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Review Article

A Review on the Medical Applications of Functional Magnetic Resonance Imaging

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Abstract

The ability to combine functional information with regular images will be a significant benefit and functional magnetic resonance imaging is an excellent example of such a tool. The development of functional magnetic resonance imaging has aided in the exact examination of brain function and identification of specific diseases. This review primarily focuses on similar advantages and achievements of functional magnetic resonance imaging procedure in a wide variety of fields, which becomes useful for the readers to urge further interest in this topic.
Keywords: BOLD, DWI, functional MRI

INTRODUCTION

This article offers a review of functional magnetic resonance imaging's (fMRI) medical applications. Magnetic resonance imaging (MRI) is a technique that produces clear images of the human body by combining magnetism and radio waves. Nuclear magnetic resonance (NMR), a physics phenomenon discovered in the 1930s in which magnetic fields and radio waves induce atoms to emit small radio signals, is the basis for MRI. The first MRI test on a live human patient was done on July 3, 1977. Magnetic resonance imaging is a non-invasive approach for visualizing internal biological structures and detecting disease that detects atoms based on how they react in a magnetic field. Computed tomography (CT) is another frequent imaging technique that employs ionizing radiation and relies on the idea of differential attenuation of x-ray beams when they strike bones and soft tissues. The contrast variation among soft tissues is very difficult to identify in a CT scan, whereas MRI images give a superior demonstration of soft tissue contrast and use non-ionizing techniques. As a result, it is suitable for brain, spine, joint, and soft tissue body component inspections. Large amount of anatomical information can be derived from MRI scans; however, we found no information about the tissues' functional and physiological features. The necessity of imaging the functional aspects of tissues led to an intriguing new breakthrough in MRI termed as "functional MRI (fMRI)." Functional magnetic resonance imaging provides pictures of brain activity during task engagement that are not intrusive. Functional magnetic resonance imaging of the brain allows the visualization of active parts of the brain during certain activities and also helps in understanding their underlying networks. It measures the metabolic changes that occur within the brain and may be used to determine the parts of the brain that handles critical functions. The base for fMRI was established on the fact that local variations in cerebral blood flow, blood volume, and blood oxygenation are caused by neuronal activity. The breakthrough occurred when it was found that blood hemoglobin exhibits magnetic characteristics that differ from the amount of oxygen it carries. Oxy-hemoglobin has diamagnetic properties, while deoxyhemoglobin formed after the removal of oxygen has paramagnetic properties.[1] The presence of deoxyhemoglobin leads to the shortening of the T2* relaxation time within the tissue voxel. These changes in the levels of oxygen in the blood will give varying MR signals. This effect of a small change in local MR signal is called the blood oxygen level-dependent effect (BOLD effect). Using visual and neural stimulus paradigms, this phenomenon was employed to create entirely non-invasive topographic maps of human brain activity.[2] In general, fMRI detects variations in blood flow to determine brain activity. It was concluded that the local differences in functional activity can change the vascular supply of the brain.[3,4]

Functional magnetic resonance imaging is a technology that compares pictures recorded during 2 states of a task: the ON state, when the subject performs a task (the activation state), and the OFF state, when the subject does not execute any activity (the baseline state). During the ON and OFF states, there is a change in the intensity of the images captured which are compared to obtain the mean difference in images, and then to get the activation maps, statistical significance tests are performed. This may be used for brain mapping, which is a collection of neuroscience procedures aiming at mapping biological quantities or qualities onto brain spatial representations, resulting in maps. Several neurological disorders demand functional information from the brain in addition to its structural details. Brain mapping methods can provide useful information on how the brain operates in both normal and pathological states. Functional magnetic resonance imaging used for brain mapping can be compared with other functional imaging methods such as optical imaging, single photon emission computed tomography, positron emission tomography (PET), and magnetic encephalography. An overview of several brain mapping methodologies, as well as fMRI signal processing approaches, was given in the study by Daimiwal et al.[5] A single image does not provide any functional information; however, this may be investigated by varying the image intensity levels over time to get the needed functional information. These maps depict the brain areas responsible for a certain sensory or motor task and provide a clear image of neural activity that may be used to better understand brain function.[5]

Resting-state fMRI is helpful for kids or adults who struggle with difficult cognitive activities including decision-making, memory, attention, judgment, etc. Some of the methods used for analysis include neural networks, seed-based methods, graph methods, clustering algorithms, independent component analysis, and pattern classifiers.[6] In the absence of any stated task, distinct parts of the sensorimotor system of the brain varied slowly and simultaneously. In resting-state fMRI, brain networks showed strong baseline activity that was reduced while individuals performed a range of cognitive activities. Resting-state fMRI is a relatively novel route for examining regional interactions in the absence of activities. It captures spontaneous low-frequency fluctuations (0.1 Hz) in the BOLD signal. Resting-state fMRI has clinical uses in presurgical planning for patients with brain tumors and epilepsy, and the technology may possibly play a role in delivering diagnostic and prognostic information for neurological and psychiatric illnesses in the future.[7,8]

Diffusion-weighted imaging (DWI) and fMRI are 2 more contrast mechanisms that have revolutionized the identification of the above-mentioned pathologic disorders. Cellular structures at microscopic levels can be characterized by the degree of diffusion in tissues, and any hindrance in the normal process caused by some abnormal pathological process can be well explained by diffusion-weighted fMRI (DfMRI). The grayscale pixel values in DWI are determined by the underlying diffusivity in voxels, with high-diffusion voxels appearing hypointense (e.g., cerebrospinal fluid) and low-diffusion voxels appearing hyper intense (e.g., acute stroke). The usual Brownian motion of water molecules is limited and slowed by the existence of cell membranes and other impediments. Diffusion-weighted functional magnetic resonance imaging shows a distinct response pattern in the visual cortex than BOLD-fMRI, according to studies. The DfMRI signal is consistently quicker at both the beginning and offset of the stimulus, implying that the DfMRI signal is more directly connected to neuronal activities than the hemodynamic response, that is the BOLD contrast.[9]

Over decades, fMRI has invaded several fields of research and we have attempted to cite briefly the areas of research, focusing wide range of readers.

MAIN POINTS

- This review article delves into functional magnetic resonance imaging (fMRI) and how it's utilised in medicine.
- fMRI adds more functional information to a scan.
- The change in blood oxygen level with activation is used in Functional Magnetic Reference (fMRI).
- fMRI is used to locate the exact region of the brain that is accountable for each act.
- fMRI may be used to diagnose a variety of disorders and can also be utilised in radiotherapy to segment normal tissue.

Psychiatry

The development of fMRI methods has made significant advances to our understanding of the brain mechanisms underlying mental disorders. Mental disease is generally related to variations in the overall organization of functional communication "throughout" the brain network, according to Zhan et al.[10] A comparable research using neuroimaging in psychiatric patients found that any changes in thinking patterns, beliefs, feelings, or behaviors that occur during psychotherapy therapies can result in a normalization of functional brain activity at a global level.[11] Another research looked at the impact of the cognitive pragmatic treatment, a rehabilitation program (CPT), where a patient fMRI was taken before and after the treatment and the patient's behavioral improvements appeared to be supported by functional alterations at the cerebral level.[12] Functional magnetic resonance imaging also pointed out the significance of psychological therapy over pharmacological therapy through a study on seriously disabled group of patients with schizophrenia.[13]

Affective Science

Functional magnetic resonance imaging has a great role in affective science which is the scientific study of emotion or affect. Studies were conducted with the understanding that the human voice is one of the most important means of social and emotional communication. It was found that specific portions of the brain were activated more on listening to a cheerful voice rather than an enraged tone. The study also discovered that only when accompanied by joyful features, cheery sounds were associated with greater activity in an unusual region.[14] It was found that neuronal activations occurred at different specific regions of the brain when the experimental fMRI was performed by inducing emotions.[15] Similar studies were carried out on rejection[16] and lie detection.[17]

Alzheimer's Disease

Functional magnetic resonance imaging studies were carried out on patients with Alzheimer's disease to evaluate the neural basis for impaired semantic memory and it helped in obtaining results consistent with several other prior researches.[18] A few functional imaging studies have looked at the functional competence of certain brain areas and their links to Alzheimer's disease memory deficits.[19] It also assisted in distinguishing the brain responses in the early stages of Alzheimer's disease from normal aging. It aids early therapy by allowing researchers to explore changes in brain function linked to the initial indications of Alzheimer's disease in vivo, possibly before the occurrence of major irreparable structural damage.[20] Furthermore, research employing fMRI has revealed that following music therapy, the activation pattern of the brain during the processing of familiar and unfamiliar music was different in Alzheimer's disease patients.[21] Improvements in graph neural networks, as well as a novel Riemannian manifold-based model fMRI, can be utilized to diagnose Alzheimer's disease more efficiently.[22]

Cancer

Small volumes of active tumor at the time of diagnosis and early disease recurrence can be detected using the novel imaging modality fMRI, which offers not only anatomic but also functional imaging. In addition to PET-CT now, fMRI has been proven to be a valuable tool for gynecologic cancer diagnosis. When PET-CT is more accurate in diagnosing ganglion disease, fMRI is more accurate in local preoperative staging.[23]

Another fMRI study was carried out between few controls and breast cancer patients to investigate the neuro-physiological differences during visuospatial working memory. Activations in locations such as the inferior frontal gyrus, insula, thalamus, and midbrain were higher in breast cancer patients than in controls during working memory.[24] One of the fMRI studies found that incorporating BOLD-fMRI and diffusion tensor imaging into radiation treatment planning for high-grade gliomas near the primary motor cortexes and corticospinal tracts is beneficial because these structures are adjacent to the target volume and can be clearly identified as organ at risks and spared during treatment.[25] A similar research looked at the use of fMRI for target delineation and key organ avoidance in brain radiation and found that it helped to identify and avoid functionally significant locations when developing treatment regimens.[26] In order to routinely adopt fMRI in clinical practice, an examination to check the reproducibility of the technique was performed on primary motor cortex as a way of providing margins of error for the radiotherapy planning stage.[27] Although studies suggest the judicious use of fMRI to help with neurosurgery planning, intraoperative electrocortical mapping remains the gold standard for locating the eloquent cerebral cortex.[28] Another research compares a careful review of morphological MRI data to the possible diagnostic advantages of presurgical fMRI. When compared to a highly deep investigation of structural 3-dimension MRI, routine presurgical fMRI provides for a superior assessment of the spatial link between brain tumor and motor cortex, greatly improving preoperative risk-benefit assessment and function-preserving surgery.[29] New functional glioma biomarkers that might help with diagnosis, treatment, and outcome prediction may come from fMRI.[30]

Other Clinical Findings

Migraine is linked to abnormal intrinsic functional activity in the limbic and primary sensory systems, according to resting-state fMRI data.[31] An fMRI scan was used to compare pre- and post-treatment functional connectivity, and the results indicated substantial differences.[32] One of the studies also showed that acupuncture might help chronic stroke patients with aphasia recover their language.[33] and acute low back pain patients[34] where the neural mechanisms of the brain associated with acupuncture were studied using fMRI. McPherson et al[35] investigated the relationship between neural systems involved in creativity and those engaged in emotion, and their findings reveal that emotions have a strong influence on activity in prefrontal and other brain networks involved in creativity. An fMRI study was conducted to investigate the neural substrates underlying the human–pet relationship, and it was discovered that mothers rated the images of their child and dog as eliciting similar levels of excitement and pleasantness but that the ratings of their dog were also positively correlated with ratings of their dog's attachment.[36] Several fMRI studies were carried out to investigate the effect of music and emotions, where they established significant correlations.[37] The fMRI study of connectivity between the neuronal networks of the brain allows for a better understanding of epileptogenesis, insomnia disease, and human speech articulation.[38-40] When depressed patients were analyzed for suicidal behavior, it was commonly observed that there occurred reduced perfusion of the prefrontal cortex, and the suicide attempters' social perception was linked to long-term neurological dysfunctions.[41] Even studies were carried out to examine the response of children's brains to food and common logos, and it was observed that the responses activated some brain regions when culturally familiar logos were viewed.[42] Also, a market survey was carried out to establish the liking of consumers for green products, in which an MRI study gave a result which was in favor of green products, while fMRI study did not point out any such trend which was the actual reflection of purchase behaviors.[43] Functional magnetic resonance imaging can be used to measure the acute pharmacological rewarding and reduced anxiety effects in alcoholics. Resting-state fMRI suggests that alcohol affects specific brain areas and may offer a neurological foundation for alcohol's effects on behavioral performance.[44] Alcohol impairs both driving behavior and brain functions linked to motor planning and control, goal-directedness, error monitoring, and memory, according to an fMRI research, making drunk drivers a huge public hazard.[45] Similar studies were carried out on the effect of marijuana smokers and other heavy smokers.[46] Another study shows the neural activity in the ventral striatum, an area of the brain that encodes feelings of subjective pleasure. Neural activity of the brain showed that there was more brain activation in the left hemisphere in the data obtained through fMRI techniques, and it can be useful in testing theories of investor behavior. It was observed that, at the moment, a subject issues a command to sell a stock at a gain, there is a sharp rise in the brain than in the right hemisphere on playing chess. Furthermore, fMRI demonstrated that the superior frontal lobes, parietal lobes, and occipital lobes were all activated bilaterally.[47,48] An fMRI research was used to examine the impact of block building games and board games on children's spatial skills, and it revealed that the block play group improved in response speed and accuracy. The brain alterations related to the 2 play regimens were evaluated using fMRI during a mental rotation task, which revealed an enhanced engagement of areas linked to spatial working memory and spatial processing memory following training.[49] Even a study on neural empathetic response of users to violent video games was carried out by Szycik et al using fMRI and found that the users were not much affected by these games in character shaping, and their research found that the effects of violent media on emotional processing can be severe and short-lived.[50] Using fMRI, Shirley et al[51] discovered which brain regions were engaged during the 3 phases of meditation compared to the control condition.

Despite the above-mentioned clinical findings, there is no baseline validation of contrast variations upon neuronal activation seen in fMRI images. A question on the credibility of fMRI signals aroused when Mr. Benneth in his poster presented the fMRI images of a dead salmon fish. The pictures of humans in different emotional states and neuronal activation occurred in the salmons brain suggesting meaningful activities were shown. Analyses were conducted utilizing separate generally used statistical tests as evidence.[52]

DISCUSSION

Functional magnetic resonance imaging has already been used to evaluate a variety of clinical functions of the human brain, detecting the onset of Parkinson's disease and noting the presence of disorders such as depression.[53] Selection of treatment modality is very crucial in the treatment of cancers as it helps in reducing the risks and improving the chances of cure. One of the major errors that occur in radiation therapy is the incorrect delineation of tumor volumes. Functional magnetic resonance imaging helps to evaluate the functional status of cells to be treated, and hence, physicians can accurately contour the diseased volumes. Other than clinical areas, the practice of taking fMRI images of the brain is spreading to areas of national security. At the time of employee screening, they are asked to get fMRI scan of the brain while performing cognitive tasks in order to check the feelings of the employee when certain extreme topics like racial prejudice, religious extremism, mental illness, psychopathology etc., come into the picture. It was concluded that it helped in lowering the risk of terrorist threats and preserving the rights of citizens.[54] The subject under examination in these cases and whoever participates in any research trial are usually healthy, but, the practical difficulty comes in the examination of sick patients who may have little capacity to perform any of the cognitive tasks. The signals obtained will be succumbed to more noise. One main drawback of fMRI is the long scanning time because of the low sensitivity of BOLD signal. This will result in more subject motion during the scanning and reduction of statistical significance of the activation maps and increases the prevalence of false activations. Motion correction tools along with recent development in software development, artificial intelligence, prediction models, and usage of different coding languages solve this drawback, and faster and more accurate images are possible with fMRI.[55-59]

Changes in blood flow, blood volume, and oxygen utilization over time are another form of physiological noise. This component accounts for two-thirds of physiological noise, which is the primary source of overall noise. Noise may also be caused by erroneous brain activity, as well as variances in mental strategy and behavior between persons and tasks within a topic. Prior to scanning, even on certain trails, individuals are instructed on how to behave or react.[60]

Other than subject-dependent noise, there are other sources of noise like thermal noise and system noise. Hence, it becomes necessary to set remarkable threshold values for the signals under study. Too high value for threshold can lead to very low output data for evaluation and very low threshold value can lead to excess noise resulting in evaluating false-positive signals. The evidence for this has been given by Benneth et al[61] in his dead salmon study. The study actually points out the necessity for multiple comparison correction. Before this controversy in 2010, around 25%-40% of the studies published on fMRI were not using the corrected comparisons. The problem lies in the analyses which are often based on low-power, small sample studies. The same was criticized by Vul et al[62] in his Voodoo correlations in neuroscience.

There is a need to find multiple techniques other than BOLD to cross-compare the results collected till date. Blood oxygen level-dependent effect is a bit noisy and it influences the signals. It was seen that the magnetic properties of the tissues change with change in temperature, that is, in the case of the brain, its temperature changes with change in activity. The early oxidation of glucose boosts brain temperature, which is then lowered as cold blood enters. Internal contrast caused by temperature changes is difficult to assess, but it can be improved by utilizing exogenous agents such as thulium compounds. We would only offer additional internal contrasts like acidity/alkalinity (pH), calcium-sensitive agents, neuronal magnetic field, and Lorentz effect to calm readers' nerves. When brain cells become active, their acid/alkaline balance changes, resulting in contrast dependent on pH. This is done far too frequently with the help of a third party. Calcium-sensitive drugs increase the sensitivity of MRI to calcium concentrations, as calcium ions are frequently used as messengers in activated neurons' cellular signaling pathways. The magnetic and electric fields in neurons are measured through neuronal magnetic field contrast.[63] A critical evaluation of MRI signals combining different contrast mechanisms is indeed necessary to evaluate the signals. Evidences are yet to be established so as to eliminate the risks of evaluating false-positive signals.

CONCLUSION

The application of fMRI is extensively wide from simple brain study to different medical and non-medical applications. There are different types of internal contrasts agents, and careful evaluation of subjects is necessary. In this study, basic principles and types and applications of functional MRI techniques are briefly introduced and reviewed. However, due to the limitation in length, the detail of each technique in-depth cannot be analyzed.

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