Functional Magnetic Resonance Imaging in the Clinical Setting

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Abstract

Functional magnetic resonance imaging (fMRI) is a relatively new imaging modality used to measure the blood oxygen levels in the brain. Task-based and resting-state fMRI are two different methods used. When a specific task is performed, there is an increase in oxygenated blood flow to the active area, providing a map to aid in the resection of a lesion in the brain without damaging vital brain tissue. Resting-state fMRI is done to assess altered connectivity of regions of the brain, specifically for patients with a mental illness. This paper discusses the major uses of fMRI in the clinical setting, including preoperative mapping for brain tumors and assessing the connectivity of networks in the brain for patients suffering from Alzheimer disease and epilepsy. Research and clinical studies have proved that this imaging modality is becoming vital in surgical planning and in predicting postoperative deficits for each patient.

Functional Magnetic Resonance Imaging in the Clinical Setting

"Functional magnetic resonance imaging (fMRI) is exceptionally beneficial in the research and treatment of neurological disorders. "It provides a means to assay differences in brain systems that underlie psychiatric illness, treatment response, and properties of brain structure and function that convey risk factor for mental diseases" (Zhan & Yu, 2015, p. 1). The use of "fMRI has an established role in the pre-surgical assessment of adult and pediatric patients being considered for brain tumor or epilepsy surgery, where the expected resection margin is close to regions of eloquent cortex" (Barras et al, 2016 p. 802). Functional MRI "is a non-invasive imaging modality that enables measurement of transient hemodynamic changes in the brain during carefully designed active tasks (paradigms) usually referring to motor, language, memory or visual functions" (Barras et al, 2016, p. 802). Functional MRI uses blood oxygen levels in the brain to aid in the preoperative planning for brain tumors, minimize postoperative neurological deficits, and identify differences in the brain systems in patients with mental illness.

Data is acquired from fMRI scans with the use of blood oxygen levels in the brain. When a certain task is performed, regions of the brain involved with that specific function become active, and there is an increase in the blood oxygen level. The brain requires more oxygen to complete a task and additional oxygenated blood is sent to the active area of the brain that is used for that particular function. The difference in the oxyhemoglobin concentration creates a magnetic resonance signal. When there is no task being performed, there is less oxygenated blood flowing to that region and the deoxyhemoglobin produces a different signal. (Gabriel, Brennan, Peck, & Holodny, 2014) "Functional MRI (fMRI) is a technique that measures hemodynamic changes after enhanced neural activity, allowing to image noninvasively and with relatively high spatiotemporal resolution, the entire network of brain areas engaged when subjects undertake particular tasks" (Pernet et al, 2016, p.37).

The difference in the amount of oxygen in the blood produces different magnetic properties. When a task is performed during an fMRI study, brain activity is detected and there is an increase in oxygenated blood, creating a stronger magnetic resonance signal. Task based fMRI uses paradigms to assess the activity of a specific region of the brain. "In most cases, small movements of the foot, hand, or tongue provide a significant signal, particularly when head motion is absent" (Gabriel et al, 2014, p. 563). "Finger-tapping paradigms are commonly used to localize sensorimotor cortex, whereas verb-generation or sentence-completion paradigms are commonly used to localize language cortex" (Chiang, Haneef, Stern, & Engel, 2017, p. S29). Eloquent brain tissue can be detected by assessing the excess oxygenated blood delivered to the areas of the brain that are involved in performing the task. In some cases, when a task is performed different areas of the brain may be activated that correspond with that particular task, but that area may not be crucial to perform that function. This imaging technique is accurate for preoperative mapping of the brain, however, caution must be taken with these corresponding areas to avoid postoperative brain damage. (Gabriel et al, 2014, p. 564)

Resting-state fMRI (RS-fMRI) is also effective in localizing active brain tissue. During resting-state fMRI, there is more deoxyhemoglobin resulting in a decrease in signal. RS-fMRI measures the amount of deoxyhemoglobin when the patient is at rest. When the brain is at rest the functional connectivity and the relationships of regions of the brain are measured with the spontaneous BOLD signal fluctuations, or the amount of deoxyhemoglobin. (Chiang et al, 2017) A RS-fMRI may be done for patients who are unable to perform a certain task such as children, patients with neurological deficits, or a patient who is unconscious. During a functional connectivity fMRI study, the patient must lie completely still for an accurate reading. This test has been used mainly to assess sensorimotor and language centers of the brain. Data acquired from RS-fMRI scans are presented as a graph or map of the location of motor or language networks in the brain.

> In patients who are not performing a task, RS-fMRI reveals areas of the brain that have synchronous BOLD activity, called resting state networks (RSNs). These networks include the somatosensory, language, and visual networks, which provide valuable information for the neurosurgeon in the preoperative setting. (Lee et al, 2016, p. 2)

One of the major advantages of RS-fMRI is that multiple networks in the brain can be identified with one scan. Multiple scans must be done for a task-based fMRI to identify the different networks with paradigms.

During the presurgical planning for brain tumor resection, data from both task-based and RS-fMRI is put into an activation map to visualize the relationship between the brain lesion, and active brain tissue. These methods of scanning demonstrate accurate measurements of the distance between a lesion in the brain to active brain tissue. The data can aid physicians in making decisions specific to each patient that include

> (1) the location and size of the craniotomy; (2) the direction and path of approach to the tumor; (3) the need for a ventriculostomy catheter and where to place it; (4) the need for electrocortical stimulation equipment to confirm the MRI findings; (5) the need for an intraoperative MRI scan; and (6) the need to vary the type of anesthesia depending on the type of anticipated stimulation mapping. Every case is different, and the MRI information can provide valuable help in decreasing morbidity and optimizing the tumor resection. (Lee et al, 2016, p. 6)

By localizing a brain tumor with fMRI, surgeons can develop treatment plans that are specific to each patient and provide the best outcome.

A multidimensional map of the brain can be created with a single fMRI scan. The map of the data acquired from fMRI scans shows the precise measurements and location of the lesion itself, and the lesion in relation to the eloquent tissues.

> For presurgical fMRI, this procedure provides information on which areas are confidently safe to be resected (gray areas), which areas should absolutely be avoided when resecting brain tissue (red areas), and in which areas the surgeon should take care because neither hypotheses can be rejected (yellow areas). (Durnez, Moerkerke, Bartsch, & Nicholas, 2013, p. 706)

Data acquired from fMRI scans is analyzed by "performing a statistical test in each voxel, which is used to classify voxels as either active or inactive—that is, related, or not, to the task of interest" (Durnez et al, 2013, p. 703). Activation maps are useful in evaluating the risks of surgery and they can be used to provide a new approach in planning, or guide the surgeon during the resection of the lesion. With so much information provided with these studies, doctors have more confidence in their decisions. In various studies, the use of preoperative maps developed with fMRI data were vital for the complete resection of the lesion with no complications. The high spatial resolution provided with fMRI scanning is important for the precision of assessing the function and organization of the brain when mapping different areas. (Gabriel et al, 2014, p. 563)

Functional MRI is commonly used to locate the sensory or motor system because it is minimally invasive and provides a large amount of data that can contribute to a patient's treatment plan. "The primary motor and sensory areas in fMRI are of particular interest for surgical planning, because iatrogenic damage to these areas can cause permanent neurologic deficits" (Gabriel et al, 2014, p. 557). Many patients who have brain tumors that are considered inoperable are now given the option of surgical resection and other treatments, with the visualization of anatomic locations of eloquent tissues gained through fMRI data. "The fMRI map correctly identified the location of the sensorimotor cortex in 96% of the cases (141 of 147 patients examined). The 4% that could not be identified displayed head motion greater than 2 mm" (Gabriel et al, 2014, p. 562).

Presurgical fMRI scans can be used to prevent postoperative complications and morbidities by measuring the distance between a brain tumor and functional brain tissue, or the Lesion to Activation Distance (LAD). Functional MRI "provides good spatial localization (as low as 1 mm) and temporal acquisition resolution (as low as 1 second)" (Gabriel et al, 2014, p. 557). The resection of a lesion in the brain can damage active brain matter and possibly cause permanent deficits. The increased spatial resolution is beneficial in localizing the borders of a lesion in the brain compared to the active brain tissue. Functional MRI is essential in directing a surgeon through the brain for resection of a tumor. The identification of eloquent areas of the brain "guides the selection of the safest trajectory to approach the lesion, the decision of whether to proceed with awake or asleep craniotomy, and it can also influence the efficiency, exposure, and choice of technique for intraoperative mapping" (Zacà, Jovicich, Nadar, Voyvodic, Pillai, 2014, p. 383). The distance between the lesion and eloquent tissues is measured "by determining the distance between the tumor edge and the edge of the cluster of BOLD activation" (Bailey et al, 2015, p. 777-778). This measurement is often used to assess the probability of postoperative neurological deficits.

Damage to tissues surrounding a lesion can result in motor or language deficits depending on the location of the lesion. “The goal of neurosurgery in patients with brain tumors is to maximize the extent of resection while minimizing morbidity” (Bailey et al, 2015, p. 776). Functional deficits are more likely to occur with a small lesion to activation distance or when a greater amount of active white matter in the brain is affected by the lesion. “A distance of 2 cm from a fMRI-identifies functional region to the surgical margin has been considered safe for resection and correlates well with the postoperative loss of function” (Manglore et al, 2013, p.144). For many patients, this small distance increases the probability of complete resection of a brain tumor with a decreased risk of complications. With the selection of the proper paradigms for task-based fMRI, patient cooperation, and the correct threshold setting, the results of the scans are very valid and can be used to predict postoperative deficits. “Pre-surgical fMRI can provide additive diagnostic information such as language-dominant hemisphere determination, or diagnosis of the relationships between brain tumors and language or motor areas before surgery” (Mahdavi et al, 2015, p. 468).

Functional MRI can be used to assess changes in brain activity for different mental illnesses such as Alzheimer disease. “Resting-state functional MR imaging yields new insights into how structurally segregated and functionally specialized brain networks are interconnected” (Kazemifar et al, 2017, p. 2). Resting-state fMRI has been used to assess the connectivity of networks in the brain compared to healthy subjects by measuring the low frequency changes of the blood oxygen level dependent signal. “Previous RS-fMRI studies have shown a reduction in functional connectivity between structures based on the *strength* of the correlation in the BOLD signal (Kazemifar et al, 2017, p. 3). When the connectivity between regions of the brain is disrupted, there is a reduction in oxygenated blood to that region. “The brain activity measurement is dependent on both the number of neuronal components and the temporal fluctuation associated with each component" (Kazemifar et al, 2017, p. 12). Patients with Alzheimer disease demonstrated a decrease in brain activity, primarily in the accumbens.

> A few RS-fMRI studies have also examined functional *network* activity in healthy subjects compared to people with Alzheimer disease. Seed based analyses have shown decreased functional connectivity (FC) in the medial temporal cortex, prefrontal cortex, precuneus, posterior cingulate, hippocampus, and thalamus in people with Alzheimer disease. (Kazemifar et al, 2017, p. 12)

Resting-state fMRI has been used in many studies to show that the connectivity is disrupted between a specific region of the brain and the hippocampus.

Functional MRI is also used to assess the connectivity of the brain in patients with epilepsy. "At present, the primary contribution of fMRI in epilepsy surgery is the identification of language-processing regions and hemispheric dominance, to predict and minimise language deficits" (Barras et al, 2016, p. 801). In many cases lesions are found in the frontal or temporal lobes of the brain resulting in the reorganization of language centers which can be identified with fMRI scans. "Estimated correlations between low-frequency fluctuations (<0.1 Hz) have been found to reproducibly reflect the underlying intrinsic neural architecture,[12] and are presumed to be generated by underlying fluctuations in neural activity" (Chiang et al, 2017, p. S26). A decrease in the blood oxygen level may cause alterations in the layout of the brain in patients with epilepsy. Functional MRI scans also detect the connectivity of networks and can help identify the EZ, which is the section of the brain where the seizures are generated. The presence of the EZ often results in weakened or altered connectivity between areas of the brain. Visualizing and comparing these changes in the brain lead to a much better understanding of the physiology in patients with epilepsy which can provide better approaches to surgery or treatments in the near future. In many studies, data acquired from both RS-fMRI and task-based fMRI are analyzed and compared on connectivity maps. This can be beneficial especially when scanning patients with Alzheimer disease or epilepsy. Task-based fMRI maps the unilateral cortex of the affected side while RS-fMRI provided a map of both hemispheres for comparison of the unaffected side. RS-MRI is able to test multiple functions at once by measuring spontaneous changes in blood oxygen level deficient levels.

Functional MRI measures blood oxygen levels in the brain to detect active brain tissue in order to develop treatment plans, decrease postoperative deficits, and provide new research about neurological disease processes. Functional MRI is less invasive, has better spatial resolution, and uses less radiation. This modality is vital for localization and resection of brain tumors because it provides more information for the surgeon to make decisions regarding each patient. Activation maps acquired with fMRI data aid in the localization of lesions and provide better visualization for determining the path of resection during surgery. The lesion to activation distance (LAD) is precisely measured with the high spatial resolution and can be used to predict postoperative neurological deficits. With the use of fMRI in the clinical setting, there is a better understanding of the anatomy and physiology of the brain in both healthy patients, and patients suffering from conditions like Alzheimer disease or epilepsy.

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