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Military Concussion – In Depth Review

According to the Defense and Veterans Brain Injury Center (DVBIC), between 2000 and late 2019 approximately 414,000 US service members have sustained a traumatic brain injury (TBI), with a majority classified as mild.[1] Between January 1 and September 30 2020 the Department of Defense (DoD) reported 12,310 TBIs, with 10,546 being classified as mild.[2] Concussions are prevalent in each branch of the military, in both stateside and deployment settings. Statistics are becoming more accurate with improved diagnostics and increased vigilance.[2] Data regarding TBI numbers is obtained from several sources, to include the Armed Forces Surveillance Branch and the Theater Medical Data Store.[2]

It is essential for physical therapists working with individuals who have sustained a TBI to recognize the immense degree of heterogeneity which exists within the military mild traumatic brain injury (mTBI) and concussion subcategory.[3] There is growing evidence of associations between mTBIs and chronic symptoms and disability, and a "watchful waiting" approach is no longer appropriate.[4] The substantial incidence of mTBI in the military and the potential for persistent and long term debilitating effects has facilitated rapidly evolving standards of care and earlier intervention.[4] Research is continuing to indicate mTBIs are not necessarily a "mild" form of TBI, but instead a "separate disease/injury state."[5] Military providers need to be especially cognizant of the potential for service members to be reluctant to report symptoms due to not wanting to be detached from their unit or unable to participate in training exercises.[6]

Criteria for classification of a mild TBI according to the Va/DoD Clinical Practice Guideline:[7]

Criteria	Mild
Structural imaging	Normal
Loss of consciousness	0-30 min
Alteration of consciousness/mental status (AOC) (must be related to trauma to the head)	Up to 24 hours
Posttraumatic amnesia (PTA)	0-1 day
Glasgow Coma Score (GCS) (best available score in first 24 hours) – *although memorandum released by DoD recommending against using GCS score to diagnose TBI*	13-15

Pathology and Pathophysiology unique to military personnel:

- **Pathology** – service members are at an increased risk for a mTBI due to the inherent nature of their profession, to include training exercises and exposure to combat zones.
    - Direct blow to the head (contact forces)[8]
        - Blunt trauma which may or may not be associated with a blast[8]
            - Ex: hitting head against interior of vehicle[8]
    - Blow elsewhere on body with forces subsequently transmitted to brain through inertial forces[8]
    - Blast trauma where the force of the pressure wave causes brain damage[8]

- Common causes of concussion for service members: physical training practices (combatives, boxing competitions, ropes courses), falls, motor-vehicle accidents and roll-over accidents, falls, jumps[6,8]

- **Pathophysiology**
  - Significant challenge in studying the neurotrauma in military related mTBI verse sport related situations as there are more "stereotyped features" of brain injury in sport settings, while military concussion is more heterogeneous and random in nature.[8] The primary injury may involve neurons, neuroglia, and vascular structures regardless of whether the injury is blast or non-blast related.[7]
  - Pathophysiology predominantly associated with rapid acceleration and deceleration of the brain by mechanical force, followed by a systemic and neuroinflammatory response:
    - Acute head or neck trauma causes meningeal inflammation and traction on pain sensitive structures.[9]
      - Deformation of meningeal blood vessels and cranial nerves[9]
      - Some individuals may have macrostructural intracranial injury visible on CT[4]
      - Most common are cerebral contusions (frontal-temporal regions), subdural hematomas, and subarachnoid hemorrhages[4]
    - Shearing forces from the acceleration-deceleration or rotation forces facilitates changes to the microscopic structure of brain and disrupts axonal integrity[10]
      - Axons stretched causing "cytoskeletal deformation" that interrupts axonal transport[3]
      - This in turn leads to accumulation of transported materials in axonal swellings or varicosities[3]
      - Microstructural changes in the white matter and alterations in fiber tract integrity have been detectable with diffusion tensor imaging (DTI).[8]
      - Pathological changes have also been found in the internal capsule, midbrain, and pons.[9]
      - If neuronal stress is large enough it will elicit a secondary biochemical response, leading to membrane depolarization and deregulated neurotransmitter release.[11] The massive release of glutamate promotes Ca2+ release intracellularly and K+ ion efflux.[11]
    - Metabolic and hemodynamic derangement by mTBI, such as cerebral edema and increased intracranial pressure acutely, and has implications on oxidative stress, cytotoxic injury, and excitatory neurotoxicity in response to the release of pro-inflammatory cytokines.[9]
    - Possibility of hormonal dysregulation from trauma-induced hypothalamic malfunction.[9]
  - Blast injury → unique injurious situation in that there is "rapid transmission of an acoustic wave through the brain tissue and accompanying blast winds."[8]
    - This can result in large intraparenchymal and subarachnoid hemorrhages and "pseudoaneurysm formation and development of vasospasm."[8]

- Neuropathological changes associated with blast injury.[8]
    - Subcortical frontal white matter shows loss of myelinated
- Associated with greater multisystem polytrauma and complicated by factors "known to exacerbate secondary injury" – i.e. hypotension, hypoxia, hypothermia.[7]

Imaging:

- CT not sensitive to structure abnormalities[4]
- MRI using diffusion tensor imaging (DTI) has detected microstructural white matter pathology and axonal injuries.[4-5]
    - Findings have supported idea of shear-induced axonal damage instead of localized trauma to brain

Genetic and Epigenetic Factors

Variability has been found in both susceptibility to and recovery from concussion, in part dependent on intrinsic factors, like an individual's genetic information.[11] There is growing research interest in identifying genetic biomarkers indicative of certain risk factors which make someone more vulnerable to concussion, as well as biomarkers predictive of clinical recovery or potential for delayed recovery to guide post injury management and return to activity.[11] A single nucleotide polymorphism, or SNP, is the most common form of genetic variation and may profoundly affect how the body reacts and responds to stress as it can alter functions or levels of protein product.[11-12] Terrell et al evaluated the association between genetic polymorphisms in APOE, exon 6 of MAPT/tau, IL-6, and IL-6 R, and sport-related concussion in a cohort of college athletes.[12] The researchers found a significant association between the IL-6R CC genotype and increased concussion risk, and the APOE4 allele was associated with reduced concussion risk which was surprising based on other studies.[12] The authors hypothesized the IL-6R CC genotype to be related to elevated levels of IL-6R levels, and possibly an increased initial severity of inflammatory response, "followed by a reduction in cognition."[12] They also note that increased brain IL-6 expression has been associated with neuropathological changes in various CNS diseases and it is likely multiple genes influence recovery and susceptibility.[12] Epigenetic aspects of mTBI are just beginning to gain traction, with most of the epigenetic mechanisms studied with animal models.[3] Following contusion TBI in rats, global hypomethylation was found early after the injury in regions of widespread necrosis and slightly delayed in more peripheral areas.[3] While DNA hypomethylation has also been found following controlled cortical impact TBI in rats, DNA hypermethylation has been found in the IGF-1 gene locus in the hippocampus.[3] In animal models exposed to blast overpressure, cell specific DNA methylation perturbations were found in neurons and glia, and were sustained months following the injury, indicating more long term persistence.[3] Research is being devoted to study the cause of DNA methylation changes and the associated enzymes responsible for triggering them, as well as how histone deacetylation following TBI may be adaptive or maladaptive.[3] Finally, the influence of CNS injury on expression levels of different microRNAs (miRNAs), that play a role in regulating various cellular functions in the brain, is being extensively studied.[3] Additionally, there is expanding research in epigenetic marks related to susceptibility for an individual who has had a concussion to suffer from a persistent symptoms, otherwise known as post-concussive syndrome (PCS).[11] It has been suggested that genetic variants of genes coding for components of NMDA receptors could be associated with concussion incidence or recovery.[11]

Personal and Environmental Factors to consider while history gathering

- Sex – Females may take longer to recover[4,10]
- History of concussive injuries may influence recovery[10-11]
- Age[10]
- Relevant co-occurring and pre-existing conditions[7]
    - Pre-injury mental health problems
    - Post-traumatic stress disorder (PTSD)[9]
        - Potential for more pronounced cognitive impairment and poorer performance on measures of attention, speed of information processing, and executive function[13]
    - Pre-existing migraine history[9]
- Sequence of events surrounding the injury[4]
    - Loss of consciousness
    - Posttraumatic amnesia
    - Confusion
    - Alcohol or substance intoxication
- Risk factors for cognitive dysfunction following concussion[13]
    - History of previous traumatic brain injury
    - History of previous neurological or psychiatric problems
    - Confounding effects of other health-related issues
    - Presence of life stressors at time of injury
    - Higher levels of symptom reporting associated with mood symptoms

Subjective Assessments which may be of benefit[6-7]

- Military Acute Concussion Evaluation 2 (MACE2)
- Defense and Veterans Pain Rating Scale (DVPRS) and symptoms report
- Military Concussion Readiness Inventory for Dizziness and Balance (MCRI-DB)
    - More appropriate than Dizziness Handicap Inventory (DHI), 36 Item Short Form Health Survey (SF-36), and Activities-specific Balance Confidence (ABC) scale for the military population
- Neurobehavioral Symptom Inventory (NSI)
- Acute Stress Reaction Questionnaire
- Borg Rating of Perceived Exertion (RPE) scale during exercise testing
- Generalized Anxiety Disorder-7
- Patient Health Questionnaire-9

Physical Examination should include the following:[7,14-16]

- Vital signs
- Mental status
    - Dual task performance
    - Attention
- Neurological Examination
- Cranial Nerve Assessment
- Manual muscle test/reflexes
- Head and cervicothoracic examination

  - Temporomandibular joint function
  - Cervical spine examination
- Postural control and motor control
  - Computerized sensory organization test
  - Functional Gait Assessment
  - Assessment of Military Multitasking Performance (AMMP), to include the Patrol-Exertion Multitask (PEMT), a more ecologically valid return to duty metric[16]
- Vestibular system evaluation[6-7]
  - Head impulse testing
  - Dynamic visual acuity
  - Dix-Hallpike
- Ocular/ophthalmologic examination
- It is essential for military personal to be assessed with complex tasks that challenge various systems (cognitive, motor, visual, vestibular) to make appropriate return to duty decisions.[16]

Systems Review: It is essential to recognize the pathophysiology of systemic manifestations following the concussive event are multifactorial and many have implications on system functioning not readily apparent to an external observer.[17] The vast symptoms associated with mTBI are indicative of the complex pathophysiological processes of cellular injury related to the brain's inflammatory response to the injury. It should be noted that most patients with a mTBI do recover within less than three months of injury (majority within seven to ten days) with rest and progressive return to activity, but a small subset may experience longer lasting systems.[18] More active management is required for patients that experience greater and more severe symptoms with longer delays in their ability to resume usual activities. Silverberg et al recommends for individuals with persistent symptoms (more than 4-6 weeks) to be referred to individual medical specialists or a specialized multidisciplinary mTBI clinics if they are not responding to treatment in the primary care setting.[4] Automated Neuropsychological Assessment Metrics (ANAM) testing should be considered as part of the comprehensive evaluation and return to duty assessment.[19] Post-concussion syndrome is characterized by a constellation of symptoms, such as post-traumatic headache, dizziness, irritability, fatigue, cognitive deficits, and blurry vision.[9] Currently increasing research is being devoted to studying the use of graded aerobic exercise to improve patient outcomes and add to management options.[20] The DoD provides stages of progressive return to activity following an acute concussion, with the objective of stage one described as "symptom resolution" and stage six "return to pre-injury activity".[15]

System	How system is affected by mTBI	Associated Impairments
Musculoskeletal – Cervicogenic Injury	Flexion-extension, rotation, cervical whiplash injury during event causing cervicalgia, abnormal muscle activity in the deep upper cervical spine, and/or cervicogenic headache.[15]	Disequilibrium[15] Lightheadedness[15] Neck pain[15] Symptoms coincide with movement of cervical spine[15]
Central Nervous System	White matter and alterations in fiber tract integrity[8]	Fatigue[13] Disturbances in attention and concentration[13] Decreased processing speed

	Dysfunctions in tracks of ascending reticular activation system[9] Changes in internal capsule, midbrain, pons[9]	Migraine and Post-traumatic headache[9]
Vestibular	Peripheral or central vestibular structures[21] • disruption of vestibulo-ocular system • impact and forces from trauma may displace the otoconia from the utricle and allow for them to migrate to other parts of the ear • shock wave from blast exposure may induce damage to inner and middle ear	Benign paroxysmal positional vertigo (BPPV)[10,22] – vertigo and nystagmus pattern VOR impairment[10,22] – visual blurring, dizziness poor visual focus, oscillopsia Visual motor sensitivity[10,22] – disorientation, dizziness, postural instability Impaired postural control[10,22] Cervicogenic dizziness[10,22] Exercise-induced dizziness[10,22] Vertigo[10,22] Blurred or unstable vision[10,22] Nausea[10,22]
Visual	Disconnect between central and spatial/peripheral vision from the injury and associated miscommunication between visual, vestibular, and proprioceptive systems.[10]	Diplopia[10] Accommodation or convergence disorder[10] Visual tracking deficits[10] Photophobia (light sensitivity)[10] Eye fatigue Impaired visual-spatial orientation[7,10]
Auditory	Greater incidence in those who sustain a blast-related mTBI due to the impact of the shock wave[7]	Altered acuity and sensitivity to noise (true abnormalities in central auditory acute/processing are rare for mTBI)[7]
Autonomic	Inertial injury and subsequent shearing forces across the brainstem leading to diffuse axonal injury to this area of the CNS associated with controlling autonomic nervous system function and cerebrovascular	Light-headedness Fatigue Exercise-induced headache Impaired cardiopulmonary response[23]

	autoregulation[23] – confirmed by diffusion tensor imaging[24] Disrupted neural connectivity contributing to ANS dysfunction[25] ANS dysfunction reduces heart rate variability[26]	-reduced heart rate variability (HRV) at rest and during exercise[18] -blunted increases in blood pressure[18]
Endocrine	Result of direct trauma or biochemical response interfering with production and regulation of inter-related hormonal processes.[18] Most vulnerable endocrine structure is the anterior pituitary gland.[18] (Higher prevalence of pituitary dysfunction following moderate-severe TBI.[26]) May be involvement of the hypothalamic-pituitary-adrenal axis.[26] More frequently affected pathways include growth hormone and gonadotropin[18] Secondary hypothyroidism and adrenal insufficiency make occur (much less frequent)[18]	Disturbances in sleep wake cycle (hypersomnia or hyposomnia) • insomnia is the most common sleep disturbance in the mTBI population.[28] Depression Fatigue[28] Weight gain[28] Low blood pressure[28] Low libido[28] Loss of muscle mass[28] Amenorrhea[28]

Activity Limitation and Participation Restrictions[6-7,10]

• Abrupt movement • Mental exertion • Riding in military vehicle/enclosed vehicles • Standing in formation • Uneven surfaces • Walking in crowds • Walking in straight line • Adrenaline rushes, stress • Bending/reaching beyond neutral • Combat load/wearing gear • Drill and ceremony • Driving • Picking things off ground • Reading print and electronic media • Maintaining equipment/vehicles • Problems with visual scanning	• Obstacle course • Ruck marching • Sprinting with quick stops • Dismounting vehicles in gear • Driving during the night • Getting up (bed/chair/toilet) • Getting in/out of bed • Navigate on rough terrain • Walking/hiking narrow paths • Climbing • Sports • Carrying heavy objects • Clearing houses • Shooting a weapon • Facing backward while flying • Sexual intercourse due to libido

Environmental Factors to consider following injury

- Hearing problems warranting the need to control environmental noise and possibly utilize white noise generators.[7] Environmental conditions with higher sensory stimulation should gradually be introduced.[7]
- Providers should be mindful of the examination environment, and make appropriate accommodations such as diming lights and speaking softer.
- There is the potential for individuals to have problems with confined areas (rooms/vehicles), excessive light, heat, staring at a TV/computer, altitude/elevation, loud noises, and changes in temperature.[6]

A comprehensive examination is essential to identifying acute and potentially enduring alterations in cognitive, motor, autonomic, and vestibular functions, especially those impairments which may not be readily apparent. Best practice for treating service members who have sustained a concussion is to prescribe a progressive return to duty with activities increasingly resumed over time in the absence of aggravating symptoms.[29]

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