Clinical Applications of fMRI: Bold Claim or Reality?

Keith R THULBORN

1University of Illinois at Chicago, rm 1191 MRI Center OCC M/C 711, Chicago, IL USA;

Introduction

The potential to map human brain function with blood oxygenation level dependent (BOLD) contrast fMRI in the setting of disease has obvious implications for pre surgical planning of all neuro-interventions (1) but also in cognitive and rehabilitation medicine. Given the rapid publication of fMRI results throughout the medical literature, there is a heightened expectation for this information to be supplied as a routine part of the clinical neuroradiology service. Experiences at meeting such requests have defined the challenges to be surmounted and have indicated solutions to meet these needs. These challenges and the solutions will be discussed in terms of patient applications on a clinical neuroradiology service.

Challenges and Solutions

Referrals: As not all patients are suitable candidates for fMRI, appropriate expectations of referring physicians must be established. In the setting of disease, the limitations of neuronal-hemodynamic coupling must be defined to establish boundaries of regions in which BOLD contrast can be interpreted reliably.

Instrument Quality Assurance (2): Given the small signal changes associated with BOLD contrast, the scanner must be optimized and routine QA performed to ensure that instrumentation limitations do not impact on the clinical interpretation of fMRI studies. The synchronization of stimulus presentation with imaging, physiological and behavioral monitoring requires appropriate additional instrumentation – the Synchronization Control System – to allow a single technologist to perform functional studies in a routine manner on the clinical service (3).

Paradigms: The stimulus paradigms must be calibrated against normal populations with appropriate matching for age, handedness, gender and education. Both block- and event-related designs can be used. Where possible, such calibrated paradigms must serve a range of clinical questions and patient populations. Patients must be prepared to reduce the novelty effects of the MR scanner and tested for visual and auditory acuity. The effects of training on behavioral responses should be minimized.

Analysis: Although there is no consensus as to how to analyze fMRI data, familiarity with the strengths and weakness of the methods used is essential to develop confidence for the interpretation of the activation maps.

Communication of Information: The reporting and display of information for the referring physician must be informative and often requires one-on-one discussion to integrate the fMRI data with the clinical scenario.

Application: Stroke Rehabilitation

Stroke is a costly disease in the United States and often devastating to the surviving patient and family. Recovery is highly variable and appears to be related to the ability of the brain to redistribute the workload away from the lost tissue caused by the stroke. Functional MRI has been used to follow this recovery process in stroke patients having problems with understanding language (receptive aphasia) and in speaking language (expressive aphasia) (4). The rate of recovery can be surprisingly rapid or unfortunately prolonged. This rate of recovery appears to relate to the redistribution of activation into areas of the remaining network. Such redistribution is dependent on having intact white matter. The white matter of myelinated neuronal axons can be thought of as being the cables connecting different processing areas of the gray matter. When the lesion involves large areas of white matter, recovery is slow, presumably due to interference with this redistribution process. Diffusion tensor and functional MRI provide tools for understanding the recovery process and have potential for establishing prognosis and aiding in the design of strategies to improve outcome.

Application: Alzheimer’s Disease

Alzheimer's disease is the most common cause of dementia in the elderly. This diagnosis has profound implications for the individual and family but it is only definitively made at autopsy. The clinical diagnosis requires extensive psychological and psychiatric testing with years of follow-up. The specificity remains low (less than 85%) even in competent hands. By using a simple oculomotor paradigm, a 6 minute fMRI test has been able to improve this specificity using a parameter based on interhemispheric differences in parietal lobe activation (5). This may portend improved diagnosis by fMRI for other diseases with cognitive disorders.

Summary

The challenges of instrumentation are decreasing as vendors begin to produce dedicated scanners for fMRI. This is evident with the production of the first FDA-cleared, very-high-field scanner (3.0T). Commercially available SCS and calibrated paradigms are also being reported. Clinical experience is still in its infancy but the level of enthusiasm is high (6). Multi-center trials should be the next step towards establishing clinical efficacy (and reimbursement) for specific clinical applications.

References


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