

**Title: Traumatic Brain Injury – Causes and Potential Therapies**

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**Reference: Patterson ZR and Holahan MR. Understanding the neuroinflammatory response following concussion to develop treatment strategies. Front.Cell.Neurosci. 6:58.doi: 10.3389/fncel.2012.00058**

**Clinical Discussion:**

Neuroinflammation is becoming more and more associated in the literature with a host of downstream comorbidities including depression, anxiety, addictive behavior, dementia and others. Concussion and the traumatic brain injury that follows can be devastating to the health and long term quality of life for those affected. In this blog I will discuss this paper as well as the potential therapies we see work in our clinic utilizing a synergistic integrative medical approach to concussion and traumatic brain injury.

The setting of this widespread issue is described in the abstract: “Mild traumatic brain injuries (mTBI) have been associated with long-term cognitive deficits relating to trauma-induced neurodegeneration. These long-term deficits include impaired memory and attention, changes in executive function, emotional instability, and sensorimotor deficits. Furthermore, individuals with concussions show a high co-morbidity with a host of psychiatric illnesses (e.g., depression, anxiety, addiction etc.) and dementia. The neurological damage seen in mTBI patients is the result of the impact forces and mechanical injury, followed by a delayed neuroimmune response that can last hours, days, and even months after the injury. As part of the neuroimmune response, a cascade of pro- and anti-inflammatory cytokines are released and can be detected at the site of injury as well as subcortical, and often contralateral, regions. It has been suggested that the delayed neuroinflammatory response to concussions is more damaging than the initial impact itself.”

The authors of this paper are at a loss for pharmaceutical answers to these issues both due to confounding effects of many standard anti-inflammatory strategies as well as lack of data: “In some cases, treatments that reduce the inflammatory response will also hinder the brain’s intrinsic repair mechanisms. At present, there is no evidence-based pharmacological treatment for concussions in humans.” While in the larger peer-reviewed literature a drug therapy may not be evident many data exist that support integrative options for mTBI. These include some common integrative therapies which have been shown to be helpful in mTBI and TBI and in my clinical experience are effective in such cases. Some of the most effective in my experience will be summarized below.

### **Potential Clinical Interventions to Consider**

#### **Glutathione:**

Animal research into TBI has shown correlation to the pathogenic environment of the CNS “The inflammatory response following mechanical brain injury is characterized by an increase in the cytokine interleukin-1 $\beta$  (IL-1 $\beta$ ) followed by a large elevation in the neurotrophin, nerve growth factor (NGF)” [2] as well as improvement in recovery by augmentation of glutathione in the CNS. [2] While direct data in humans on the effects of glutathione supplementation in TBI and mTBI are lacking the known cytokine triggers of damage as well as pathways involved are largely manipulated by glutathione in the direction of healing. Nerve regeneration has been documented in an intravenous glutathione trial in humans with post-radiation nerve damage. [3] In this study it was shown that the cofactors for glutathione cycling and function, when given with intravenous glutathione, were effective at aiding nerve regeneration which has similar pathogenesis to radiation damage.

If intravenous glutathione is unavailable then liposomal glutathione and oral nutrient cofactor use can be supportive.

#### **Curcumin:**

In this paper they review multiple cytokine triggers for the neuroinflammatory cascade following mTBI. In many papers the ability of curcumin to modulate these cytokines have been elucidated. [4-6] In addition to this data there is human clinical data showing that outcomes in CNS inflammatory depression improved with curcumin administration. [7]

Curcumin is a well-known integrative therapy and in cases of TBI and mTBI is a very appropriate inclusion into a treatment protocol.

#### **Boswellia:**

In many of the same ways as are known about curcumin, boswellia herb can modulate the inflammatory cytokines involved in the pathogenesis of mTBI. [8] As with curcumin boswellia can be considered in any case of mTBI as a potential therapy.

#### **Neurosteroids:**

Neurosteroids are the CNS steroids involved in the anti-inflammatory activity as well as the repair mechanisms of the nervous system. [9, 10] Neurosteroids are also showing promise in the therapy of

TBI. [10, 11] The most studied neurosteroids include Pregnenolone, Progesterone and more recently DHEA. The effects of the neurosteroids are opposed by estrogens in the CNS.

The optimization of DHEA levels and the use of Pregnenolone and Progesterone as therapeutic interventions have shown in our clinical experience to be synergistic in the treatment of TBI and mTBI.

#### **Hyperbaric Oxygen Therapy:**

Hyperbaric Oxygen Therapy (HBOT) has been used for years in TBI and other non-healing injury states. A recent study showed that HBOT can induce neuroplasticity leading to repair of chronically impaired brain functions and improved quality of life in mTBI patients, even at late chronic stage. [12] In our own clinic we have likewise seen synergy with HBOT therapy and the others mentioned above in cases of TBI and mTBI. In a recent clinical trial which is in pre-publication [13] patients with mild to moderate TBI improved in the following areas after 35 treatments: Significant improvements 8/8 ANAM mood, 6/7 ANAM neurocognitive, and 7/10 CNS Vital Signs cognitive measures. Additionally earlier intervention with HBOT, younger patients, military, and increased number of HBOTs correlated with improved outcomes.

#### **Summary:**

While the authors of the Patterson paper do not come to any therapeutic conclusions using pharmaceutical therapies in mTBI an integrative medical approach can offer many well researched potential therapies. In our clinical experience no single therapy equals the synergy of a multifaceted approach. The combination of the therapies mentioned above, as well as many others known in integrative medicine are the best approach for the patient with TBI and mTBI.

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