

Functional Neuroimaging: Current Status

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Editorial

Despite increasing complexity of neurosurgical procedures; they have become safer over the last few decades which can be clearly attributed to rapid advancement in technology coupled with dramatic improvement in radiological imaging. Today neurosurgical treatment is increasingly benefitted by rapid developments in radiological imaging and post processing techniques leading to decreased invasiveness and improved safety. With increasing expectation from patients and greater understanding of biology of intracranial pathologies, the limitations of structural imaging became more obvious leading to development of imaging modalities to link function with imaging providing robust clinical information with potential to impact the clinical management and outcome. Initially driven by improvement in structural imaging, the last few years have witnessed tremendous advances in the field of functional neuroimaging and brain mapping techniques [1]. In the last two decades a variety of functional imaging techniques have been developed which are increasingly able to give surgeons an understanding not only of the complex anatomical relationships of brain lesions, but also of the functional relationship of the lesion to surrounding key cortical areas and white matter structures.

Functional imaging assesses brain function in real time and uses the neuroimaging technology to measure an aspect of brain function, often with a view to understand the relationship between activity in certain brain areas and specific mental functions [1,2]. These techniques, initially used as research tools mainly in cognitive neuroscience and neuropsychology are increasingly deployed in the clinical arena. Clinical functional studies such as direct Electroconvulsive Stimulation testing (ECS) and intracarotid amytal (Wada) testing which were once considered "gold standard" are now complemented by newer, less invasive techniques, such as functional Magnetic Resonance Imaging (fMRI) and Transcranial Magnetic Stimulation (TMS) [1,3].

Common methods of functional neuroimaging include Positron Emission Tomography (PET), fMRI, multichannel Electroencephalography (EEG) or Magnetoencephalography (MEG), and Near Infrared Spectroscopic Imaging (NIRSI) [3-6]. PET, fMRI and NIRSI rely on measurement of localized changes in cerebral blood flow related to neural activity while EEG and MEG directly measure electric brain activity. The most common fMRI technique detects blood flow-related changes in venous deoxyhemoglobin content, the so-called Blood Oxygenation Level Dependent (BOLD) contrast technique, to generate functional maps of neural activation and deactivation [4]. Though started as a primarily research tool, the role of fMRI has been rapidly evolving in management of various neurosurgical disorders. fMRI has found wider clinical applications mainly in presurgical evaluation of patients for epilepsy surgery and management of intracranial lesions involving/located adjacent to the eloquent cortex [1]. Recent studies have demonstrated the potential role of fMRI to provide a more accurate picture of the neurophysiologic sequelae of brain injury and a better predictive value of clinical outcome in pediatric patients with brain injury [7]. Other than that, fMRI is being used as a biomarker for disease, to monitor therapy, or for studying pharmacologic efficacy [8-10]. PET on the other hand is based on the principle of intravenous injection of very small amount of labeled compound (called radiopharmaceutical or radiotracer) into the patient and after an appropri-

ate uptake period; the concentration of tracer in tissue is measured by the scanner. The role of PET in neurooncology has been vital in (1) providing a global picture of the tumor and thus guiding the appropriate site for stereotactic biopsy; (2) prediction of biologic behavior and aggressiveness of the tumor, thereby aiding in prognosis and (3) differentiating recurrent tumor from treatment-related changes (e.g., radiation necrosis and postsurgical changes) which has significant clinical implication [5]. Again the sensitivity and specificity of (18)F-FDG in evaluating recurrent tumor and treatment-induced changes can be improved significantly by co-registration with structural MRI [5,8]. Also there has been development of newer amino acid PET tracers which are more sensitive than the commonly used (18) F-FDG in imaging recurrent tumors (particularly recurrent low-grade tumors) and in differentiating between recurrent tumors and treatment-induced changes [11-13]. PET and SPECT have become an integral component in the presurgical evaluation of epilepsy surgery patients leading to better characterization of epileptic foci translating into better outcome following epilepsy surgery especially in patients with negative MRI [5,14], and a sensitive imaging tool in evaluation of Alzheimer's disease [15]. Clinical application of MEG recently have provided another technique for localization of epileptic discharges, determination of the hemispheric dominance of verbal processing, and the ability to locate eloquent cortex [2]. MEG measures the post synaptic neural activity originating in the pyramidal cells of the cerebral cortex and is supposed to localize neural activity more accurately than EEG as magnetic fields are less perturbed than electrical potentials by overlying brain structures. MEG has been used increasingly as a tool in presurgical evaluation of patients with brain tumors and epilepsy; however its high cost remains a concern [2,3]. In summary, the application of functional neuroimaging in evaluation of intracranial tumors, epilepsy, stroke, trauma, chronic pain, schizophrenia, depression, and obsessive-compulsive disorder is increasing at a rapid pace and is expected to play a major role over the next few years.

Considering a number of functional neuroimaging techniques available, the appropriate neuroimaging technique used for a particular study is dictated by the specific question being addressed, limitations and cost factors. For instance, MEG records the magnetic fluctuations that occur when a population of neurons is active. This is excellent for measuring the time-course of neural events (on the order of milliseconds,) but is poor at measuring where those events happen [2]. PET and fMRI measure changes in the composition of blood near a neural event. Because measurable blood changes are slow (on the order of seconds), these methods are much worse at measur-

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ing the time-course of neural events, but are generally better at measuring the location [4,5]. An active area of functional neuroimaging research involves examining the functional connectivity of spatially remote brain regions [16]. Combination of fMRI and PET studies may enable creation of functional connectivity maps of distinct spatial distributions of temporally correlated brain regions called functional networks. A direct method to measure functional connectivity is to observe how stimulation of one part of the brain will affect other areas. This can be done noninvasively in humans by combining TMS with one of the functional neuroimaging tools such as PET, fMRI, or EEG. Apart from the avoiding intraoperative awake testing through preoperative localization of certain functions away from the surgical bed utilizing advanced functional neuroimaging, the functional data also has the potential to be combined with Diffusion Tensor Imaging (DTI) identifying the trajectory of the nerve fibers so they can be avoided during surgery preventing complications. As fMRI indirectly measures neuronal activity based on oxygenation levels, a significant site of neuronal activity may escape recognition if they do not generate an adequate hemodynamic response. Signal changes during BOLD imaging are dependent on magnetic field strength and may need higher than the usual 1.5 T sequences. Though higher magnetic strength has the potential to pick up the BOLD signals the problems of greater susceptibility artifacts needs to be addressed with increasing magnetic field. Additionally, the BOLD signal itself is not yet entirely understood: the relationship between positive and negative BOLD signals and alterations in neural activity has not been fully established [4]. Hence knowledge of strength and limitations of various functional neuroimaging techniques is vital in directing appropriate work up. Infact combination of functional neuroimaging techniques with advanced structural MRI (fMRI with DTI, PET with MRI and MEG with MRI and DWI) seems very promising in further increasing the overall localization and diagnostic accuracy of current radiological techniques [3,11].

To summarize, there has been an exponential growth in functional neuroimaging techniques over the last few years which has drastically changed the way we treat disorders of the nervous system. There are limitations with each techniques and functional neuroimaging is no exception. The challenges ahead lie in selecting the best functional neuroimaging technique with possible combining of both functional and advanced structural radiological imaging data to further enhance the efficacy and safety of neurointerventions. This issue of Open Access Radiology journal dedicated to functional neuroimaging discuss the current status of functional neuroimaging techniques though articles from experts from a wide range of disciplines related to brain imaging. The benefits of articles from various experts in the field in combination with the open access nature of the journal grant to all users a free and easy access to the scientific literature with no limitations.

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