

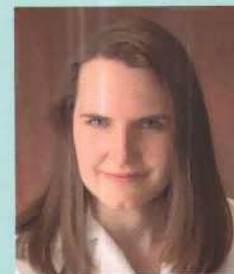
# Window Into The Brain

*New advances in sports concussion management:  
Functional Brain Imaging*

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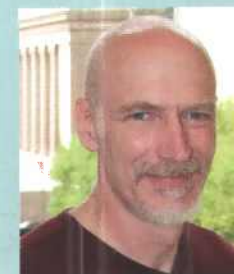
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The past decade has witnessed an explosion in research aimed at understanding recovery from sports-related mild traumatic brain injury (concussion). The dramatic rise in research appears to be the outgrowth of an increased awareness of the dangers of concussion in conjunction with the considerable advances in the neurosciences. Research in this area has resulted in radical changes in the clinical management of sports concussion. Only 10 years ago, there were more than 20 separate return-to-play guidelines, and none of these guidelines had undergone validation through research. This led to considerable confusion among sports medicine practitioners. More recently, return-to-play directives have been increasingly based on new advances in research.

The orthopedic surgeon plays a key role in the clinical management of concussion in athletes. The orthopedist is often the first health professional to evaluate the athlete after concussion, and they frequently have the responsibility of making complex

and difficult return-to-play decisions. Therefore, it is crucial that they have a current grasp of new and evolving research.

#### NEW FRONTIERS IN CONCUSSION MANAGEMENT

Until quite recently, little was known about changes in brain function following concussion, and our understanding was based solely on animal research. For example, in the late 1990s,

David Hovda, PhD, director of the University of California, Los Angeles, Brain Injury Research Center, and his associates demonstrated a "metabolic mismatch" characterized by increased energy demand within the brain, accompanied by a decrease in cerebral blood flow, presumably secondary to the accumulation of endothelial  $Ca^{++}$ , leading to widespread cerebral neurovascular constriction. In this animal model, concussion was found to last up to 2 weeks post-injury. This mismatch between energy demand and supply within the brain has since been postulated to leave the brain more vulnerable to a second injury, possibly helping to explain the rare but often fatal "second impact syndrome" seen in children and young adults. This metabolic dysfunction was also thought to provide the basis for the less severe, though occasionally incapacitating, post-concussion syndrome (eg, postconcussion symptoms that persist months and even years after injury).

Although extremely important in advancing our base of knowledge, this initial animal research in the 1990s did not provide information that was directly applicable to humans.

Understanding the metabolic process of concussion in humans is important for several reasons:

First, an understanding of how the brain recovers following concussion could eventually lead to the development of clinical return-to-play guidelines based on neurological recovery, rather than on purely clinical sympto-



Figure 1. Young athlete being prepared for an fMRI study.

matology. Therefore, athletes could be cleared or held from play based on more objective evidence of when brain function has returned to normal.

Second, currently utilized anatomical brain imaging technology is notoriously insensitive to concussion and is therefore of little value in managing the injury. The development of advanced brain scanning technology that allows for the examination of brain function rather than brain structure could lead to a major paradigm shift in the diagnosis and treatment of concussion as well as nonsport-related brain injuries.

#### FUNCTIONAL BRAIN IMAGING

Although neuropsychological testing has increasingly been utilized as both a research and a clinical tool, an intense focus on the development of sophisticated brain imaging techniques has emerged in the past several years. This interest grew out of new technological advances in brain imaging in addition to frustration regarding the well-known lack of sensitivity of more traditional anatomic imaging techniques such as CT and MRI. Although useful in identifying brain injury in more severe cases, CT and MRI scans are not often helpful in identifying more subtle brain-related changes that are thought to occur on a metabolic rather than an anatomic level.

Functional magnetic resonance imaging (fMRI) is based on the measurement of specific correlates of brain activation such as cerebral blood flow and oxygenation. Unlike traditional MRI technology that provides images that display changes in brain anatomy, fMRI utilizes an MRI scanner that has been adapted to measure changes in brain metabolism in response to different cognitive activities.

Figure 1 shows a young athlete being prepared for an fMRI study. The athlete's head is encased in a hood that assures a rigid head position as well as providing a small, illuminated screen on which the test stimuli are projected. Once the athlete is moved back into the bore of the MRI magnet, specific memory tests are projected onto the screen. The athlete responds to these stimuli by clicking a mouse (shown) or other input device.

Our program at the University of Pittsburgh currently utilizes several different cognitive tasks to evaluate the brain's response to concussion. The N-Back test is a standard test of working memory during which the athlete is shown a series of letters on the screen and is required to

indicate whether each letter is a target or nontarget letter by pushing a button. For the 0-Back condition, the athlete merely responds each time the target letter (for example, "x") is presented. The task is then made increasingly difficult by requiring the subject to recall whether the letter presented was the same as the letter presented one (1-back) or two trials previously (2-back).

The administration of specific neuropsychological tests to nonconcussed individuals during the fMRI scanning process results in measurable and predictable changes in brain activity that can be contrasted with the performance of athletes following concussion.

fMRI involves no exposure to radiation and can be safely utilized in children. Furthermore,

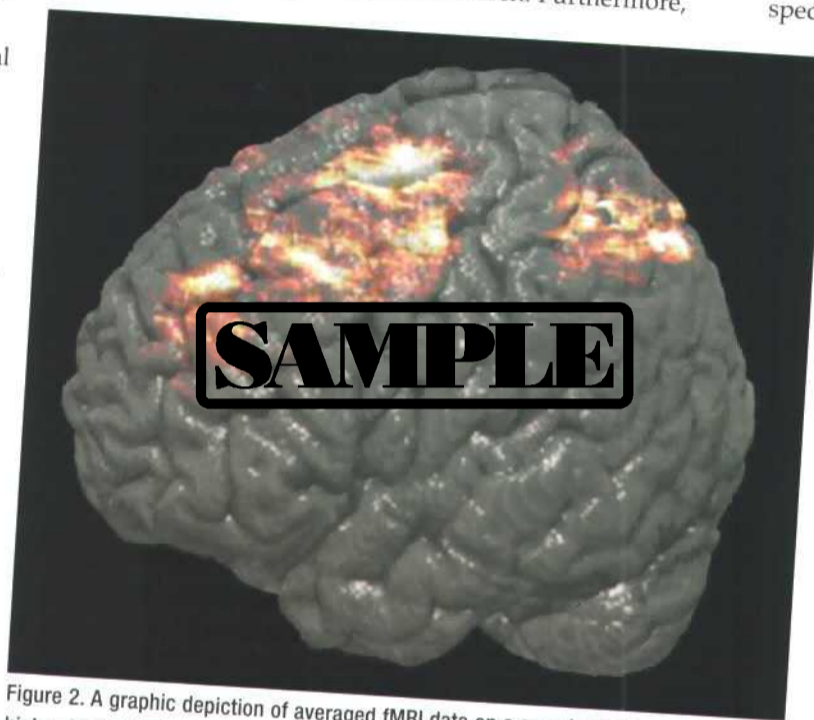


Figure 2. A graphic depiction of averaged fMRI data on a sample of 13 concussed high school athletes who had undergone fMRI evaluation.

repeat evaluations can also be undertaken with minimal risk. This promotes the assessment of changes in neural substrata that may occur with mild concussion and makes it possible to track the recovery process. Potentially, one of the most important uses of functional MRI scanning is the ability to provide validity data regarding the sensitivity and specificity of neuropsychological testing to detect subtle changes in brain function.

Although a promising tool, fMRI has been implemented only in a few centers internationally. In the United States, the laboratory at the University of Pittsburgh represents one of a handful of research programs structured to collect both neuropsychological and fMRI data in athletes.

This multiyear, prospective study, funded by the National Institutes of Health, relies on the prior baseline neuropsychological testing (ImPACT) of a very large cohort (more than 2,000) of male and female high school and college athletes. In the event of an injury, the athletes undergo repeat neuropsychological and fMRI evaluations within 7 days of injury. An additional fMRI scan and follow-up ImPACT testing are completed when the patient is asymptomatic. This has allowed us to evaluate the correlation between fMRI and neuropsychological testing results.

To date, the University of Pittsburgh/Carnegie Mellon University project has evaluated more than 165 concussed athletes. We have found specific patterns of increased cerebral blood flow (hyperactivation) in brain regions known to be highly involved in memory, thus directly linking concussion to changes in brain metabolism.

Figure 2 provides a graphic depiction of averaged fMRI data on a sample of 13 concussed high school athletes who had undergone fMRI evaluation. As the memory task becomes more difficult, the illumination shows areas of hyperactivation in the dorsolateral prefrontal cortex. This area of the brain is highly involved in working memory (eg, the capacity of the athlete to recall information in the face of interference and distraction). Therefore, this pattern of hyperactivation appears to be reflecting a need for the concussed brain to increase its metabolic activity in response to the task becoming more difficult.

The management of sports-related concussion is an area of intense interest in the field of sports medicine, and clinical concussion management continues to evolve at a rapid rate. Increasingly, changes in concussion management will come from advances in the neurosciences that will undoubtedly involve the development and implementation of new brain imaging techniques. Functional MRI appears to be a highly promising technology that will lead to increasingly sophisticated concussion management strategies. OTR

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## NFL Players Recover Faster Than High School Players

A research study undertaken by the NFL's Committee on Mild Traumatic Brain Injury (MTBI) revealed that professional football players recover faster from concussions than high school players. The study was the first to provide a direct comparison of neurocognitive recovery in athletes, within days of concussion occurrence, by using a computerized neurocognitive testing tool called ImPACT.

Developed by Mark R. Lovell, PhD, director of neuropsychological testing for the NFL and director of the UPMC Sports Medicine Concussion Program, the device is a computerized test battery that athletes can complete on a laptop or desktop computer within about 30 minutes. According to Lovell, the athletes were evaluated with formal tests of reac-

tion time, concentration, and memory, and the results underscore the critical need for preventing younger athletes from returning to play before they have fully recovered from concussions.

As a group, the NFL players studied returned to preinjury baseline neurocognitive performance in 1 week, with the majority of athletes having normal performance 2 days after injury. By comparison, the high school athletes demonstrated a slower injury recovery and longer lasting neuropsychological effects, according to the principal investigator Elliott Pellman, MD, chairman of the NFL MTBI committee. Pellman said the most dramatic difference was on tests measuring speed and reaction time.