AN ANALYSIS OF TECHNIQUES FOR FUNCTIONAL BRAIN CONNECTIVITY DETECTION ON fMRI

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Abstract:

Our brain is a complex integrative network of functionally linked brain regions. Multiple spatially distributed, but functionally linked brain regions continuously share information with each other, together forming interconnected resting-state communities. With the use of resting-state fMRI we can explore the functional connections of the brain network, using seed-based, ICA-based and/or cluster-based methods. Recent studies have shown that functional communication within the human brain is not just random, but organized according to an efficient topology that combines efficient local information processing with efficient global information integration. This integration of information may be facilitated by important hub-regions, as suggested by the observed heavy tailed connectivity distributions of functional brain networks. Interestingly, most pronounced functional connections are found between regions that are known to share a common function, suggesting that resting-state fMRI oscillations may reflect ongoing functional communication between brain regions during rest. Around eight resting-state networks have been consistently reported, overlapping the primary motor, visual and auditory network, the default mode network and known higher order attention networks. Functional connections of resting-state networks tend to be strongly related to structural white matter connections, suggesting the existence of an underlying structural core of functional connectivity networks in the human brain. Recently, the use of graph theory in combination with resting-state fMRI has provided a new platform to explore the overall structure of local and global functional connectivity in the human brain.

To use functional magnetic resonance imaging (fMRI) to investigate functional connectivity, and hence, underlying neural networks, in never-treated, first-episode patients with schizophrenia using a word fluency paradigm known to activate prefrontal, anterior cingulated, and thalamic regions. Abnormal connectivity between the prefrontal cortex (PFC) and other brain regions has been demonstrated in chronic, medicated patients in previous positron emission tomography (PET) studies, but has not to our knowledge, previously been demonstrated using both first-episode, drug-naïve patients and fMRI technology.

Keywords:

Brain connectivity, Brain network, FMRI

Introduction:

The brain is the most complex organ in humans and is responsible for controlling the body. Since time immemorial, it has been an object of fascination. Although the brain is related to the mind, still today the mechanisms by which it gives rise to thought and consciousness are not completely understood. Magnetic resonance imaging (MRI) is a non-invasive and relatively safe imaging method that allows the visualization of the structure and many of the pathologies of the human brain in vivo, and that more recently is able to study the brain functions. MRI came into clinical use in the early 1980s, a few years before the first successful functional magnetic resonance imaging (fMRI) experiment in 1991 (Bandettini, 2012). The availability of MRI scanners has increased rapidly in most European countries over the past two decades (OECD, 2012). For example in the Netherlands, the number of MRI units per capita increased tenfold between 1990 and 2010 (OECD, 2012). Similarly, in Italy, the number of MRI scanners per capita increased by nearly six times between 1997 and 2010 (OECD, 2012). The success of fMRI is believed to be a result of the good accessibility to MRI scanners, the parallel development of computing power and the advances on brain physiology and MRI signal knowledge (Bandettini, 2012).

In the fMRI field, a task paradigm is the manner (timing, duration and magnitude) in which a stimulus is presented to the subject being scanned in order to activate certain brain regions. The stimulus used depends on which brain functions need to be studied, and may be for example motor (as illustrated above), sensorial, language or cognitive. The most commonly used paradigm designs are block design and event-related design.

The human brain which is the centre of the nervous system controls both voluntary and involuntary actions in accordance with the situations. Apart from that the brain controls the sense organs, emotions and also responsible for various movements for the proper functioning of the human body. Any impairment or damage to the brain causes imbalance in the functioning of the body. In order to diagnose and to assess the nature of impairment or damage, the same can be done with fMRI.

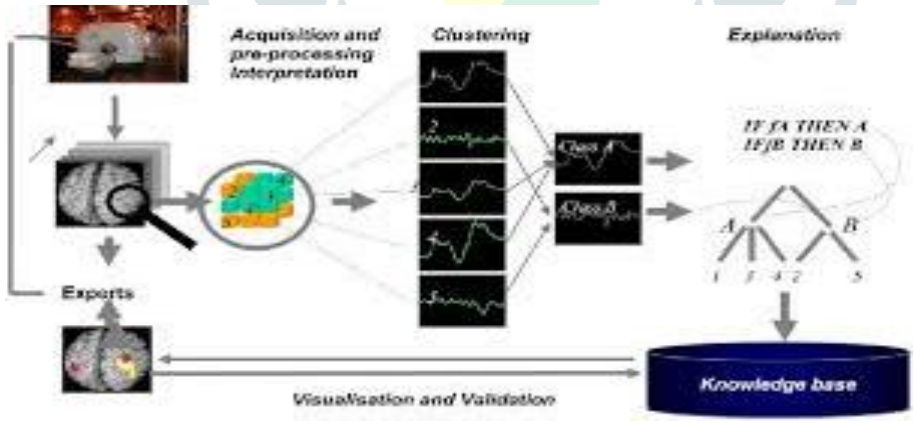
Literature Survey:

Many of the techniques of digital image processing, or digital picture processing as it often was called, were developed in the 1960s at the Jet Propulsion Laboratory, Massachusetts Institute of Technology, Bell Laboratories, and University of Maryland. A few researches such as application to satellite images, wire-photo standards conversion, medical imaging, videophone, character recognition,

and photograph enhancement were also carried out [1]. SuezouNakadateet al [2] discussed the use of digital image processing techniques for electronic speckle pattern interferometry. A digital TV-image processing system with a large frame memory allows them to perform precise and flexible operations such as subtraction, summation, and level slicing. Digital image processing techniques made it easy compared with analog techniques to generate high contrast fringes. Satoshi Kawataet al [3] discussed the characteristics of the iterative image-restoration method modified by the reblurring procedure through an analysis in frequency space. An iterative method for solving simultaneous linear equations for image restoration has an inherent problem of convergence. The introduction of the procedure called "reblur" solved this convergence problem. This reblurring procedure also served to suppress noise amplification. Two-dimensional simulations using this method indicated that a noisy image degraded by linear motion can be well restored without noticeable noise amplification.

Methodology:

Whole brain gradient-echo, echoplanar fMRI (TR 3s, TE 45 ms, FOV 24 cm, and matrix 64 × 64) was performed using a 1.5T GE scanner. Twenty-seven contiguous, sagittal 5 mm slices were acquired in order to provide coverage of the entire brain. Each subject also underwent a 3D SPGR anatomic reference scan (TR 26 ms, TE 9 ms, FOV 24 cm, matrix 256×192×128, 1.5 mm thick sagittal images) during the same scanning session as the functional runs.



The fMRI data sets were processed in AFNI, using a cross-correlation analysis with a sinusoidal stimulus waveform function (Cox, 1996). Twelve different activation maps were created for each individual subject by using combinations of four correlation coefficients ($r = .39$, $p < .01$; $r = .42$, $p < .005$; $r = .46$, $p < .001$; $r = .50$, $p < .0001$) and three cluster volumes [70 mm^3 (1 voxel, i.e., no clustering), 140 mm^3 (2 voxels), 700mm^3 (10 voxels)]. The cross-correlation coefficient [r] represented the association between the time-course of the signal intensity and the stimulus waveform function. The probability of a false positive activation [p] was estimated by a data

reshuffling analysis corresponding to each particular r-value (Bullmore *et al*., 1996). The cluster volumes, comprised of 2 and 10 voxels, were defined in a manner that accepted all neighboring voxels sharing a side, edge, or corner. No spatial smoothing was used. Regions of interest were manually outlined on a coronal MRI anatomic template formed from the 3d SPGR scans of all 8 subjects which had been combined in Talairach space. The medial temporal lobe was divided into four anatomic compartments. These regions of interest were the posterior hippocampal formation, anterior hippocampal formation, parahippocampal gyrus, and entorhinal cortex. Figure 1 shows two views of the ROIs.Functional magnetic resonance imaging (fMRI) is well established as a method for the detection and delineation of regions of the brain that change their level of activation in response to specific experimental conditions. fMRI studies typically use "snapshot" imaging methods such as echo-planar sequences that are sensitive to changes in blood-oxygenation-level-dependent (BOLD) signal, which reflects neuronal activation, albeit indirectly [1. fMRI studies produce activation maps that typically depict the average level of engagement during a specific task or in response to a specific stimulus of different regions in the brain. These may be compared between conditions or between subjects to evaluate the relative magnitudes of different responses. This is the basis of using fMRI for brain mapping and for comparing the activation patterns produced by different stimuli or between groups. However, appropriate fMRI data may also be analyzed in greater depth to reveal how components of large-scale distributed neural systems are coupled together in performing specific functions. The organization, interrelationship and integrated performance of these different regions are generally described by the term "functional connectivity."

For this review, we will restrict our use of "functional connectivity" to mean the quantification of the operational interactions of multiple spatially distinct brain regions that are engaged simultaneously in a task. We will further restrict our discussion to connectivity measures derived from fMRI activation data alone. Currently, there is no consensus on the most accurate or efficient method of detecting or measuring functional connectivity using fMRI [2, although there are considerable interest and activity in this field. However, while specific analytic techniques vary, a common feature of multiple fMRI assessments of connectivity is the use of correlations or co variances of activities derived from BOLD data. The objectives of this article are to introduce and explain several types of proposed analyses that attempt to quantify connectivity using such statistical properties. In addition, we will discuss the origins and nature of three primary sources of variance in these data: inter subject variance, task-related variance and intrinsic or steady-state variance. Finally, we will identify some confounding factors in the measurement of functional connectivity that may obfuscate conclusions in practical applications. We postulate that the ultimate value of fMRI in studies of brain function will depend not only on our ability to map activity patterns to reveal neural functional architecture but also on our ability to understand how brain regions work together to accomplish specific tasks and behaviors. Methods for assessing functional connectivity are key for obtaining such insights.

Analyzing the Data:

The goal of fMRI data analysis is to detect correlations between brain activation and a task the subject performs during the scan. It also aims to discover correlations with the specific cognitive states, such as memory and recognition, induced in the subject. The BOLD signature of activation is relatively weak, however, so other sources of noise in the acquired data must be carefully controlled. This means that a series of processing steps must be performed on the acquired images before the actual statistical search for task-related activation can begin. Nevertheless, it is possible to predict, for example, the emotions a person is experiencing solely from their fMRI, with a high degree of accuracy. To this day, the Numerical Distance Effect is a valuable tool used for investigating the cognitive aspects of number-space association in synaesthesia. In number-space synaesthetes, the NDE is found to be larger when the arrangement of the stimulus matches that of the synaesthetic representation. That is, the NDE for synaesthetes representing numbers from left-to-right will be larger when the display contains number pairs from left-to-right than from rightto-left. Previous studies have examined the NDE when number was a task relevant dimension. A few studies used passive viewing of single digits or non-symbolic quantities (array of dots) to address quantity coding in the parietal cortex. These studies are in agreement with the idea that quantities are represented in the parietal cortex in the absence of an explicit task.

Conclusion:

In conclusion, recent resting-state fMRI studies examining functional connectivity between brain regions have revealed new fundamental insights in the organization of the human brain and provide a new and promising platform to examine hypothesized disconnectivity effects in neurologic and psychiatric brain diseases. In this review, we have described and compared a number of analysis techniques that have been developed to probe the function of cognitive networks using intersubject task-related or intrinsic variations in BOLD fMRI signals. Specific experimental hypotheses and the appropriateness of various assumptions will drive the choice of methodology for any particular experiment. Functional MRI's unique contribution to the investigation and understanding of neural connectivity is its combined spatial and temporal resolution in a noninvasive technique. Although fMRI has temporal resolution less than the true speed of neural interactions, it provides whole-brain coverage at spatial resolutions of millimeters and is an ideal tool for measuring intrinsic steady-state hemodynamic fluctuations within single subjects in particular. Evidence that connectivity measures based on hemodynamic fluctuations measurable by fMRI reflect meaningful aspects of cognitive processing in terms of task, load, behavior and pathology or psychiatric diagnosis continues to accumulate.

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