Traumatic brain injury in the shadow of post-traumatic stress disorder.

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Foreword

Since 2004, my work has been dedicated to redefining our understanding of Post-Traumatic Stress Disorder (PTSD) in relation to Traumatic Brain Injury (TBI). Based on the science, I have long maintained that PTSD is not a standalone psychiatric condition but rather a continuum of an untreated or misdiagnosed traumatic brain injury. In recent years, a growing body of research has recognized that nearly all cases of PTSD can be traced back to a predisposing traumatic event. This realization underscores a critical gap in our comprehension of subclinical trauma and the molecular and biochemical shifts it triggers within the brain.

One of the most significant yet overlooked mechanisms in this process is **mechanotransduction**—a phenomenon (Hemphill et al., 2015) where physical forces cause cellular vibrations that release free radicals and biochemical mediators. These, in turn, activate microglia, leading to the release of pro-inflammatory cytokines (Gordon et al., 2025). This cascade of neuroinflammatory events is particularly prevalent in subconcussive brain traumas, where symptoms may not manifest immediately but instead emerge insidiously over time. Chronic neuroinflammation resulting from this altered neurochemistry disrupts the synthesis of neurosteroids and neurotransmitters by damaging the enzymes essential for their production. Additionally, it alters neuroreceptor function, limiting the efficacy of pharmacological interventions, including psychedelics, which fail to achieve their full therapeutic potential in the presence of unresolved neuroinflammatory processes (Gordon et al., 2023).

As you will explore in the pages ahead, PTSD is not an isolated disorder but rather the culmination of a series of neurobiological responses to trauma. Given this perspective, the logical and most effective course of action is to address the underlying neurochemical disruptions that drive these symptoms rather than merely managing the symptoms themselves. By shifting our focus toward treating the root causes—neuroinflammation, oxidative stress, and neurotransmitter imbalances—we can pave the way for more precise and effective interventions that restore neurological function and improve outcomes for those affected by PTSD.

Let's Begin

Post-traumatic stress disorder is a profound and life-altering condition that emerges in the wake of trauma. While it is often associated with psychological distress and emotional upheaval, a growing body of evidence underscores the fundamental role of physical trauma in the development of this disorder. Unlike other psychiatric conditions, PTSD necessitates a precipitating traumatic event, making it unique in its etiology and progression. While psychological stressors can contribute to PTSD, it is physical trauma—direct harm to the body through injury, combat exposure, accidents, or assault—that serves as the primary catalyst for the disorder (Katrinli et al., 2022). Understanding PTSD through the lens of physical trauma not only refines our comprehension of its origins but also enhances approaches to prevention, diagnosis, and treatment (Gordon et al., 2023). √

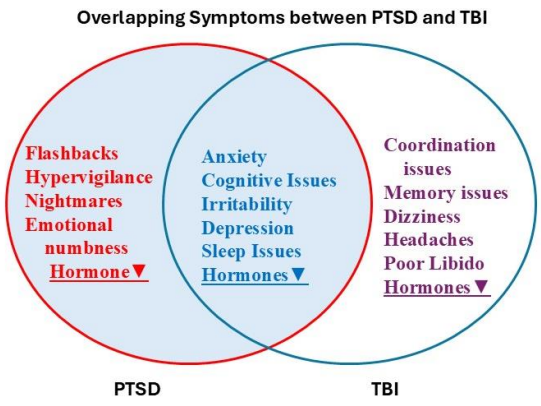
Decades of research have explored the pathways through which physical trauma precipitates PTSD. Studies indicate that the body's physiological response to injury—particularly the activation of the immune system

and inflammatory pathways—plays a pivotal role in the onset and severity of PTSD symptoms. When the body experiences physical trauma, a cascade of biological responses ensues, including the release of stress hormones, activation of immune responses, and changes in neural circuits responsible for fear and memory processing (Michopoulos et al., 2017). These physiological disruptions create an environment conducive to the development of PTSD, suggesting that the disorder is not merely a psychological consequence of trauma but also a condition deeply rooted in the body's biological response to injury both past and present.

The immune system has emerged as a critical player in this dynamic. Research has shown that individuals with PTSD exhibit elevated levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Passos et al., 2015). These markers are commonly associated with physical trauma, indicating that the inflammatory response triggered by injury may contribute directly to the development of PTSD. The body's attempt to heal itself following trauma may, paradoxically, predispose individuals to the chronic symptoms of PTSD, including heightened anxiety, hyperarousal, and cognitive impairments.

One of the most well-documented physiological responses to physical trauma is the activation of the hypothalamic-pituitary-adrenal (HPA) axis. This system regulates the body's response to stress by modulating the release of cortisol, a hormone critical for managing inflammation and immune function. However, in individuals who develop PTSD, this regulatory system becomes dysregulated. Studies have demonstrated that PTSD patients often exhibit lower baseline cortisol levels, which paradoxically leads to an exaggerated inflammatory response (Yehuda et al., 2015). This imbalance further exacerbates symptoms of hypervigilance and emotional dysregulation, and the hallmark features of PTSD.

Beyond systemic inflammation, physical trauma has been shown to induce neuroinflammation, a process in which the brain's immune cells, particularly microglia, become activated in response to injury. Neuroinflammation can lead to neuronal damage and alterations in brain regions implicated in PTSD, such as the amygdala, hippocampus, and prefrontal cortex (Franklin et al., 2018). The amygdala, responsible for processing fear and emotional responses, becomes hyperactive in PTSD patients, resulting in heightened anxiety and exaggerated startle responses. Concurrently, the hippocampus, which plays a crucial role in memory and contextualizing fear, often exhibits reduced volume and impaired function in individuals with PTSD. These neurological changes underscore the profound impact that physical trauma has on the brain's architecture and function, further reinforcing its role as the primary driver of PTSD.



One of the most compelling pieces of evidence linking physical trauma to PTSD is the high incidence of the disorder among individuals who have suffered TBIs. Military veterans, athletes, and accident survivors who experience TBI are at a significantly higher risk of developing PTSD (Stein et al., 2016). The overlap between TBI and PTSD symptoms—such as cognitive deficits, mood disturbances, and heightened stress responses—suggests that the physical damage to the brain serves as a foundational element in PTSD pathology. Studies have shown that even mild TBIs, often referred to as concussions, can trigger inflammatory processes in the brain that persist long after the initial injury (Glatt et al., 2013). This chronic neuroinflammation is believed to contribute to the persistent

symptoms of PTSD, highlighting the need for treatments that primarily address this neurochemical disorder fueled by inflammation.

Brain Region	PTSD	TBI
Amygdala	Hyperactive, leading to heightened fear and emotional responses. (DHT▼)	Can be damaged, affecting emotional regulation and fear processing.
Hippocampus	Reduced volume and impaired function, leading to memory deficits and difficulty contextualizing fear.	Can suffer structural damage, leading to memory impairment and cognitive dysfunction.
Prefrontal Cortex	Dysfunctional regulation of the amygdala, contributing to emotional dysregulation.	Often impaired, affecting decision-making, impulse control, and executive function. (▼ AlloP5)
Hypothalamic-Pituitary-Adrenal (HPA) Axis	Dysregulated, leading to abnormal cortisol levels and increased inflammation.	Can be disrupted, affecting stress response and hormonal regulation. (▼GnRH)
Microglia Activation (Neuroinflammation)	Chronic activation leads to neuronal damage and persistent symptoms.	Neuroinflammation contributes to cognitive and mood disturbances. Loss of hypothalamic-pituitary regulation of LH.
Cortical Structures	Functional impairments in fear processing and emotional regulation.	Physical damage can impair sensory processing and cognition.

From an evolutionary perspective, PTSD can be seen as a maladaptive extension of the body's natural response to danger. In ancestral environments, individuals who survived physical trauma needed heightened vigilance and rapid threat detection to avoid further harm. This survival mechanism, governed by the amygdala and stress response systems, would have been advantageous in dangerous settings. However, in modern society, where immediate physical threats are less frequent, this hyperactive threat response becomes pathological, manifesting as PTSD (Gilpin et al., 2015). The persistence of these heightened responses in the absence of ongoing danger underscores the importance of physical trauma as the primary instigator of the disorder.

Recognizing physical trauma as the principal precipitating factor for PTSD has significant implications for treatment and prevention. Current therapeutic approaches often focus on psychological interventions such as cognitive-behavioral therapy (CBT) and exposure therapy. While these methods may be effective for some individuals, they do not address the underlying biological disruptions caused by physical trauma. Integrating medical treatments that target inflammation, neuroprotection, and hormonal regulation could enhance recovery outcomes for PTSD patients (Hori & Kim, 2019).

Emerging therapies, such as anti-inflammatory medications, neurosteroids, and regenerative treatments, show promise in mitigating the long-term effects of physical trauma on the brain. For instance, studies on progesterone and other neurosteroids suggest they may have protective effects against neuroinflammation and HPA axis dysregulation, potentially reducing PTSD severity (Sumner et al., 2020). Additionally, interventions that promote physical healing, such as hyperbaric oxygen therapy (HBOT) and transcranial magnetic stimulation (TMS), are being explored as adjunctive treatments for PTSD.

Prevention strategies should also prioritize the early identification and treatment of physical trauma. Immediate medical intervention following injury, including the use of anti-inflammatory agents and neuroprotective compounds, may reduce the risk of PTSD development (Boscarino, 2004). Furthermore, monitoring individuals with a history of physical trauma—such as military personnel, first responders, and survivors of severe accidents—for early signs of PTSD could facilitate timely and effective interventions.

The prevailing narrative surrounding PTSD often emphasizes psychological trauma, yet the evidence strongly supports physical trauma as the primary driver of the disorder. From systemic inflammation and neuroimmune activation to hormonal imbalances and structural brain changes, the physiological consequences of physical trauma create the conditions necessary for PTSD to take hold. By reframing our

understanding of PTSD through the lens of physical trauma, we can develop more comprehensive and effective treatment strategies that address both the mind and the body.

The Millennium's Approach to Assessment and Treatment

Since 2004, the Millennium has been running a 28-point biomarker panel consisting of key neurosteroids, neuroactive steroids, and biomarkers that reflect and influence hormonal homeostasis. The results of this panel are fed into an AI software application (MOA) that applies a multi-phasic, cross-correlational analysis of all markers looking for patterns suggestive of trauma (inflammation) induced biochemical alterations. The AI software can also identify deficiency states and the influence of certain medications on hormone systems such as an increase in Growth Hormone (GH) from bupropion, L-dopa, amantadine, and Mucuna pruriens. An elevation in GH can influence the levels of prolactin, luteinizing hormone, testosterone, and the thyroid T4 to T3 ratio.

Once the results are entered into the MOA, a twelve-page report is generated which provides diagnoses, suggests additional blood testing, and may suggest performing a specific neuroradiologic study to rule out a suspicious brain tumor (pituitary adenoma). Most importantly, and based upon these results, a predictive treatment option is offered which includes hormones and nutraceutical products to address deficiencies and to curtail neuroinflammation. Treatment is driven by the results of these laboratory tests.

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The Millennium Health Centers, Inc.

The Millennium Health Centers, Inc. (MHC) is a pioneering force in mental and cognitive health, dedicated to addressing the hidden causes of neuroinflammation and neuropsychiatric disorders. With over 30 years of expertise, MHC challenges conventional symptom-based treatments, prioritizing root-cause analysis and innovative, science-backed interventions to restore optimal brain function and overall well-being. Since 2009, MHC has focused on the needs of our veterans providing a personalized approach to recovery.

MHC utilizes precision medicine to evaluate and correct biochemical imbalances caused by neuroinflammation. Research shows that inflammation-related disruptions in hormones like pregnenolone, DHEA, testosterone, and thyroid hormones significantly impact mental and cognitive function. Our goal: restore balance and enhance resilience naturally.

Conventional treatments rely on pharmaceuticals to mask symptoms, often leading to polypharmacy without resolving the root cause. Objective testing such as neurosteroids (hormones) and markers for inflammation are frequently lacking and many individuals—especially veterans and first responders—are placed on multiple medications, experiencing minimal relief and deteriorating quality of life.

Rather than relying on lifelong medication or chronic hormonal replacement, MHC prioritizes restoring the body's *natural* hormone production to optimal levels by correcting the known causative factors impeding production. Many times, this can be achieved due to the ability of the 28-point biomarker panel being analyzed and interpreted by an AI software application (MOA).

Additional information:

- Learn more: TBIHelpNow.org
- **Enroll today**: tbimedlegal.com
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