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Tools and techniques to image functional brain activity

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Abstract. Neuroeconomics has become a unified discipline which bring together economy, psychology, sociology and neuroscience trying to build a general theory of human behavior. In fact, the study of the neurobiological and computational basis of value-based human decision-making has emerged as a meaningful field of research during the last years. Various studies using neuroimaging and neurophysiologic techniques suggest the principles of human choice analyzing economically relevant brain processes. However, the human mind is still a "black box" as we still don't know how to foreshadow an individual action in a given situation. The new methodologies in human neuroscience (with an emphasis on those to be applied by gathering neuroelectromagnetic brain signals) are helping to predict how the brain operates. Here, we review the utility of these non-invasive neuroimaging approaches towards greater understanding of dynamic brain networks. We compare different methods as electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), Single-Photon and Positron Emitted Tomography (SPECT and PET), and Near-infrared Spectroscopy (NIRS), identifying the benefits and advantages as well as the weakness and disadvantages of each of them. It is important to keep in mind these features, the main drawbacks and limitations in the spatial and temporal domains, while trying to "read the brain" or when looking for the most suitable tool to study a concrete issue.

Keywords: Electroencephalography; Magnetoencephalography; functional Magnetic Resonance Imaging; Single-Photon and Positron Emitted Tomography;Near-infrared Spectroscopy.

1. Introduction

One of the key issues in neuroscience concerns the processes that underlie and connect sensation and action by revealing the neural principles of value-based decisions and its predictability [Sanfey et al., 2006]. In fact, the brain employes multiple levels of processing when making decisions, and the neural activity is characterized by electrophysiological functions which correspond with neuronal dynamics [Jerbi et al., 2009]. As neuronal communication is an electrochemical process, all these processes require energy consumption and the brain constantly needs glucose and oxygen which both are supplied by the blood flow [Hirsch et al., 2012]. The non-invasive neuroimaging modalities are based on biophysical related either on neuronal electrophysiology or in the metabolism and/or hemodynamics of the brain. Electrophysiological signals are almost immediate, but the metabolic and hemodynamic systems are slower, and only reflect indirectly the neural activity [Bruyns-Haylett et al., 2010].

When dealing with the word *functional brain imaging* we refer to a set of particular mathematical techniques to be applied on hemodynamic or electromagnetic spatio-temporal information of brain activity. Such information is gathered by a large number of different sensors and acquisition devices that return structural and functional maps of the cerebral regions of interest. These functional brain imaging techniques applied to human studies (with different degree of invasiveness) exploit interactions between cerebral tissues and different kind of electromagnetic or metabolic energies. The collected data from brain activity are then used to create spatio-temporal maps of the distribution of the estimated variable (blood assumption, generation of electrical or magnetic field).). Currently, by the modern medical imaging devices based on the properties of the resonance of water to the variation of high magnetic fields (i.e. Magnetic Resonance Imaging), the brain could be "read" in a not invasive way both at structural and at functional levels [Tong and Pratte, 2012]: i) approaches depending on behavioral manipulations often compare signal variations between a control and an experimental condition; ii) metabolic measures indicate absolute level of the function in a particular condition; iii) structural images show differences between different kinds of brain areas and tissues (such as gray and white matter), blood vessels and bones, lying on their different physical properties such as tissue density or molecular characteristics; and then, iv) functional images highlight the physiological activity of the brain by presenting, for instance, metabolism activity, blood flow, chemical composition, electrical and magnetic activity that are related to neuronal activity and that support the link between neural activity and behavior [Serences and Saproo, 2012].

The armamentarium of neuroimaging is multifaceted and versatile, and in the last years has deeply advanced improving spatial and temporal resolution. The progress and new development of the technology applied to neuroimaging led to new tools to investigate the brain functioning: how the human being perceive, process, evaluate, react and utilize the personal variation in decisión-making in everyday interactions [Gluth et al., 2012]. Moreover, mathematical analysis are need in order to decode the information about the brain processing and understand the data obtained by all the functional tools used in human cognitive (and affective) neuroscience. Therefore, the interpretation of neuroimaging signals should be done keeping in mind the mechanisms analyze for the diverse tools, and it is compulsory to proceed with caution as it is heterogeneous for different regions in the brain. In addition, it is important to keep in mind that all of the techniques have strengths and weakness: the value of these techniques is related to its accessibility, the time of analysis, its costs both of the equipment and the personnel time, as well as the possibility to manipulate and the capacity of moving from one place to another.

1.1. Functional brain imaging techniques

We discuss the technical approaches and the variations in the signal amplitude (by means of time and space resolution) measured by EEG, MEG, fMRI, PET/SPECT AND NIRS, resulting from experimental manipulation of the behavior and its correlate with changes in cerebral functions. Conversely, other brain imaging techniques such as the Transcranial Magnetic Stimulation (TMS; not treated here for space limitation) direct affects the recorded signals through a stimulation of brain tissues by a rapid fluctuation of the magnetic field inducing a modification of the electric activity in the underlying neurons [Shafi et al., 2012].

2. Electro- and Magnetoencephalography (EEG and MEG)

The measurement of the electromagnetic fields generated by the neural assemblies in humans could be performed either by using electrodes (for the gathering of the electrical component of the brain field) or superconducting quantum interference device (SQUID) sensors (for the collection of the magnetic component of brain activity). Both EEG for the recording of the electric modality and MEG for the recording of the magnetic modality allow non-invasive measurement of a group of neuronal cells on a millisecond scale as temporal resolution but presents a relatively low spatial resolution, on the order of cm. The EEG, firstly explored by Hans Berger in 1924 [Gloor, 1994], and the more recent MEG, introduced by David Cohen [Cohen, 1968], measure electric and magnetic signals, respectively, resulting from postsynaptic potentials in the apical dendrites of the cerebral cortex pyramidal cells. These potentials generate currents flowing within the neuron [Spruston, 2008]. If a multitude of cells lay in a parallel configuration, they summate because of the creation of electrical dipoles. This synchronization leads to a measurable potential difference on the scalp surface, a voltage that can be measured by EEG. The burst discharge by pyramidal cells may be detectable with MEG and EEG when 10 000-50 000 neurons are synchronously active [Murakami and Okada, 2006]. Perpendicularly to these currents, a magnetic field arises which can be measured by MEG. In both electric and magnetic

modalities, these signals can be used to monitor the brain activity in the temporal and frequency domain, especially for studying cerebral functions when a temporal resolution on the scale of milliseconds is required [Hamalainen et al., 1993; Hari, 1990, 2007; Hari and Lounasmaa, 1989; Babiloni et al., 2001, 2002, 2003; Urbano et al., 1997]. For instance, different frequency profiles are associated to sleepiness, alertness or to a different cognitive, emotional state or lateralization. These signals can be also observed within a temporal window related to cognitive function of interest, for instance, low frequencies desynchronization can be experienced just before a motor response but prefrontal neurons are known to change activity depending on expected reward [Kobayashi et al., 2010].

2.1. EEG

EEG measures scalp potential differences by means of electrodes that have to be located on the skin. These voltage oscillations, varying between 10 to 100 mV, can be recorded over time for each applied electrode. Scalp electrodes used for EEG recordings are usually big and distant from each other. They are able to detect synchronizations of the electric activity of large number of neurons [Fries, 2009]. However, EEG is not able to detect action potentials as generates signals with big amplitude (70-110 mV) but in a short temporal window (0.3 ms) (Table 1). Hence, a synchronous firing of action potentials of neighboring neurons is highly unlikely. Instead, the postsynaptic potentials are the generators of the extracellular electric field that can be recorded by the EEG. If compared to the action potentials, despite a lower amplitude (0.1-10 mV), their temporal window is longer (10-20 ms) allowing the summation of neighboring cells activity [Baillet et., 2001]. In addition, these neurons have also to be disposed in a regular shape in order to arise a sufficient EEG activity to be measured on the scalp surface [De Vico Fallani et al., 2007]. The spatial properties of the neurons assure the reciprocal amplification of their extracellular electric field. For instance, the dendritic trees of neighboring pyramidal cells are arranged parallel one to each other through the cortical surface. Then, at the synapsis an excitatory neurotransmitter that causes a flow of positive extracellular ions at the postsynaptic membrane can depolarize it. This process leads to a lack of extracellular positive ions in the apical dendrites of the postsynaptic neuron. At the same time, a redistribution of intracellular positive ions occurs. These ions flow from apical dendrites to cell nucleus depolarizing the membrane and creating an extracellular potential. Subsequently, positive ions become available at extracellular level, in the cell body and in the basal dendrites. A migration of positive ions from the cell body and from basal dendrites to apical dendrites appears as a current flow. This configuration arises extracellular potentials that can be detected at the scalp level by electrodes.

2.2. MEG

Scalp magnetic fields can be measured by using SQUID containing very sensitive detectors transforming the magnetic field in current values. These SQUIDs are necessary because the summation of the amplitude of magnetic fields generated by pyramidal neurons detected on the scalp is very low, around 10 fT, whereas environmental noise ranges between 106 to 109 fT. SQUIDs are kept immersed in liquid helium at a temperature around -4ºC (below the absolute zero). To perform a MEG recording, an insulating vessel, called dewar, containing the helium is brought close to the head of the subject. Modern neuromagnetometers contains hundreds of SQUIDs disposed in a helmet in order to cover the whole subject's scalp. Nowadays, more than one hundred laboratories spread all around the world use these devices to record MEG signals. Cerebral areas activations can be estimated by MEG signals by solving the so-called "spatial inverse problem" returning neural generators of the measured scalp signals. Such a solution can be represented as discrete current dipoles, acting as ideal local currents, or as distributed current patterns. In order to employ a good volume conductor modeling neuronal sources measured by MEG signals, usually a sphere is largely used for these purposes. From a computational point of view, more realistic and elegant head models can be employed as well. In an ideal sphere, only tangential currents to the surface will generate a magnetic field propagating outside the sphere, whereas the magnetic field produced by other currents will be confined inside the volume for symmetrical reasons. Because of the anatomical organization of the cerebral cortex, signals recorded by MEG mainly come from fissural cortices where apical dendrites of pyramidal cells are tangent to the skull surface. In such as dendrites, currents flowing in several directions lead to a considerable signal cancellation at macroscopic level for MEG recordings [Irimia et al., 2012]. Even if only the 1% of this neurophysiological effect is acquired, it has been demonstrated that this small fraction is a good indicator of the local signaling. In fact, the synchronization of small subpopulations of neurons can explain the bigger part of the global signal [Hari et al., 1997].

2.3. Advantages of EEG and MEG

EEG and MEG are the tools less expensive and more widely available than anyone of the others, and all the devices used can be easily portable and sufficiently friendly for the subjects to be analyzed.

Moreover, EEG and MEG have a great temporal resolution (< 1 ms) than means that it can be measured both timing and evolution of the neural activity at the timescale as well as the oscillatory and synchronized activity (neural signals at fast time scale) that provides additional information (Table 2).

2.4. Disadvantages of EEG and MEG

As showed, both EEG and MEG techniques are not able to provide any anatomical information that is one of its major limitations. However, there are realistic head models that are available to approximate the signals generators location, starting from the sensors position on the scalp. The precision and the spatial resolution of source localization obtainable through MEG or high-density EEG and realistic head models is quite high (on the order of fraction of cm) and allows to create images of the cerebral neuronal activity in a non-invasive manner. Such as methods have been used in many experimental and clinical studies validating the correctness of the source localization with other neuroimaging techniques or by means of intracranial recordings [Lachaux et al., 2012]. Therefore, a sufficient number of electrodes, realistic head models and correct values of conductivity are necessary to properly exploit the capability of the source localization [Brodbeck et al., 2011; Ryynanen et al., 2006; Malmivuo, 2012] (Table 2).

2.5. Comparing EEG and MEG

Comparing with the EEG, MEG signals are less distorted since magnetic fields are transparent to skull as well as to other extra cerebral tissues. Hence, activated cerebral sites could be identified in a more reliable manner [Hari, 2011], even if there is no direct evidence for this statement. EEG signals measure voltage differences between two electrodes, which can affect each other in the electric field detection. Instead, the signal measured with a MEG sensor reflects the cerebral activity without being influenced by others. Conversely, EEG is able to equally detect the different orientations of the sources, whereas MEG can only detect superficial sources [Malmivuo, 2012; Ahlfors et al., 2010]. Finally, the cost of advanced EEG systems can varies in the range of thousands dollars, whereas that of a MEG system is much more expensive (around millions of dollars).

Table 1. Temporal resolution, spatial resolution, and origin of the signals of each neuroimaging technique.

	Temporal resolution	Spatial resolution	Origin of the signals
EEG MEG	**< 1ms**	**Poor**	- Cortical Columns* - Their primary sources are the synaptic currents flowing through the apical dendrites of pyramidal neurons (cortical layers).
fMRI	**every 2" but it's improving**	**3 mm**	- Hemodynamics events. - BOLD contrast ➔ de-oxyhemoglobin is paramagnetic. - Its concentration depends (inversely) on blood oxygenation levels (on demand of metabolic demands). - Reflects more synaptic activity than spiking activity (not action potential firing).
PET SPECT	**1 min**	**1 cm**	- The radioactive decay involves the creation of positrons that are quickly destroyed when nearby electrons, and then create 2 photons. - PET captures the photons pairs.
NIRS	**Good**	**Poorer**	- Non-invasive measurement of the amount and oxygen content of hemoglobin. - NIR can typically penetrate much farther into a sample than mid infrared radiation

Very poor | Poor | Good

(*) The columns facilitate the formation of regionally synchronized synaptic currents

3. functional Magnetic Resonance Imaging (fMRI)

fMRI became the mainstay of research in clinical and cognitive neuroscience being the dominant paradigm for assessing behavior-related brain physiological changes in humans [Huettel et al., 2004]. Magnetic resonance techniques have been using since the seventies as have multiple applications in structural brain images. However, their use for cerebral functions analysis was only started in 1990 when it was shown that the variation of oxygen in the blood hemoglobin modulates the magnetic resonance signal in veins [Ogawa et al., 1990]. This finding led to the development of magnetic resonance imaging sequences able to follow changes of blood flow in the brain without the need of contrasting exogenous agents to be injected (eg, PET). However, the relation between the blood oxygen-level dependent (BOLD) signal and underlying neural activity remains an open and actively researched question even if it has been demonstrated the coupling of cerebral blood flow and oxygen consumption during physiological activation [Uludag et al., 2004]. Then, the accepted theory is that BOLD signal correlates strongly with the underlying local field potential (LFP) which mainly means peri-synaptic activity [Logothetis, 2008], and that neural activity indirectly drives the BOLD signal. Then, at least for neocortex, BOLD signal reflects peri-synaptic activity in the form of the local field potential rather than the spiking rate of individual neurons [Ekstrom, 2010]. The BOLD response provides an indirect measure of cerebral activation being able to reveal activated cerebral regions during cognitive and perceptual tasks. However, as the vascular and the local circuitry-based explanations challenge the BOLD-LFP coupling model, it could be predicted when BOLD can be expected to reflect neural processing and when the underlying relation with BOLD may be more complex than a direct correspondence [Ekstrom, 2010].

3.1. Technical considerations of fMRI

The rapid diffusion of fMRI has been promoted by the very high number of magnets already existing for clinical purposes (to obtain functional resonance images of the whole body). These resonance techniques rely on quantum mechanics properties of hydrogenous protons. Each proton has its own spin and can be considered as a little magnet. In the same way, the magnet rotates around the Earth's gravitational field, the proton around an external magnetic field. The frequency of precession linearly depends on the amplitude of the magnetic field: the greater the amplitude of the magnetic field, the faster the proton's precession motion. For instance, if the proton lies in a magnetic field of 3T amplitude, it precesses at a frequency of 128 MHz. When an experimental subject goes into a strong magnetic field (ranging between 1.5 or 3T, but can be of 7T and more), a percentage of protons (around 5/6 parts per million) array along the direction of the external magnetic field applied. In fact, from an energetic point of view, aligning along the antiparallel direction would result more expensive. This unbalance creates a consequent magnetization along the direction of the external magnetic field. Protons can be then excited by applying an external short magnetic field, orthogonal to the steady one, oscillating at the same precession frequency (the resonance frequency). After a relaxation time, protons revert to their initial position losing the synchronicity with respect to the neighboring ones. Once gained the starting electromagnetic balance, they emit a signal at the same resonance radiofrequency. As relaxation times depend on the surrounding environment of protons in the tissue and on local magnetic field, it is possible to obtain images depending on the tissue's properties. The prevailing protons' sources in the human body are water and fat, and the MRI measures how protons behave within water and fat in different tissues. In the case of fMRI, the tissue of interest is the blood, and it has been demonstrated that water in the blood behaves differently depending on the oxygen level in the hemoglobin [Ogawa et al., 1990]: the effect of the de-oxygenated hemoglobin on the magnetic field is different with and without oxygen. When the blood hemoglobin lacks oxygen, it earns magnetic properties disturbing the magnetization effects in its proximity and producing a reduction in amplitude of the measured signal. Conversely, the oxygenated hemoglobin causes lower effects on close molecules, and in consequence generates a signal with higher amplitude during the magnetic resonance scanning. This is the BOLD signal. Neuronal activations provoke an enhancement of blood flow in the activated areas and in the neighboring regions, while the oxygen consumption does not increase equally. The result is a decrease of the amount of de-oxygenated venous blood in the activated cerebral areas. De-oxyhemoglobin owns paramagnetic properties and causes small perturbations of the magnetic field in the surrounding tissues generating a positive BOLD signal. Oxyhemoglobin does not generate such a perturbation because it owns diamagnetic properties. In this way, protons surrounding blood cells containing de-oxyhemoglobin will experiment with a different magnetic field from that of others and resulting changes of the precession frequency will modify the amplitude of the magnetic resonance signal measured [Naselaris et al., 2011]. For instance, a sustained decreased BOLD signal (negative

BOLD) does not unequivocally imply decreased neuronal activity, but can also result from increased neuronal activity, depending on the complex interplay between hemodynamics and metabolism [Shmuel et al., 2006]. Furthermore, whether a negative BOLD results from an increase or decrease of neuronal activity might depend on brain region and state.

3.2. Advantages of fMRI

One of the main advantages of fMRI is the possibility of evaluate the whole brain with uniform sensitivity, with high spatial resolution and high specificity, and because it is the best combination of spatiotemporal resolution and anatomical coverage (Table 1). Moreover, fMRI represents a very powerful method to investigate cerebral activations, especially for its non-invasiveness and its highest spatial resolution (3 mm) (Table 2).

3.3. Disadvantages of fMRI

One of the main limitation of fMRI is its poor temporal resolution (on the order of few seconds). It is worth of note that this temporal resolution depends from the intrinsic time constant of the physiologic phenomena analyzed (i.e. increase or decrease of de-oxyhemoglobin concentration in blood flow, a process that could take seconds) and not by the technical limitation of the measuring device. However, by increasing the strength of the magnetic field (at 7 Tesla or more) it can be detected small variation of the percentage of de-oxy-hemoglobin concentration in blood. Another limitation of fMRI it's on the fact that measures a variable that has an indirect link with respect to neuronal activity. In fact, the BOLD signal reflects mass activity of the more than 1 million neurons in a single voxel. In addition, fMRI activations cannot be quantified from a metabolic point of view but only analyzing their percentage variations by comparing the signal with respect to a control condition. In fact, it is almost impossible to affirm if the registered activity is top-down or bottom-up, or neuromodulatory. On the other hand, resonance scanners are noisy and the narrow room can let subjects feel uncomfortable. Moreover, in order to provide the best images, subjects are able to not move during the recording and paradigms requiring vocalization or limb movements can deteriorate the quality of the image. In addition, subject's intolerance to discomfort and immobility could modify cerebral functioning and activations. Finally, the high cost of this technology (the apparatus, the technical expertise, the price of each study, and the data storage and management) is one of the main disadvantages of fMRI for daily studies (Table 2).

4. Positron Emission Tomography and Single-Photon Emission Computed Tomography (PET and SPECT)

The born of nuclear medicine in 1940 and its subsequent research and development concerning radioactive isotopes and gamma rays detectors, greatly contributed to the genesis of brain imaging techniques such as the PET and the SPECT [Garcia-Alloza and Bacskai, 2004]. Both generate images of blood flow and brain metabolic processes through measurements of radioactive energy emitted by radioactive isotopes intravenously injected, and consequently spread in the cerebral circulatory system. The isotopes circulate in the brain releasing positrons. Once an electron is collided and destroyed, they release two gamma rays travelling in the opposite direction. Coincidence detectors determine the collision source along with the numbers of occurring collisions, providing information regarding the location and the concentration of that compound in the brain that allows reconstructing a tridimensional image of the metabolic effects on radioactive isotopes in the brain. Several isotopes can be used to measure blood flow (eg, oxygen), blood volume (eg, carbon monoxide), or metabolic processes such as glucose metabolism or dopamine synthesis (eg, fluorine) [Mountz, 2007; Mountz et al., 2003]. PET and SPECT tracers differently interact with the brain but share the same radioactive decaying principles and detecting measures. Some tracers accumulate in the brain while others pass through just for a short time period.

4.1. Advantages of PET and SPECT

Both PET and SPECT have the advantage to precisely measure and quantify the radioactive degree injected in the sample to exactly determine the glucose metabolism rate, blood flow or oxygen consumption. However, this operation involves arterial blood, and then elevates the invasiveness of this technique. Conversely, these methods allow vascular characterization needing small doses of radiation. In medical and clinical terms, PET and SPECT are useful tools for molecular and metabolic imaging, mainly when combining high resolution of today's PET/CT systems [Levin, 2012] or with ultra-high field 7.0 T fMRI [Cho et al., 2008] (Table 2).

4.2. Disadvantages of PET and SPECT

The main concern and major limitation of both PET and SPECT is related to the lack of structural information that makes difficult to assess the precise location of tissue with metabolic uptake. On the other hand another weakness concerns the temporal resolution because of the low sensibility of radiations detectors. The acquisition time in PET ranges around 40 seconds while SPECT requires longer times because needs to accumulate the tracer before taking the image. In general, PET and SPECT techniques have a lower temporal resolution compared with a spatial resolution of 5-10mm which is improving [Abraham and Feng, 2011]. Similar to fMRI: i) in PET/SPECT analysis, subjects motion during scans degrades image quality and its analysis, and ii) the costs of these techniques are particularly high (Table 2).

5. Near-infrared spectroscopy (NIRS)

NIRS is neuroimaging technology for mapping the functioning human cortex. NIRS was discovered in 1977 when Frans Jöbsis showed the high degree of the brain tissue transparency in the InfraRed ligth range (650–1000 nm), and how, using transillumination spectroscopy, he could capture real-time non-invasive detection of hemoglobin (Hb, the oxygen transport red blood cell protein) oxygenation [Jöbsis, 1977]. It is known that the absorption spectrum of hemoglobin depends on its level of oxygenation. In fact, the relatively high attenuation of NIR light in tissue is due to the "chromophore" hemoglobin located in small vessels (b1 mm in diameter) of the microcirculation (capillary, arteriolar and venular beds). Then, NIRS allows the quantitative monitoring of different parameters as: cerebral oxyhemoglobin (O(2) Hb), deoxyhemoglobin (HHb), oxyhemoglobin (O2Hb), and total hemoglobin (tHb). The last, tHb, is proportional to the cerebral blood volume by the hematocrit.

In summary, NIRS is based on the fact that: i) the brain is relatively transparent to light in the InfraRed spectral window; ii) NIR light is able to penetrate human tissues (the skin, the scalp, and the brain), and iii) its tissue transport is scattering (about 100 times more probable than absorption). With these measures, since 1997, NIRS as a non-invasive and safe technique has contributed in making advances toward the functional activity of the brain during cognitive tasks.

5.1. Technical considerations

Technically NIRS comprises: i) a laser diode and/or light emitting diode light sources spanning the optical window between 650 and 1000 nm, and 2) flexible fiber optics to carry the NIR light to (source) and from (detector) tissues. NIRS can be use wireless and at any place without the need for subjects restraint or sedation. Adequate depth of NIR light penetration can be achieved using a source-detector distance around 3 cm. The light is injected through the scalp and diffuses in all directions inside the tissues of the head (scalp, skull, and subarachnoid space filled with cerebrospinal fluid). This occurs both before and after passing through the brain tissue the sensitivity of each source-detector pair exhibits a banana-shaped profile. This distortion of the spatial sensitivity is caused by the optical heterogeneity in the head (for instance, the low scattering subarachnoid space). NIRS can obtain data from "brain activity" but the spatial sensitivity tends to distribute horizontally along the gray matter. However, it is important to note that currently there is high temporal resolution multi-channel systems which combine different NIRS techniques with deep data analysis systems which can provide display the results in the form of a map or image over a specific cortical área. In addition, the functional NIRS (fNIRS) can obtain simultaneous multiple measurements with multi-channel systems "even in normal daily activities" [Ferrari and Quaresima, 2012].

5.2. Advantages of NIRS

The main benefit of NIRS is its real-time resolution and noninvasively monitoring of brain tissue oxygen saturation (SO2) as well as the changes in the concentration of oxyhemoglobin, deoxyhemoglobin, and total hemoglobin.

The new fiber optics (which carry the NIR light to source and from detector tissues) are flexible and very suitable for any head position and posture, then very friendly for users and subjects as does not require strict motion restriction and can be used in a daily life environment. Moroever, new apparatus are ease to use, wireless, and its devices can be transported [Hoshi, 2007] (Table 2).

5.3. Disadvantages of NIRS

NIRS has poor spatial localization and can only analyze the brain cortical surface (underneath the skull) because its power of penetration is low. NIRS is weakly sensitive to blood vessels >1 mm because they completely absorb the light. As the arterial blood volume fraction is approximately 30% in

the human brain [Ogawa et al., 1990], NIRS obtains the information of oxygenation changes occurring mainly within the venous compartment. Last but not least, the price of the device is currently still high (Table 2).

6. Final remarks

Neuroimaging techniques are able to identify areas and cerebral networks activated in clinical and experimental conditions and provide information concerning relationships between brain signals and behavior. Functional brain imaging provides cerebral maps showing the activity of distributed neural networks involved in motor or mental tasks both in clinical purposes and experimental applications such as cognitive neuroscience including. The aim of the application of neuroimaging techniques in cognitive neuroscience is to understand how brain functioning mediates cognition and human behavior such as memory, attention, emotion, and decision-making. Thanks to the technological advancement of modern techniques of brain imaging, cerebral functions can be detailed studied both in time and in space. However, there are main concerns related to the time and to the space.

Table 2. Advantages and disadvantages of each neuroimaging technique.

	Pros	Cons
EEG	- Less expensive and more widely available than the others techniques - It can be easily portable - Great temporal resolution (< 1ms) (it can be analyzed both timing and evolution of neural activity at the timescale) - Oscillatory and synchronized activity (neural signals at fast time scale) can be studied - Are relatively tolerant to subject movements - Hardware costs are lowers when compared with all other techniques	- Don't provide anatomically information on the brain structures. Relatively poor spatial resolution (few or one cm) Sensitive to the activity of the upper layer of the cortex but not to the subcortical structures - EEG requires intense analysis and interpretation -
MEG	- Great temporal resolution (< 1ms) (it can be analyzed both timing and evolution of neural activity at the timescale) - Oscillatory and synchronized activity (neural signals at fast time scale) can be studied)	- Hardware costs are elevate (million of dollars) - It cannot be portable - Is not tolerant to subject movements Relatively moderate spatial resolution (one cm or few mm) Sensitive to the activity of the upper layer of the cortex but not to the subcortical structures
fMRI	- The best combination of spatiotemporal resolution and anatomical coverage - Have a good spatial resolution (3 mm) - Have an improving temporal resolution (every 2")	- Expensive - Don't localize the activity temporally - The temporal inverse problem - The BOLD signal reflects mass activity (more 1 million neurons in a voxel) - Mesure synaptic conductances more than neuronal spiking - Difficult to know if the activity is top-down, bottom-up or neuromodulatory - Not possible movements of the head or of the body during the exploration - Some subjects are not able to go into t machine
PET SPECT	- Can mesure blood flow in absolute terms (mL/min) - Can measure cellular-level metabolic changes - Use of tracers to mesure specific cerebral metabolism and neurotransmission	- Expensive - No good spatial resolution (1 cm) - Deficient temporal resolution (1 min) - Exposure to radioactive material (in very low doses) forbidden for pregnant women - Obtaining radioactivity and managing the ligands
NIRS	- Higher temporal resolution than fMRI - Higher specific measures of oxygenated and deoxygenate hemoglobin than fMRI	- Very poor spatial localization - Only able to scan dorsal cortical surface (underneath the skull)

	- It can be easily portable and it's unobtrusive, which enables investigations in freely moving subjects - Wireless instrumentation is available	- Expensive

6.1. Time concerns

PET and fMRI techniques are limited in their temporal resolution by the time scale of the brain physiology involved, and not by the technical constraints of the acquisition devices. The time scale of the increase of the cerebral blood flow due to the hyperactivity of the brain tissues is completed in a time range of several seconds. Thus, fMRI is not the most suitable method for the investigation of brain activity in the time domain. In relation to the PET, this technique has been an important achievement to study human cognitive functions in the early stages of neuroimaging. However, PET has similar temporal disadvantages as fMRI but lower anatomical resolution and currently the new apparatus combined PET and CT49, as CT provides detailed anatomical structures to the PET molecular images but the temporal problems is still present.

6.2. Space concerns

The measurement of the electromagnetic fields generated by the neural assemblies in humans could be performed by using electrodes (for the gathering of the electrical component of the brain field) or superconducting quantum interference device (SQUID) sensors (for the collection of the magnetic component of brain activity). Both EEG, for the recording of the electric modality, and the MEG, for the recording of the magnetic modality, allow non-invasive measurement of a group of neuronal cells on a millisecond scale but presents a relatively low spatial resolution, on the order of cm. Such problem states that different electromagnetic sources configurations can generate the same electromagnetic activity on the scalp as gathered by the sensors. In this case, measuring a maximum of activity at a certain scalp point does not mean that signal's generators are located in the underlying cortex level [Fender, 1987]. In this way, the analysis of electric and magnetic fields distribution on the scalp surface does not provide exact information about signals' sources. The only way to obtain a distribution of the electric and magnetic sources is to solve the inverse problem by introducing a priori assumptions about the generation of EEG and MEG signals [Fuchs et al., 1999; Michel and He, 2011].

Summing up, from the technical point of view, the major advantages of optical methods of brain imaging include spatial resolution in the cm range, temporal resolution in the millisecond range, and the ease with which devices can be transported enabling investigations in freely moving subjects. Other properties can be the potential to measure intracellular/intravascular events simultaneously, and molecular and biochemical specificity. However, as none of the current tools have all these specifications together, it is compulsory to choose the best of them for the purpose of each concret study.

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