IRMf data several methods, algorithms mathematical have been elaborated for the calculation's regions of cerebral activations that demand complex software tools and powerful computer platforms, either in the medical clinics or in the centers of research on the IRMf due to the complexity and to the volume of the data treated. To extract the activity as experiment result, we have used the mathematic linear model general with least square method to study the application of Student T-test, then see the activity lower then 0.05 and apply it on a glass of Talairach.*

Index Terms--: IRM, IRMf, BOLD, PET, neuronal Activity

1. INTRODUCTION

The IRM became the instrument privilege's survey in vivo for anatomy normal and pathological brain. Otherwise, the survey of the cerebral drip permits to get some information on the working of the brain and on its viability. Some recent developments showed that the IRM permits to study the cortical organization of the cerebral functions, while detecting the local variations of drip associated to the neuronal activity (functional IRM, IRMf). Indeed, it is known that every motor, sensory, or cognitive function, can be assigned to one or several cerebral anatomical regions. [1], [2].

The techniques of functional imagery as the SPECT (Single Photon Broadcast Tomography) and the TEP (Tomography by Broadcast of Positons) measure the regional cerebral blood debit for the injection of a radioactive scorer (water marked to the O₁₅ in TEP) in period of "rest", then during the execution of a task and localize by taking difference from the activated regions (imagery of activation), but the clinical use of this techniques rest limited because of their technical complexity, of their weak

spatial and temporal resolution, and of the few of available facilities.

IRMf present multiple advantages for the survey of the functions cerebral in vivo among the patients and the normal subjects. Indeed, it doesn't require injection of radioactive tracer, present a temporal and spatial resolution until now unequaled, and is extensively available on the clinical sites. Otherwise, whereas in TEP, the middle of several topics is often necessary to get a report signal on noise being sufficient, the IRMf is especially suitable to an individual's survey, what makes the first tool of functional imagery of it comfortably usable in clinic. The advantages of the IRMf in the survey of the cerebral activation are:[1],[2],[3],[4]

- Excellent spatial resolution
- Good temporal resolution
- Absence of ionizing radiation, technique non invasive not of exogenous contrast product injection
- Possible Acquisition in all plans and 3D volume rendering.

The fMRI has been developed in the beginning of the years 1990 when some more and more powerful computers were coupled to the devices of IRM. The time of registration can be as short as 40 milliseconds and the resolution of the order of the millimeter is the best of all functional imagery techniques. The last scanners of fMRI can produce four images per second of the brain, what permits to follow the displacement of the neuronal activity during a complex task.

2. IMAGERY BY FUNCTIONAL MAGNETIC RESONANCE (IRMf)

To the difference of the magnetic resonance that permits to visualize the anatomy of the cerebral structures, the imagery by functional magnetic resonance (IRMf) informs us on the activity of the different cerebral regions. The equipment that surrounds the patient and the working of basis is appreciably the same that with the IRMf, but the computers that analyze the signal differ (Fig1). [2], [5],[6],[7],[8].



Fig.1. Picture of G.Boynton: [2], [5], [7].

The physiological phenomenon on which leans the IRMf (all as the TEP besides) was put in evidence at the end of the 19th century when some neurosurgeons established that the cognitive functions modify the cerebral blood circulation locally. Indeed, when a group of neurons becomes more active, a local vasodilatation of the

cerebral blood capillaries occurs automatically to bring blood more, and therefore of oxygen, toward these more active regions.

However hemoglobin, this protein possessing an atom of iron that transports the oxygen has different magnetic properties depending on whether it transports the oxygen or that it has been riddled some by the consumption of the most active neurons. It is the concentration of desoxyhemoglobin (hemoglobin riddled of its oxygen) that the IMRf is going to detect. Indeed, this molecule has the property to be paramagnetic: its presence generates in its neighborhood a weak disruption of the magnetic field.

Without entering in the details, let's mention that the increase of the cerebral blood debit in a more active region of the brain is always superior to the demand of oxygen increased of this region. Therefore, it is the decrease of the rate of desoxyhemoglobin (dilute in a bigger oxygenated blood volume) that the IRMf is going to make an increase of the activity of this region corresponds.

While subtracting the intensity of the different regions of this picture of a thereafter another one that has been recorded previously before the task to accomplish, one observes a difference in some zones that "ignite" at the regions the more irrigated and therefore the most active to the level of the neuronal activity (fig2). [2], [4], [5], [8],[9], [10].

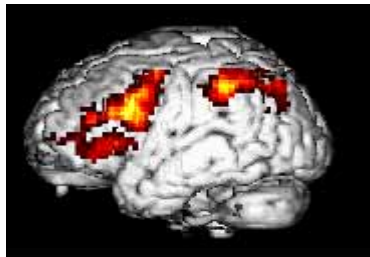


Fig.2. Functional magnetic resonance of G.Boynton . [2], [4], [5]. [10].

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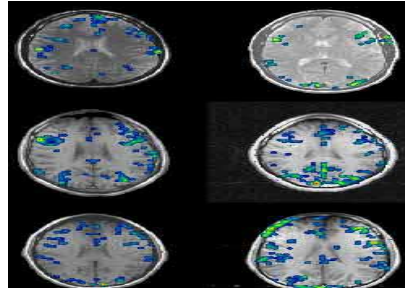


Fig.3. Functional magnetic resonance during the test of Stroop for six different patients demonstrating the big variability between the participants. (Source: Dr David C. Osmon) [2], [5],[8], [9], [10]

The IRMF, which can be used without the injection of stain in the patient's organism, is appreciated very in fundamental research (fig3). Another of its big advantages is that the same machine can provide a structural and functional picture of the same brain, facilitating the anatomy-functional correspondences thus.

The IRMF is often considered as the technique of imagery producing the most impressive results. But the costs of these devices and maintains them are as impressive, so that its use must often be shared and there are lists of waiting.

3. PRINCIPLES AND MECHANISMS OF THE IRMF

3.1. Cerebral drip and activation

3.1.1. Cerebral drip

The word "drip" makes reference to the local contribution of elements useful to the life of the cells (oxygen, nutriments, hormones, chemical mediators...) and to the evacuation of the products's catabolism or synthesis (CO₂, NO, hormones, mediators...). The exchanges between blood and texture don't take place that to the level of the capillary network.

The brain at the man receives a debit of blood of 50 to 60 ml/100 g/min (either to the total 750 ml/min). The consumption of oxygen is essentially the fact of the gray substance (40 to 45 ml/min of oxygen). The increase of the CO₂ entails a cerebral vasodilatation, whereas the hypocapnie entails a cerebral vasoconstriction on the contrary, the hypoxia being a weaker stimulus of the cerebral vasoreactivity. [2],[11]

3.1.2. Activation-Drip coupling

The neuronal activity comes with a depolarisation of the membrane. During the potential of action, some ions are exchanged between the surroundings extra and intracellular. The pump to sodium-potassium that has like role to maintain constant the ionic distribution consumes the energy and induced of the modifications of the metabolism and the extraction of the oxygen, of the metabolism of glucose, of the concentration in lactate. It is likely that the increase of the concentrations of CO₂, H⁺, NO, K⁺ and glutamate, free at the time of the neuronal activity, succeeded to a local

dilation of the vessels. It follows a secondary increase of the blood flux and the blood volume, whose delay varies between 0,1 s and 4 s and reaches its maximum in 8 to 10 s.

At the time of the cerebral activation, this increase important of the local blood flux overcompensates the increase curbed of the oxygen consumption. The consequence of these two phenomena is a paradoxical blood hyper oxygenation on the venous side of the capillaries downstream the activated region (fig 4).

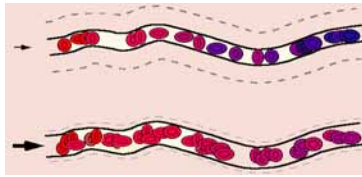


Fig. 4. Hyper oxygenation capillaroveineuse during the activation.[5],[11]

To the state basal, the oxygen is consumed quickly. The local deoxyhemoglobin concentration is important to the exit of the capillary. During activation, one notes an increase of the debit and the volume blood in the capillary. The oxygen in excess is not consumed and the concentration in desoxyhemoglobine is decreased. [2], [5], [11], [10] .

A venous hyper oxygenation exists therefore in relation to the state activates (fig.5)

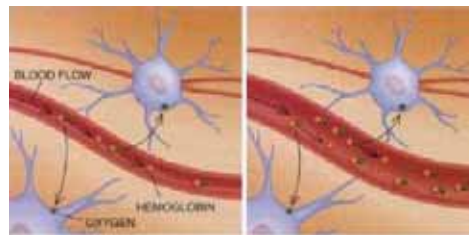


Fig.5: Effect BOLD: No cerebral activity (Fig. of left). Increase of the blood volume and the rate of oxyhemoglobin because of a cerebral activity (Fig. of right). [5], [11], [12]

Remark:

Oxyhemoglobin: diamagnetic.

Dice-oxyhemoglobin: paramagnétique.

3.2. Techniques of functional IRM

The metabolic answers and hemodynamics in relation with a cerebral activity being localized remarkably, it is possible to get a cartography of drip that either a precise reflection of the cerebral functional zones.

The methods of survey of the drip by IRM used principles developed in nuclear medicine as the use of tracers initially. But these techniques are relatively difficult to put in work and don't offer a sufficient temporal resolution to follow "in real time" the neuronal activity. Some techniques in development measure the variations of flux regardless's blood oxygenation while

using methods of magnetic marking's protons of the circulating blood. But currently, the technique of IRMf the more used detects the variations of oxygenation and a blood flux bound to the neuronal activity, and has been called BOLD (Blood Oxygenation Level Dependent). [2],[5],[9],[8], [10].

4. INSTALLATION OF THE PATIENT

The patient must be installed comfortably, because the immobility of the head is essential (holds of mosses, elastic bandaging, masks in plastic thermoformables...), the technique being based on a comparison of the pictures acquired sequentially during the test.

4.1. Protocol of activation and acquirement of the pictures

The technical IRMf-BOLD being based on the comparison of pictures acquired during two different functional states (activity vs rest, or activity vs references), all sequence of activation in IRMf must include these two different states, that are alternated according to one precise fashion (paradigm of activation) (fig 6). For example, in a survey of the primary motor cortex of the hand, one asks the patient initially to remain immobile, then to move the fingers of the hand, and this cycle is repeated several times. During the whole length of the paradigm, some pictures are acquired to a fast cadence (all 3 to 10 seconds according to the cases), always the same in order to be able to compare their signal during rest (or the state of reference) and the activation. To the total, one acquires fluently between 500 and 2000 pictures by IRMf set.

The very big variety of the neurological functions capable to be tested in IRMf explains that innumerable paradigms of activation can be finalized according to the calm question. These paradigms sometimes require particular facilities (all non magnetic in order to can be placed in the room of the imager): video projector adapted and reflecting mirror to present to the patient of the stimuli on a screen placed to its feet at the end of the tunnel, bound joystick to a computer to record the answers of the topic, special helmet with earphones in case of auditory stimuli, etc... In any case, one is careful to avoid the movements of the patient's head, what even obliges to test the language in a silent way, in order to avoid the movements of the face. [2], [8], [11]



Fig.6. Classic paradigm of activation for the survey in BOLD. An alternation of phases of activation and rest (or reference) is used. [2][11]5. TREATMENT OF THE DATA

5. ANALYSE STATISTIC

5.1. Diagrams synoptic

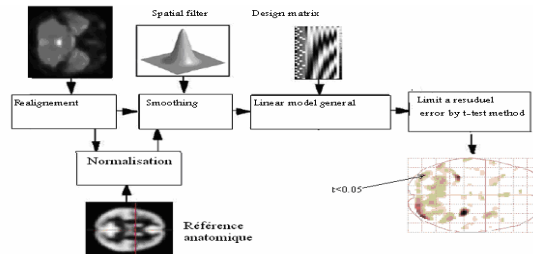


Fig.7. General working of the treatment of the pictures of IRMf [11],[12],[13],[14]

The objective of the treatment of the data in IRMf is to detect and to localize the zones activated from sets of pictures. The variations of signal bound to the activation are not very visible to the naked œil and require a statistical treatment of the pictures with the help of specialized software. This treatment takes place in several stages: pre-treatment, treatment, presentation of the results, either directly to the console with software constructors, and either on workstations. Many software have been developed by the laboratories of recherche.fig7

- Pre-treatment. [11], [13], [15]
 - Detection and correction of the artifacts of movements (Recalage of the pictures) .
 - Correction of geometric distortions. Filterings...
 - Normalization in the space of Talairach
- Treatment (statistical test Choices). [13], [15], [16]
 - Subtraction
 - Parametric cartography (Z, t, ANOVA) or non parametric
 - Analysis of interrelationship
 - Multiple linear regression
 - Regrouping of data (Dated clustering)
- Presentation of the results. [13], [2], [14]
 - Superposition to an anatomical picture 2D
 - Superposition to an anatomical picture 3D (returned surfacique)
 - Coordinated of Talairach

5.2. Least square method

By using matrix formulation to calculate the activity by the method of T-test

5.2.1. The contrasts of time hemodynamic(t-test)

For calculate t-test it is necessary know that: [1]

- To every position in the brain, one l module activity during the time by a set of function that represents that that we know function (paradigm or noise).
- One adjusts by least squares the weight of each of these functions to adjust to best the data (to minimize the variance of the residues). One gets valued parameters. (The weights of these functions), of the adjusted data and of the residues.

- One test then these weights (One test then these weights (them): Creation "contrast" and one calculates a statistical (equation (1))

$$t = \frac{\text{contrast of estimated parameter}}{\sqrt{\text{variance estimate}}} = \frac{C' \cdot \beta}{\sqrt{\sigma^2 \cdot C'(X^T \cdot X)^{-1} \cdot C'}} \quad (1)$$

$$\hat{\sigma}^2 = \frac{\varepsilon^T \varepsilon}{M - p} \quad (2)$$

with

$\hat{\sigma}^2$: Estimated of σ , M : The time and P: A parameter .

If we think that 1 regressor in our matrix of the drawing (for example β_1) could lead to an interesting activation, we calculate:

$$1\beta_1 + 0\beta_2 + 0\beta_3 + 0\beta_4 \quad (C' = 1 \ 0 \ 0 \ 0)$$

One gets a statistical card in t. to test the simultaneous influence of several columns of the experimental drawing matrix, one uses a F. test [13],[14].

5.3. Presentation of our results

a. Algorithm :

- Extraction of the IRMf data (temporal Set in a specific Voxel)
- Definition of the experimental protocol: Auditory stimulation based on words bi syllabic to a report of 60 per minute.
- Evaluation of the general linear Model
- Definition of contrasts them
- Execution of t-test

b. Data of IRMf :

The IRMf data are pictures of the brain in format ANALYZES acquired by the functional imagery technique (BOLD/EPI) with a scanner (Siemens MAGNETOM Vision system) of which the magnetic field equal to 2T.

The experience is executed on only one topic in only one session. The protocol consists to scanner one volume of (64x64x 64 3mm x 3mm x 3mm voxels) every 7 second (TR=7s). Therefore we got 96 acquisitions after have suppress the first four pictures due to the undesirable effects of T1 fashion. We have only one condition (auditory Stimulation) executed in successive alternation separated by equal rest times formed of block of 6 acquisitions. As result see (Fig: 8,9,10,11)

Example: Survey the section10 of data bus snrfM00223: elapsed time =46.1400s

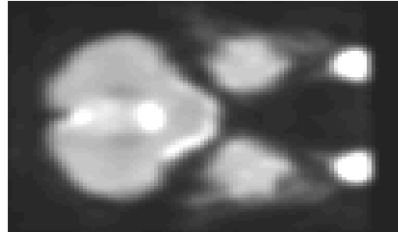


Fig.8. Section of image chosen (number 5)

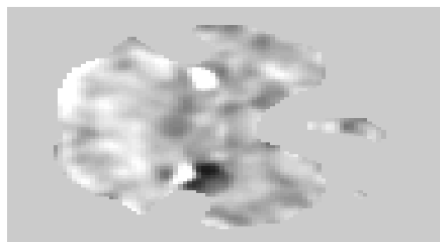


Fig.9. Execution of t-test for all the section

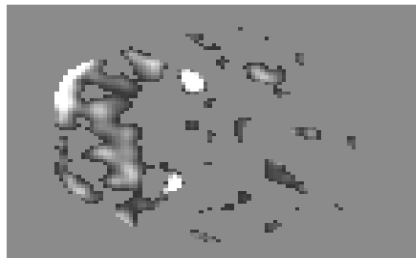


Fig.10. Image masked to extract the Activity for t-test inf (to 0.05)

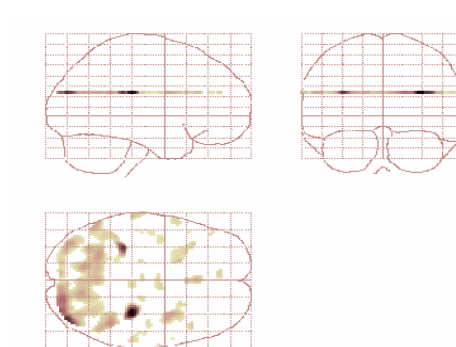


Fig.11. Project the precedent figure on 'glass' of Talairach

Note:

We can't inject our safe result only if we normalized a bus of data in the beginning of analysis, to be on that our result becomes to apply correctly on the glass Talairach.

6. CONCLUSION

The development of the different techniques of imagery stands art:

Semi-rapids, fast and ultra - rapids and their future impact on the cost of the IRM in clinical routine marked in a remarkable way the diagnostic medical. However, subject to a sufficient reduction of the price of the exam and because of its character "no - invasive" that is called cerebral functional IRM and that permits more analysis non invasive an analysis dynamic many physiological or pathological states and is revolutionizing the clinical approach of the neurological and neurochirurgical patients, as well as research on the organization of the cerebral functions, because it is strictly the first means non invasive to establish a cerebral functional cartography.

The clinical impact of the functional IRM will be major account held of its multiple advantages, but its diffusion will depend mainly on the available super-quick imagery possibilities on the facilities of IRM of the hospitable services.

It is however important to underline that the functional IRM is again in methodological development phase, that non resolute remains of numerous questions, concerning as well the techniques of acquirement, that the analysis of the data and the interpretation of the results. Outside of again limited some indications, the clinical assessment of the technique remains to make, before this one can go in protocols of exploration in routine. [1],[9]

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