# Functional MR Imaging: Blood Oxygen Level–Dependent and Resting State Techniques in Mild Traumatic Brain Injury

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**KEYWORDS**

• Functional MR imaging • Blood oxygen level dependent • Resting state • Mild traumatic brain injury

**KEY POINTS**

- There are numerous changes in resting state functional MR imaging postconcussion.
- Although the overall time-course of mTBI-associated effects on functional connectivity are still being elucidated, some general trends with respect to initial injury, persistent change and recovery have begun to emerge in the literature.
- There seems to be a period of acute post-injury default mode network hyperconnectivity, followed by a period of decreased connectivity before later connectivity normalization in some patients.

## INTRODUCTION

Concussions are clinically diagnosed from behavioral observations, patient-reported symptoms, and physical examination. Neurocognitive testing may be used and is often helpful; however, it is not required for diagnosis. No biomarkers to reliably diagnose concussion have been incorporated into routine clinical practice, and conventional neuroimaging methods are typically negative. Furthermore, the same limitations that exist for initial diagnosis are also present in monitoring recovery.[1] Functional MR (fMR) imaging is an evolving form of neuroimaging that permits quantitative measurement of brain function that may one day aid diagnosis and can be repeated longitudinally for evaluation of recovery.[2] It has been posited that fMR imaging is a more sensitive tool for postconcussion neuropsychological evaluation than classic testing methods.[3]

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fMR imaging quantifies brain activity based on the relationship between neural activity and localized hemodynamic responses. Although the exact mechanism has not been determined, neural activity typically induces a hemodynamic response that results in a net effect of increased oxyhemoglobin level in relation to deoxyhemoglobin level in the local microvasculature. With increased ratio of oxyhemoglobin to deoxyhemoglobin, there is a reduction in local magnetic susceptibility, which can be measured using blood oxygen level–dependent (BOLD) contrast where increased signal results.

There are 2 broad approaches to using this BOLD contrast in functional neuroimaging. In task-fMR imaging, a specific sensorimotor or cognitive task is performed by the patient, and correlations of BOLD signal with task modulation are computed. Any brain region that shows BOLD oscillations that are synchronous with the performance of the task are considered to be relevant to performance of that task. More recently, a task-free paradigm has emerged, now described as resting state fMR (rs-fMR) imaging, in which the patient does not perform a specific task while BOLD images are acquired. The patient thus engages in undirected processes throughout the acquisition. Despite this lack of task-oriented cognitive control through the acquisition, fairly consistent spatial patterns of temporal BOLD correlations have been shown using rs-fMR imaging. Spatially distinct regions of the brain that show temporally synchronous BOLD signal (and by inference neural activity) have been characterized as various intrinsic resting state brain networks.[4]

There are significant benefits of rs-fMR imaging compared with task-fMR imaging. Because no task is explicitly performed in rs-fMR imaging, this technique can be used to negate the confounding issue of patient performance, which can be variable depending on the population that is being studied. This advantage lends itself to greater uniformity in data acquisition if the imaging parameters are kept constant across sites. Furthermore, with task-fMR imaging, only a specific subset of cognitive processes are interrogated; in contrast, rs-fMR imaging provides information about multiple brain networks across the entire brain. Given the ease of acquisition compared with task-fMR imaging, as well as the breadth of information acquired, rs-fMR imaging has in most cases supplanted task-fMR imaging for investigation of brain function across a wide variety of brain disorders; and this article therefore focuses on rs-fMR imaging in the context of concussions.

Alterations of functional connectivity assessed by rs-fMR imaging are described with respect to the chronology of presentation, starting with the immediate postconcussive time frame and extending to years postinjury. In addition, this article uses the terms mild traumatic brain injury (mTBI) and concussion interchangeably, although there is active debate about the specific meaning of these terms in both the clinical and research domains.

## ACUTE MILD TRAUMATIC BRAIN INJURY

In the recent literature, the acute phase of an mTBI is typically considered the initial 30-day period postinjury. The time period immediately following an mTBI is characterized by rapid changes in which the brain presumably attempts to recover from the initial concussive insult. rs-fMR imaging has shown variable patterns depending on the timing of imaging in the acute phase.[5] This variability is understandable because both the primary injury and early inflammatory response occur during this period and subsequently begin to heal.[6] The primary injury is a direct result of impact exposure and may include primarily axonal injury resulting from the sudden deformation of brain. The inflammatory response follows this neuronal injury as edema, neurotransmitter release, and vascular dysfunction. This early time period can be particularly difficult for patients as they attempt to manage their symptoms, which often include headache, cognitive fogging, emotional lability, insomnia, and slowed reaction times.[7] Although almost all concussive symptoms resolve within 10 days, some patients can be burdened with a more prolonged postconcussive syndrome (PCS) that can continue for months and even years. For young athletes busy in both athletics and academics, the immediate postconcussive period can be particularly stressful because their return to play depends on a successful return to school.

In the setting of all this neurocognitive change, rs-fMR imaging attempts to provide imaging correlates of concussion and relate them to concussive symptoms, time postinjury, degree of recovery, and other variables in order to characterize the brain-related functional impact of injury. Through repeated imaging across the acute and chronic phases of injury, some trends have begun to emerge, showing an expected pattern of mTBI recovery compared with large control groups. Most consistently explored are the default mode network (DMN) and task-positive networks (TPNs). The DMN primarily consists of coordinated activities of the posterior cingulate cortex, medial prefrontal cortex, hippocampus, and parahippocampus, and it has been described to be involved in introspection, memory, planning, and daydreaming.[8] In contrast, the TPN is anticorrelated with the DMN and is typically active during