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Modeling Changes in Cellular Micro-Environment in Mild to Moderate Head Trauma

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Introduction

Mild to moderate traumatic brain injury (TBI) are typically a result of the head being struck or strike by an object or undergo a whiplash motion:

- Mild TBI (mTBI) is defined by the Management of Concussion/mTBI Working Group as Normal imagining; a brief period of loss of consciousness (LOC) less than 30 minutes; post traumatic-amnesia (PTA) less than a day; and with Glasgow Coma Scale (GSC)of 13-15;
- Moderate TBI is classified as LOC more than 30 minutes but less than 24 hours; PTA greater than a day but less than 7; GSC between 9 and 12;

Mild TBI is extremely common. An estimation of 42 million people worldwide suffer from mTBI or concussion every year. A severe TBI is a well-known risk factor for various types of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS) [1]. Recently, large studies have identified mTBI as a risk factor for various symptoms in physical, cognitive and emotional domains with different level of severity from patient to patient [2]. If not treated properly, it could also lead to long-term TBI sequelae.

Populations most susceptible to traumatic brain injury:
· Soldiers · Athletes · Children · Older adults

In this work, we have modeled mTBI to identify the source of fatigue and the relation of sleep issue and fatigue, which one comes first and how. This model may help develop mTBI treatment while there is virtually none at this time.

Methods

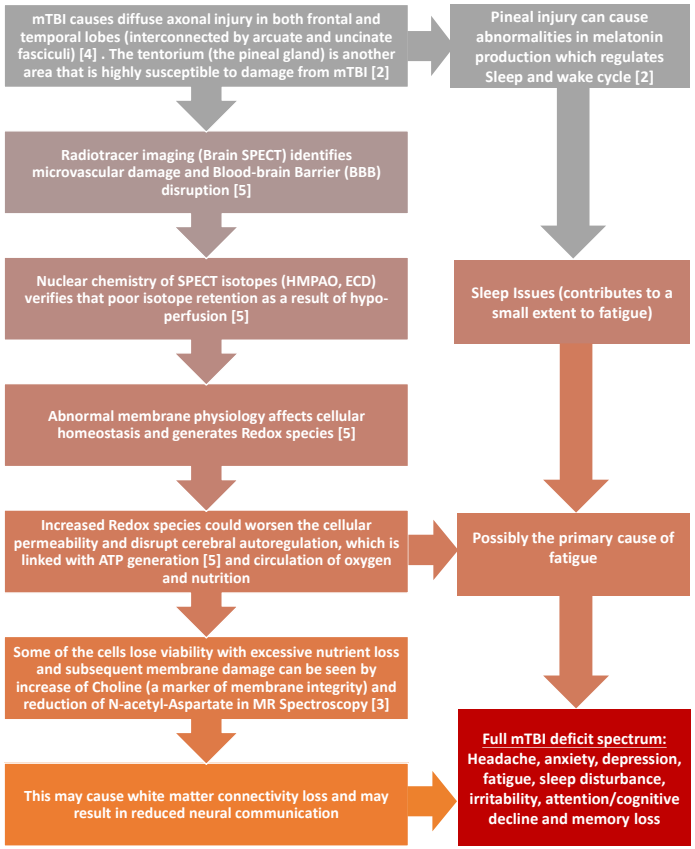
We have evaluated 15 published works containing keywords like: mild traumatic brain injury, sleep disorders/issues, and effects of mTBI and have identified the following 6 articles that have conclusively observed or discussed at least one dominant deficits due to mTBI. The model we proposed is a predictive/explanatory algorithm as a plausible, progressive sequence, often times each stage accelerates the next stage and is shown as a cause effect flow diagram in result.

Result

One may explain mTBI symptoms for 10-20% patients that go through almost all of the full set of sequential events described here. However, most patients often stop at some intermediate stage and are able to repair some of the abnormal symptoms leading to partial or full recovery.

Our model (the flow chart shown below) describes the sequence of events, which we propose could occur after one or repeated mTBI in terms of microscopic cellular and macroscopic tissue effects.

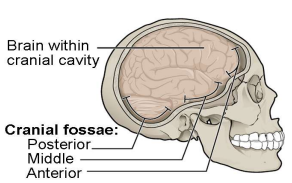
The reasoning behind this model was derived from Bigler's work that various deficits lead progressively as the flow chart model shows when the affected cells or tissues are anatomically connected or proximally located:



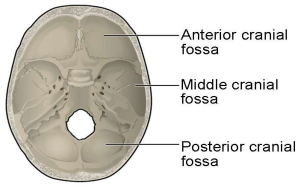
Causal Analysis and Discussion

Despite the fact that much is known about nervous systems and brain structure, the effects of mTBI in the cellular microenvironment of the brain is not fully understood. Often, conventional neuroimaging has failed to detect any changes in mTBI patients. MR spectroscopy, on the other hand, is able to identify neurochemical abnormalities in mTBI [3].

Our model emphasizes following three main effects due to tissue connectivity or functional dependence describe below:
1A) Structural-wise, frontal and temporal lobes are connected and both are vulnerable regions for brain traumatic injury, due to their location in the anterior and cranial fossa of the skull [4]. **1B)** The sliding stress on the frontal and temporal lobes against the fossae can cause microvascular damage, which is identified as the reason for cerebral perfusion abnormalities in frontal and temporal lobes [5]. **2)** The frontal lobe is known to be responsible for high-level cognitive processing and damage to the frontal lobe could cause cognitive symptoms of mTBI. **3A)** Another region that is susceptible to injury is the pineal gland, which is located anterior to the tentorial ridge and subject to pressure effects from CSF. **3B)** The pineal gland controls the homeostasis of sleep and could be the source of sleep-wake disturbances in mTBI patients [2]. We also agree that sleep deprivation could add to other post-concussion symptoms, mainly to fatigue and impair neuro-recovery [6].



Lateral View



Superior View

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