María A. Pastor

New Perspectives on the Interpretation of Human Brain Images

Neue Perspektiven bei der Interpretation von Bildern des menschlichen Gehirns

Zusammenfassung

Functional Magnetic Resonance Imaging (fMRI) erlaubt nicht nur die Sichtbarmachung der Hirnanatomie, sondern auch die Messung der hämodynamischen Veränderungen, die durch neurale Aktivität bedingt sind. fMRI macht sich biochemische Eigenschaften des Blutes zu Nutze, welche als naturgegebener paramagnetischer Kontrast bei der Lokalisation und Verteilung neuraler Populationen in komplexen zerebralen Netzwerken fungieren. Mittlerweile wurde die fMRI zu einem attraktiven Werkzeug für Psychologie, Neurophysiologie und Sozialwissenschaften. Allerdings sollte man sich der Grenzen bei der Interpretation von Daten bewusst sein, die von diesem Surrogat für Signale aus neuronaler Massenaktivität gewonnen werden. Die Korrelation von Hirnaktivität mit bewussten menschlichen Handlungen würde dabei hilfreich sein, jene Hirnregionen zu identifizieren, die für diese zuständig sind, ohne das Wesen des Bewusstseins selbst erklären zu wollen. Ein multidisziplinärer Zugang zu Kognition und Verhalten des Menschen ist nötig, um Aspekte zu behandeln, die zwar ontologisch an das Gehirn gebunden, jedoch nicht das Gehirn selbst sind.

Schlüsselwörter: Functional Magnetic Resonance Imaging (fMRI), Sauerstoffsättigung (BOLD), neurale Verarbeitung, Neurowissenschaften

Abstract

Functional Magnetic Resonance Imaging (fMRI) allows not only visualization of brain anatomy but also measuring haemodynamic changes which reflect neural activity. fMRI takes advantage of the blood biochemical properties as a natural paramagnetic contrast to localize distributed activity of neural populations in complex brain networks. Currently, fMRI has become an attractive aid to psychology, neurophysiology and social sciences. However, when interpreting the data, we should consider the limitations of this surrogate signal which reflects neuronal mass activity. The correlation of brain activity with conscious human actions would help to identify cerebral regions involved in these actions but not the nature of consciousness. A multidisciplinary approach to human cognition and behaviour is needed to tackle elements that, even ontologically united to the brain activity, are not the brain.

Keywords: Functional Magnetic Resonance Imaging (fMRI), Blood Oxigen Level Dependent (BOLD), Neural Processing, Neurosciences

María A. Pastor, MD, PhD Associate Professor, Functional Imaging Laboratory, Department of Neurosciences, Center for Applied Medical Research, University of Navarra School of Medicine, E-31008 Pamplona mapastor@unav.es Brain imaging has developed exponentially in the last four decades providing an incredible amount of information to the neurosciences. Magnetic resonance Image applied to the medical equipments since the 1980s has been an efficient tool for clinical diagnosis and neuroscience research. Magnetic resonance Image was primarily used to record structural images of different organs including the brain. The possible modifications of the magnetic field have also provided information on vascularisation, perfusion and biochemical spectroscopy studies of the tissues.

With the advent of fast sequences and higher field scanners applied to human studies, functional magnetic resonance Image allows not only visualization of brain anatomy but also localization measurement of haemodynamic changes which reflect neural activity increments. MRI has the advantadges of generating no radiation, its lower cost and its technical versatility.

The basis of functional magnetic resonance Image were preceded by the discovering that blood perfusion of the brain may act as a natural paramagnetic contrast. Linus Pauling and Charles Coryell described in 1936 the magnetic properties of haemoglobin, oxyhemoglobin and carbon monoxyhemoglobin which are essential components of the blood. In their paper they refer that Faraday investigating the magnetic characteristics of dried blood had made a note: "must try recent fluid blood". The note was dated November 1845.

In 1973 Magnetic resonance images were first observed on a test tube sample by Paul Lauterbur. In 1977, Raymond Damadian obtained magnetic resonance images of the whole human body and in the same year, Peter Mansfield developed the echo-planar imaging (EPI) technique, which is the fastest MRI technique till today to produce images. The Nobel Prize in Physiology or Medicine 2003 was jointly awarded to Paul C. Lauterbur and Peter Mansfield "for their discoveries concerning magnetic resonance imaging".

The existence of a natural paramagnetic con-

trast, the blood, was not considered for a long time. Nevertheless the rediscovering of paramagnetic properties of the blood enhanced by the exchange of oxygen during their functional supply to the brain tissue, has become one of the most attractive methods applied to psychology, neurophysiology and even to social sciences.

The year 1990 was a landmark in neuroimage because of the application of magnetic resonance Echo-planar imaging (EPI) sequences. Ogawa and collaborators reported new extremely fast sequences of magnetic resonance able to detect the signal produced by changes in oxygenation and deoxigenation of circulating blood in the rat brain during visual stimulation (Blood oxygen level dependent, BOLD).1 This experiment was performed successfully in humans during visual stimulation reproducing a BOLD signal located in the occipital visual cortex.² EPI is a unique imaging method since it can record an MR image, in about 40 to 100 ms. The speed at which images are obtained gives us insight into dynamic processes of the brain based in local blood volume changes and oxygen consumption changes (BOLD).

The MRI mapping techniques using intrinsic blood-tissue contrast have fulfilled a role of defining functional human neuroanatomy with an unprecedented spatial-temporal resolution. In addition, the analyses of the neural-related activity helped not only to the localization of distributed neural populations but also to investigate neural information processing ranging from small neuronal groups to complex neural networks. The functional MRI sequences may detect in a short period of time the brain activity elicited by the task requested inside the scanner. This technique allows measuring a surrogate of synaptic activity of a working neuronal population reflected on blood supply demand and oxygen consumption with increased glucose utilization.³

When a subject is asked to remember a list of words, inside the scanner cerebral areas in charge of verbal memory increase their activity. Using functional MRI sequences we are able to record BOLD signal changes as the result of neural activation in the brain regions involved in the task which increase their signal strength.

Currently, we use high-field and faster scanners which help reduce motion-related artefacts and inhomogeneities in MR images. The software has become user friendly and technically acceptable even in a non-academic environment. Thanks to technological developments and non-invasive characteristics, the clinical applicability of these techniques is rising. We are able to obtain BOLD activity in tissue with enough signal to noise ratio during the scanner time performing a wide possibility of actions. We can measure from the individual brain at the neuronal field level during the most primary sensorial functions such as the detection of a light touch or visualization of a light from the highest cognitive actions such as decision-making. The whole brain could be mapped showing the entire network of brain areas engaged while subjects perform a particular task can be delineated. Signal sensitivity is good enough to discriminate duration of the stimuli presented such as a light sound, touch in the order of hundreds of milliseconds.

The technique allows reconstructing the topographical localization in the cortex of the active neural populations such as the tonotopy of the auditory cortex, the retinotopy of the visual cortex, etc. This bulk of knowledge promises to improve our insights in physiology, psychology and cognitive sciences both in health and disease. Specific areas such as vision physiology have benefitted enormously from functional neuroimaging.

There is an increasing interest to predict brain activity using functional magnetic resonance imaging in primary sensorial examinations, complex perception, motor activity and cognitive functions. The signal measured can be correlated with activity of interconnected clusters. The more accurate the correlation of brain activity with mental states and cognitive functions would help to understand cerebral regions intervening in these functions and the processing timing. But we cannot expect to understand what the mental states and processes are at a functional level or how they are coupled with brain activity.

In the coming years, spatial and temporal resolution of magnetic resonance brain-scanning will continue to improve. The development of this field will yield to technical innovations in neurobiological measurement, neurogenetics and molecular and cellular biology. From the early 2000's some social studies have been pointing at human reactions such as empathy, trust, lies, etc....

However, we should keep in mind the limitations of this functional magnetic resonance imaging technique when interpreting the data. It is a measure of a surrogate signal which reflects neuronal mass activity. For the simplest sensory information to be processed are required excitatory synapses as well as recurrent inhibition mediated by interneurons. Both excitatory and inhibitory mechanisms act together and both have a significant influence on cerebral blood flow changes. Neuronal populations are interconnected with converging inhibitory and excitatory influences and also are under the effect of modulators.

Independently of BOLD signal physical and biological constraints, we face limitations in the design when trying to explore complex perception and cognitive functions. The more we study cognitive paradigms in humans the more obvious appears that measurements of every component of the subject complex individual behaviour cannot be recorded. We face the possibility that additional processes not detected by the scanning techniques available, are just as important as those detected. The reasons are multiple: some because the technical resolution both spatial and temporal characteristics of functional magnetic resonance imaging is limited; some because of the superimposition of networks of neurons subserving different functions, or because of temporal overlapping; some of them because individual peculiarities are lost in the statistical analyses; some because there are psychologically complex functions which are undefined by

previous knowledge obtained from focal lesions.

The observation of an increased cerebral blood flow consequence of electrical synaptic activity as a result of a simple perceptual or motor design is not difficult to interpret. With the help of neurophysiology, a broad field of traditional research in neurosciences, we have got a guide about field activity and how the regions interact as components of a complex integrated system. Thereby bringing us closer to understanding what physiological mechanisms are capable of supporting cognitive functions. There is a bulk of findings regarding correlations between individual brain activity and mental processes, e. g.

But when analyzing complex tasks or cognitive paradigms, -such as perceptual discrimination, decision making or purposeful actions-, the pattern of activation is artificially fragmented because of analyses requirements and thus is even more difficult to attribute the activations to the process of reasoning or action the subject has planned to solve the presented problem. In addition the simplest human activities tested with neuroimage, such as voluntary movement, in spite of the efforts to explain the generator of the decision to move have not lead to any conclusion.

Recently, a colleague, Professor of Economics, remarked in a widely distributed email that neuroeconomics is about the silliest thing he could think of. Upon which another colleague, an understanding psychiatrist, replied that many neuroscientists assume that the brain controls the behaviour. This is the sort of argument and discussion one can also hear, with different levels of intensity, in the lecture halls and corridors of conferences. Who is right?⁴ The anecdote that professor Schultz writes in the introduction of his paper about Neuroeconomics could be applied to many other areas of cognitive neuroscience, opposite positions are determined, and possibly we could make the effort to analyze which aspects of any of those antagonistic views are definite or need a more critical analysis.

There is an option followed by some Neuroscientists that is to consider the human brain as a generator of any human activity, such as memorizing, analyzing or decision-making. Their goal is to decipher brain activity from cognitive functions to free will decisions using decoding-based methods. Their hope is that based in the experience of the fast technical growing in hardware and acquisition methods in the last decades, more sophisticated equipment together with image analyses methods might ultimately discover that individual acts of conscious willing occur simultaneously with specific brain activity instigating our actions. The elementary definition of this line of thought is that functional magnetic resonance imaging will be a mind reader.

Interestingly, the development of functional brain imaging techniques is reflected in the knowledge about its limitations and possibilities. For example, a frequently made assumption is that the mind can be subdivided into modules or parts whose activity can then be studied with functional magnetic resonance imaging. If this assumption is false, then even if the brain's architecture is modular, we would never be able to map mind modules onto brain structures, because a unified mind has no components to speak of. Even if true, the challenge remains in coming up with the correct recursive decompositions in each of which any given cognitive capacity, however abstract, is divided into increasingly smaller functional units that are localized to specific brain parts, which in turn can be detected and studied with functional magnetic resonance imaging. This is not a neuroimaging problem but a cognitive one.5

The fact is that although we are measuring spatially and temporally neural correlates of any human action, thought or imagery, we do not know the triggers and planning that precede these activities. We can design a task in which conscious behaviour is relevant and we can get the neural correlates of the conscious action but not the nature of consciousness. Another option is to admit that neuroscience has limited capability for a thoroughly human explanation of consciousness, freedom and creativity. There is a need to approach a multidisciplinary study of human cognition and behaviour to be able to tackle elements that, even ontologically united to the brain activity, are not the brain. There is a need for dialogue about being human between neurosciences, psychology, anthropology and philosophy.

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Further Literature

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