

**Concussion and pathophysiology (literature search) – Dr Ryan Kohler – December 2011**

### The pathophysiology of concussions in youth

Shrey DW, Griesbach GS, Giza CC, Physical Medicine And Rehabilitation Clinics Of North America 2011 Nov; Vol. 22 (4), pp. 577-602

Mild traumatic brain injury, especially sport-related concussion, is common among young persons. Consequences of transient pathophysiologic dysfunction must be considered in the context of a developing or immature brain, as must the potential for an accumulation of damage with repeated exposure. This review summarizes the underlying neurometabolic cascade of concussion, with emphasis on the young brain in terms of acute pathophysiology, vulnerability, alterations in plasticity and activation, axonal injury, and cumulative risk from chronic, repetitive damage, and discusses their implications in the context of clinical care for the concussed youth, highlighting areas for future investigation.

### The pathophysiology of concussion


Concussion is defined as a biomechanically induced brain injury characterized by the absence of gross anatomic lesions. Early and late clinical symptoms, including impairments of memory and attention, headache, and alteration of mental status, are the result of neuronal dysfunction mostly caused by functional rather than structural abnormalities. The mechanical insult initiates a complex cascade of metabolic events leading to perturbation of delicate neuronal homeostatic balances. Starting from neurotoxicity, energetic metabolism disturbance caused by the initial mitochondrial dysfunction seems to be the main biochemical explanation for most postconcussive signs and symptoms. Furthermore, concussed cells enter a peculiar state of vulnerability, and if a second concussion is sustained while they are in this state, they may be irreversibly damaged by the occurrence of swelling. This condition of concussion-induced brain vulnerability is the basic pathophysiologic of the second impact syndrome. N-acetylaspartate, a brain-specific compound representative of neuronal metabolic wellness, is proving a valid surrogate marker of the post-traumatic biochemical damage, and its utility in monitoring the recovery of the aforementioned "functional" disturbance as a concussion marker is emerging, because it is easily detectable through proton magnetic resonance spectroscopy.

### Cerebrovascular pathophysiology following mild traumatic brain injury


Mild traumatic brain injury (mTBI) or sport-induced concussion has recently become prominent concern not only in the athletic setting (i.e. sports venue) but also in the general population. The majority of research to date has aimed at understanding the neurological and neuropsychological outcomes of injury as well as return-to-play guidelines. Remaining relatively unexamined has been the pathophysiological aspect of mTBI. Recent technological advances including transcranial Doppler ultrasound and near infrared spectroscopy have allowed researchers to examine the systemic effects of mTBI from rest to exercise, and during both asymptomatic and symptomatic conditions. In this review, we focus on the current research available from both human
and experimental (animal) studies surrounding the pathophysiology of mTBI. First, the quest for a unified definition of mTBI, its historical development and implications for future research is discussed. Finally, the impact of mTBI on the control and regulation of cerebral blood flow, cerebrovascular reactivity, cerebral oxygenation and neuroautonomic cardiovascular regulation, all of which may be compromised with mTBI, is discussed.

The molecular pathophysiology of concussive brain injury
Concussion or mild traumatic brain injury (mTBI) is a condition that affects hundreds of thousands of patients worldwide. Understanding the pathophysiology of this disorder can help manage its acute and chronic repercussions. Immediately following mTBI, there are several metabolic, hemodynamic, structural, and electric changes that alter normal cerebral function. These alterations can increase the brain's vulnerability to repeat injury and long-term disability. This review evaluates current studies from the bench to the bedside of mTBI. Acute and chronic effects of concussion are measured in both animal and clinical studies. Also, the effect of repeat concussions is analyzed. Concussion-induced pathophysiology with regards to glucose metabolism changes, mitochondrial dysfunction, axonal injury, and structural damage are evaluated. Translational studies such as functional magnetic resonance imaging, magnetic resonance spectroscopy and diffusion tensor imaging prove to be effective clinical tools for both prognostic and treatment parameters. Understanding the neurobiology of concussion will lead to development and validation of physiological biomarkers of this common injury. These biomarkers (eg, laboratory tests, imaging, electrophysiology) will then allow for improved detection, better functional assessment and evidence-based return to play recommendations.

Pathophysiology of Sports-Related Concussion: An Update on Basic Science and Translational Research
Giza, Christopher C.; DiFiori, John P., Sports Health: A Multidisciplinary Approach 01/01/2011, Vol. 3 Issue 1, p46
Abstract: Context: Concussions that occur during participation in athletic events affect millions of individuals each year. Although our understanding of the pathophysiology of concussion has grown considerably in recent years, much remains to be elucidated. This article reviews basic science and relevant translational clinical research regarding several aspects of concussion. Evidence Acquisition: A literature search was conducted using PubMed from 1966 to 2010, with an emphasis on work published within the past 10 years. Additional articles were identified from the bibliography of recent reviews. Results: Basic science and clinical data both indicate that there is a period of increased vulnerability to repeated injury following a concussion and that its duration is variable. Growing evidence indicates that postinjury activity is likely to affect recovery from brain injury. Data suggest that long-term sequelae may result from prior concussion—particularly, repeated injuries. The unique aspects of cerebral development may account for differences in the effects of concussion in children and adolescents when compared with adults. Conclusions: The available pathophysiological data from basic science and clinical studies have increased the evidence base for concussion management strategies—the approaches to which may differ between young athletes and adults.
Acute hemispheric swelling associated with thin subdural hematomas: pathophysiology of repetitive head injury in sports


The most common head injury in sports is concussion, and repeated concussions occurring within a short period occasionally can be fatal. Acute subdural hematoma is the most common severe head injury and can be associated with severe neurologic disability and death in sports. We investigated severe brain damage resulting from repetitive head injury in sports, and evaluated the pathophysiology of sports-related repetitive injury.

Management of concussion and post-concussion syndrome

Willer B, Leddy JJ, Current Treatment Options In Neurology 2006 Sep; Vol. 8 (5), pp. 415-26

Concussion and mild traumatic brain injury (mTBI) are common clinical problems. However, the literature is not consistent in defining how concussion and mTBI are related. Although most patients with concussion recover within days to weeks, approximately 10% develop persistent signs and symptoms of post-concussion syndrome (PCS). There are no scientifically established treatments for concussion or PCS and thus rest and cognitive rehabilitation are traditionally applied, with limited effectiveness. This article presents a clinical model to suggest that concussion evolves to become mTBI after PCS has developed, representing a more severe form of brain injury. The basic pathophysiology of concussion is presented, followed by a recommended approach to the clinical evaluation of concussion in the emergency department and the physician’s office. We evaluate the limited evidence-based pharmacologic treatment of acute concussion symptoms and PCS symptoms and also discuss return to activity recommendations, with an emphasis on athletes. Lastly, we suggest a promising new direction for helping patients recover from PCS.

Concussion: the history of clinical and pathophysiological concepts and misconceptions.

McCrory PR, Berkovic SF, Neurology 2001 Dec 26; Vol. 57 (12), pp. 2283-9

Concussion is a well-recognized clinical entity; however, its pathophysiologic basis remains a mystery. One unresolved issue is whether concussion is associated with lesser degrees of diffuse structural change seen in severe traumatic brain injury, or is the mechanism entirely caused by reversible functional changes. This issue is clouded not only by the lack of critical data, but also by confusion in terminology, even in contemporary literature. This confusion began in ancient times when no distinction was made between the transient effects of concussion and severe traumatic brain injury. The first clear separate recognition of concussion was made by the Persian physician, Rhazes, in the 10th century. Lanfrancus subsequently expanded this concept as brain “commotion” in the 13th century, although other Renaissance physicians continued to obscure this concept. By the 18th century, a variety of hypotheses for concussion had emerged. The 19th century discovery of petechial hemorrhagic lesions in severe traumatic brain injury led to these being posited as the basis of concussion, and a similar logic was used later to suggest diffuse axonal injury was responsible. The neuropathology and pathophysiology of concussion has important implications in neurology, sports medicine, medicolegal medicine, and in the understanding of consciousness. Fresh approaches to these questions are needed and modern research tools, including functional imaging and experimental studies of ion-channel function, could help elucidate this puzzle that has evolved over the past 3,000 years.

The neurometabolic cascade of concussion

Abstract: To review the underlying pathophysiologic processes of concussive brain injury and relate these neurometabolic changes to clinical sports-related issues such as injury to the developing brain, overuse injury, and repeated concussion. Over 100 articles from both basic science and clinical medical literature selected for relevance to concussive brain injury, postinjury pathophysiology, and recovery of function. The primary elements of the pathophysiologic cascade following concussive brain injury include abrupt neuronal depolarization, release of excitatory neurotransmitters, ionic shifts, changes in glucose metabolism, altered cerebral blood flow, and impaired axonal function. These alterations can be correlated with periods of postconcussion vulnerability and with neurobehavioral abnormalities. While the time course of these changes is well understood in experimental animal models, it is only beginning to be characterized following human concussion. Following concussion, cerebral pathophysiology can be adversely affected for days in animals and weeks in humans. Significant changes in cerebral glucose metabolism can exist even in head-injured patients with normal Glasgow Coma Scores, underscoring the need for indepth clinical assessment in an effort to uncover neurocognitive correlates of altered cerebral physiology. Improved guidelines for clinical management of concussion may be formulated as the functional significance and duration of these postinjury neurometabolic derangements are better delineated.

**Evidence-based review of sport-related concussion: basic science**


The evidence base for sport-related concussive brain injury is reviewed in this paper. In the past, pathophysiological understanding of this common condition has been extrapolated from studies of severe brain trauma. More recent scientific study demonstrates that this approach is unsatisfactory, and the clinical features of concussion represent a predominantly functional brain injury rather than manifest by structural or neuropathological damage. Such understanding of this condition remains incomplete at this stage.