Repetitive Head Injury Syndrome

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Background

Primary head injury can be catastrophic, but the effects of repetitive head injuries must also be considered. Second-impact syndrome (SIS), a term coined in 1984, describes the situation in which an individual sustains a second head injury before the symptoms from the first head injury have resolved.

The second injury may occur from days to weeks following the first. Loss of consciousness is not a requirement of this condition, the impact may seem relatively mild, and the athlete may appear only dazed initially. However, this second impact causes cerebral edema and herniation, leading to collapse and death within minutes. Only 17 cases of confirmed SIS have been reported in the medical literature. Thus, the true risk and pathophysiology of SIS has not been clearly established.

Importantly, even if the effects of the initial brain injury have already resolved (6-18 mo post injury), the effect of multiple concussions over time remains significant and can result in long-term neurologic and functional deficits. These multiple brain insults can still be termed repetitive head injury syndrome, but they do not fit the classification of SIS. True SIS would most likely have a devastating outcome.

A study of American high school and college football players demonstrated 94 catastrophic head injuries (significant intracranial bleeding or edema) over a 13-year period. Of these, only 2 occurred at the college level. Seventy-one percent of high school players suffering such injuries had a previous concussion in the same season, with 39% playing with residual symptoms. On the other hand, results from a study of concussion by the National Football League demonstrated no cases of SIS or catastrophic head injury in players returning to play in the same game after resolution of symptoms.

The outcome of multiple minor head injuries over a prolonged period has not been well studied and is not well understood. The preponderance of data assessing the impact of repetitive head injuries on short- and long-term neurologic (cognitive) performance has been focused on the sports of boxing and American football.

Numerous studies of professional boxers have shown that repeated brain injury can lead to chronic encephalopathy, termed dementia pugilistica. Likewise, the autopsies of 2 former professional football players with a history multiple concussions demonstrated changes that were consistent with chronic encephalopathy. Another investigation of retired professional football players showed a 3-fold increase of depression in players with a history of 3 or more concussions. Older studies of American and Australian rules football showed no effect from repetitive mild head injuries. However, more recent studies of collegiate football players showed an association between multiple concussions and reduced cognitive performance, prolonged recovery, and the increased likelihood of subsequent concussions.
Evidence has also been gleaned from other sports that involve head impact. Nonrandomized studies of soccer players who have had multiple minor concussions have demonstrated that these individuals performed worse on neuropsychologic tests compared with a control group.\[^{16, 17, 18, 19}\]

Neuropsychologic testing is the standard for monitoring cognitive recovery after concussion. However, 2 studies suggest that abnormalities in visual motor and motor cortex function persist after neuropsychologic testing has normalized.\[^{8, 20}\] Slower recovery in patients with a second concussion was also seen.

Basic science research is also ongoing. Experiments in concussed rats demonstrated prolonged abnormalities in metabolic markers of brain activity when a second impact was administered at 3 days\[^{21, 22}\] This implies there may be a metabolic window of vulnerability to a second impact that leads to chronic or prolonged symptoms. Clinically useful biomarkers for brain injury are also being investigated.

**Update on chronic traumatic encephalopathy**

The effects of single or multiple TBIs in later-life are poorly understood, particularly in mild TBI (mTBI). Recent studies suggest that even mTBI can lead to an increased risk of later-life cognitive impairment and neurodegenerative disease, especially when repeated injuries are involved.\[^{23, 24, 25}\] TBIs of mixed severity have been associated with an elevated incidence of Alzheimer disease (AD) and other dementias\[^{26, 27, 28}\] and a reduced age of onset for AD,\[^{29}\] although not in all studies.\[^{30}\]

It has long been suspected that repeated concussions can result in dementialike symptoms many years after injury, a condition labeled chronic traumatic encephalopathy (CTE). The brain structures damaged in CTE are critical for memory and executive function.\[^{31, 32}\]

CTE has been studied in boxing, wherein retired boxers developed dementia at a higher rate and a younger age compared with the general population.\[^{33}\] More recently, brain autopsies of athletes in various sports with confirmed CTE have demonstrated tau-immunoreactive neurofibrillary tangles and neuropil threads,\[^{25, 34}\] suggesting that pathological processes similar to AD may be involved.

A critical gap in the literature exists with respect to later-life neuropsychological functioning after TBI. In a study of individuals with TBI of varying initial severity, researchers found later-life cognitive impairments when compared with a control group in the areas of episodic memory, short-term memory, visuospatial processing, object naming, and semantic processing.\[^{35}\]

Regarding CTE specifically, neuropsychological deficits have been observed but appropriate norms do exist.\[^{36}\]

A meta-analysis found no cognitive effects in 289 amateur boxers;\[^{37}\] however, a large survey study suggested that multiple concussions increase the risk of later-life cognitive dysfunction. Recently, the diagnosis of mild cognitive impairment (MCI, also known as insipient dementia) and self-reported memory problems were more common among football players who reported...
3 or more concussions than those who reported none.\cite{23, 24} Although several cross-sectional studies in sports injury populations have been performed later in life, the long-term effects of TBI in nonsports populations (military, civilian) remain poorly defined.

The possibility of a link between mTBI and CTE or early dementia has widespread implications for military service members and veterans. TBI is an important source of morbidity in the ongoing global war on terrorism (GWOT).\cite{38} TBI has been called the "signature injury" of Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), and Operation New Dawn (OND), affecting up to 20% of all service members deployed in theatre. More than 233,000 TBIs have been officially reported in OIF/OEF/OND between 2000 and 2012 (www.dvbic.org/tbi-numbers.aspx), nearly 80% of which are mild.\cite{39} Explosive munitions in the form of improvised explosive devices (IEDs) have caused the overwhelming majority of these identified cases. The prevalence is likely higher than the above-reported numbers, given the frequency of blast exposure in the GWOT and the fact that mTBI may go unrecognized during and even after deployment.

Missed or delayed diagnosis of mTBI is attributed to the subtlety of symptoms, the overlap of clinical signs and the common effects of heightened arousal and activity in times of combat, a lack of knowledge as to the specifics of diagnosis and detection, greater attention paid to more visible concomitant injuries, and a reduced subjective awareness related to cognitive deficits in the acute period on behalf of the injured service member.\cite{40}

At present, a definitive diagnosis of CTE is made on postmortem examination, using a battery of immunohistochemical markers to define pathognomonic histopathologic features of this disease process, such as tau-immunoreactive neurofibrillary tangles and neuropil threads. There are no clear in vivo diagnostic tools to diagnose CTE. Identification of such a tool or set of tools would provide key data to clinicians caring for this patient population, aid in conducting epidemiological studies to explore the natural history of CTE, and provide objective diagnostic endpoints to support clinical trials to explore therapies for this disease process. Much more attention in recent years has been put towards the early detection of dementia than that of CTE.

In recent years, significant effort has been devoted to the creation of imaging agents that selectively accumulate at sites of interest and emit a signal that can be detected by either positron emission tomography (PET) or single-photon emission computed tomography (SPECT). In contrast to CT and MRI sequences, PET and SPECT have the significant advantage of providing information on changes occurring at the cellular or molecular level. To date, a number of targeted imaging agents have been cataloged at the NIH MICAD Web site: http://www.ncbi.nlm.nih.gov/books/bookres.fcgi/micad/home.html.

In studies of aging, sensory and motor changes have been observed that precede dementia in the domains of olfaction, eye movement, and balance. Olfactory impairment has been identified as a preclinical marker of AD.\cite{41} Olfactory function is also reduced after brain injury.\cite{42, 43}
Researchers have recently demonstrated that early neuromotor impairments are predictive of late global outcome after TBI. [44] Using video-oculography, saccadic eye movement abnormalities have been described in patients with cortical neurodegeneration (AD) and/or nigrostriatal neurodegeneration (Parkinson disease). [45] Furthermore, eye movement abnormalities have been identified in adults with postconcussive syndrome. [46] Research has also demonstrated the utility of a mobile video-oculography device. [47, 48]

Finally, balance impairments (as measured by computerized posturography (CPT) are more common in dementias of all types compared with controls [49] and have been demonstrated acutely after mild TBI. [50] CPT score is predictive of recurrent falls in persons with balance and vestibular disorders. [51]

Tau proteins (collectively termed "total-tau") are a logical indicator of CTE and, more broadly, TBI-onset neurodegeneration. Total-tau in cerebrospinal fluid (CSF) is one of the most predictive biomarkers for clinical use in neurodegenerative disorders associated with cognitive impairment. [52] While serum total-tau has been less predictive than CSF for age-onset neurodegenerative disease (eg, AD), it has been demonstrated to be discriminative in other pathologic causes of brain dysfunction, including higher-risk mTBI patients. [53]

Given the unique pathology associated with CTE and tau accumulation more broadly and around blood vessels, it is entirely plausible that long-term neurodegeneration following trauma may selectively present elevated serum-tau levels. It is further postulated that long-term serum-tau levels in posttraumatic subjects will be less age-dependent than CSF-tau levels in age-onset neurodegeneration. The authors’ contention is entirely consistent with the known pathobiology of CTE, specifically the excessive tau accumulations seen across broad cortical areas with a focus around blood vessels in regions of geometric inflection that are most stressed by the deformation forces of brain trauma.

CTE has also been characterized by widespread TDP-43 proteinopathy. [54] TDP-43 is involved in regulating translation in mitochondrial RNA in the brain. It has been associated with the physiological response to traumatic axotomy. [55] Blood levels of TDP-43 are elevated in association with a variety of neurodegenerative conditions, to include frontotemporal lobar degenerations, amyotrophic lateral sclerosis (ALS), and AD. [56, 57] However, no publication to date has examined it as a biofluid marker for CTE. As in the case of tau, TDP-43 fibrillaries accumulate at anatomical points of geometric inflection in the brains of CTE subjects. Given that trauma focuses deformation forces in these areas, it is highly plausible that TDP-43 accumulation is in contact with the compromised microvasculature and, as such, would be present in the blood of trauma patients with latent CTE.

Beta-amyloid (Ab) peptides are yet other biomarkers with diagnostic and prognostic utility for a broad number of neurodegenerative disorders. [52] Ab plaques are common immediately after TBI, [58] and Ab continues to accumulate in traumatized axons that survive. [59] Recently, it has been reported that Ab plaques are diffusely yet widely present throughout the brains of moderate-to-severe TBI subjects at 1 year or longer following injury. [58] Plaques were also found to be predominantly in a fibrillary form that resembled AD pathology more than acute TBI. Importantly, diffuse, widespread fibrillary Ab accumulation resembles CTE pathology. [60] Until
recently, CSF has been the only biofluid found to provide reliable Ab measures. However, the latest blood Ab assays are providing predictive and prognostic performance in MCI and AD that is considered particularly useful for longitudinal monitoring and so it holds relevance to the present application.\cite{61}

While blood assays are most often developed for disease biomarkers, urine provides certain distinct advantages. Precedence exists in the form of a urine assay for neural thread protein (NTP), which is already available as a clinical test for neurodegenerative disorders.\cite{62} Recently NTP has shown particular promise for the early prediction of AD.\cite{63} Importantly, NTP is related to tau pathobiology in connection with neurodegeneration,\cite{62} and is thus likely to correlate with other tauopathies such as CTE. In addition to NTP, urine may also provide ready access for Ab measures. Complicating blood Ab assays is the interaction with predominant protein. However, normal renal filtration removes this confound, allowing smaller metabolites, possibly Ab peptides, to be detected more easily. The authors further suspect that smaller breakdown products of tau protein may be accessible in urine for the same reasons, which are readily detected by total-tau antibody.\cite{64}

Possession of the APoE-ε4 allele is a risk factor for dementia.\cite{33} Carriers may have altered brain activity, even at a young age.\cite{65} Long-term, but not short-term, effects of TBI may be influenced by APOE. APOE was not associated with poorer neuropsychological performance 1 month after mild or moderate TBI.\cite{66} However, TBI was found to increase AD risk of APOE 10-fold\cite{67} and cognitive decline after 30 years was greater in TBI patients with the APoE-ε4 allele compared with those without.\cite{68} Environmental factors, in particular multiple concussions, may influence the effects of APOE. Boxers with the APoE-ε4 allele who had participated in many bouts were more likely to have CTE, while the allele was not a risk factor in boxers who had only experienced a few fights.\cite{58}

Certainly, more research is needed to better understand the chronic and catastrophic effects of repetitive head injuries.\textbf{Epidemiology}

The National Center for Catastrophic Sports Injury Research in Chapel Hill, NC, reported 35 cases of SIS among American football players from 1980-1993. Seventeen were confirmed by necropsy, surgery, or magnetic resonance imaging (MRI) findings. Eighteen were probable cases of SIS, despite inconclusive necropsy findings.

The number of reported SIS cases increased from 1992-1998, but this increase is thought to be due to more frequent recognition and reporting. Some clinicians believe that SIS is overreported. Boden et al reported an average of 7.08 catastrophic head injuries per year in high school football, compared with 0.15 for college football from 1989-2002.\cite{1} The incidence was 0.67/100,000 for high school players and 0.21/100,000 for college players. Thirty-nine percent of the affected athletes reported playing with residual symptoms.\cite{1} There were 8 fatalities, of which 1 individual had cerebral edema as the only radiographic finding. It was unclear as to whether a second impact occurred in this case.

With the advent and improvement of the helmet in American football and with the introduction of new rules that make spearing illegal, the incidence of head-injury fatalities has decreased
from 2.64 cases per 100,000 persons in 1968 to 0.20 cases per 100,000 persons since 1977. The US Centers for Disease Control and Prevention estimates a 20% rate of concussion from football brain injuries (predominantly high-school and college level), which equates to an estimated 300,000 concussions per year.

Collins et al showed that 20% of the college football players they studied had 2 or more concussions during their career. [7] Furthermore, a study by Daniel et al found that the symptoms of an estimated 60,000 football players who suffer concussion may persist for 4 or more months in up to 24% of these individuals. [20]


Schulz et al reported on a prospective cohort study of North Carolina high-school athletes followed from 1996–1999. [69] Subjects were clustered by school and sport, and the sample included 15,802 athletes, with 1–8 seasons of follow-up per athlete. Concussion rates ranged from 9.36 concussions per 100,000 athlete-exposures in cheerleading to 33.09 concussions per 100,000 athlete-exposures in football, where "athlete-exposure" is 1 athlete participating in 1 practice or game. The overall rate of concussion was 17.15 concussions per 100,000 athlete-exposures.

Cheerleading was the only sport for which the practice rate of concussions was greater than the game rate. [69] Almost two thirds of cheerleading concussions involved 2-level pyramids. Concussion rates were elevated for athletes with a history of concussion, and they increased with the increasing level of body contact permitted in the sport.

Powell and Barber-Foss reported a 2-year review of 235 US certified athletic high-school training records. The authors estimated a total of 62,816 cases of mild traumatic brain injury (TBI) annually among high-school varsity athletes, with football accounting for approximately 63% of these cases and a varied incidence among 10 other popular sports. [70]

Matser et al showed that 23% of the amateur soccer players they studied had 2-5 concussions during their career. [16] Boden et al found that the overall prevalence of college soccer-related concussions was 0.6 cases per 1000 athlete-exposures for men and 0.4 cases per 1000 athlete-exposures for women. [17] The authors reported that the vast majority (72%) of these concussions were grade 1, and none were grade 3. [17]

The actual number of athletes who may be affected by repeated minor head injuries is largely unknown.

**Functional Anatomy**

SIS is thought to occur because of a loss of autoregulation of the cerebral blood flow, which leads to vascular engorgement, increased intracranial pressure (ICP), and eventual herniation.
This herniation may involve the medial temporal lobe and may occur medially across the falx cerebri or inferiorly through the tentorium. Herniation can also force the cerebellar tonsils to move inferiorly through the foramen magnum. The athlete’s condition rapidly worsens, and brainstem failure occurs in 2-5 minutes.

**Sport-Specific Biomechanics**

The brain is protected by bone and is cushioned by tough meninges and cerebrospinal fluid. Despite these protective surroundings, blunt-force trauma to the head can cause injury to the site of impact (coup injury) and the site immediately opposite of the impact (contrecoup injury). Factors that dissipate the force (eg, equipment, neck muscle strength) can minimize this trauma.

**History**

The history is a key element in evaluating an athlete with a suspected head injury. However, the athlete may not be able to provide a good history because of slowed mentation or confusion. In such cases, obtain the history from a teammate, coach, or observer. Symptoms of a head injury may include the following:

- Headache
- Memory impairment
- Confusion
- Diplopia
- Fatigue
- Photophobia, phonophobia, or both
- Blurred vision
- Dizziness
- Hemiplegia
- Nausea
- Sensory loss
- Impairment of hand-eye coordination
- Irritability
- Depression

**Physical**

The goals of the physical evaluation are to (1) recognize that a head injury may have occurred, (2) determine which athletes require immediate transport to a medical facility, and (3) decide when the athlete can return to competition. Emergency management includes the ABCs of first
aid. That is, assess and manage the individual's airway, breathing, and circulation. Signs of head injury include the following:

- Altered levels of consciousness
- Posttraumatic or retrograde amnesia
- Gait abnormalities
- Weakness
- Visual abnormalities
- Sensory loss
- Pupillary concordance and/or accommodation
- Poor concentration
- Apprehension
- Increased symptoms with exertion
- Focal symptoms – Facial or extremity twitching, smelling of atypical odors, tasting of atypical tastes
- Generalized symptoms – Tonic-clonic movements of body, incontinence, altered level of arousal

The brief neurologic examination should be performed without moving the athlete until the patient's ABCs and spine are deemed stable. The following are assessed:

- Verbal quality and appropriateness
- Memory (eg, to event), orientation (eg, to date), cognitive (eg, ability to perform the serial 7 s test)
- Visual findings – Pupillary size and reaction, tracking, nystagmus, gross visual fields, diplopia
- Motor findings – Coordination (finger to nose), strength (focal findings), balance (eg, single-leg stance, heel to toe)
- Romberg test results
- Tone
- Reflexes
- Sensory abnormalities – Touch, pinch, and pain

**Causes**

Factors that may increase the risk of a poor outcome with a repetitive head injury include the following:

- Previous head injury
- Persistence of symptoms from a previous head injury
  - Headache
  - Labyrinthine dysfunction (balance disorder)
  - Visual, motor, or sensory changes
  - Mental difficulties that affect thought and memory processes
• Alcohol or illicit drug use

Laboratory Studies

No laboratory tests help in diagnosing repetitive head injury. Most cases are diagnosed on the basis of the clinical findings.

Imaging Studies

Imaging studies are reserved for athletes with more significant injuries, such as those that cause loss of consciousness, persistent symptoms, neurologic deficits, or neurologic deterioration. Imaging studies should be considered in all athletes who have had more than 1 concussion. In addition, imaging studies should be ordered if symptoms last longer than 12 hours. Consultation with a neurosurgeon is imperative if any imaging findings are abnormal.

• Plain skull radiography yields few findings in persons with mild brain trauma, and it should not be ordered unless facial fractures are suspected. Plain film radiography (cervical spine [C-spine] radiographs) can be ordered to rule out neck pathology, which can occur with head trauma.
• Head computed tomography (CT) scanning is sensitive for detecting intracranial pathology associated with blunt-force trauma, even in a mild head injury (eg, Glasgow Coma Scale score of 13-15).
  o Nonenhanced CT scanning is the imaging examination of choice because acute hemorrhage must be excluded before performing contrast-enhanced CT scanning.
  o The advantages of CT scanning compared with MRI include (1) more rapid image acquisition in an emergency situation; (2) better depiction of bone; (3) lower cost, although cost should not influence clinical decision making in a potentially life-threatening situation such as the setting of a head injury; (4) correlation of negative results with a successful outcome; and (5) better sensitivity in detecting skull fractures.
  o Compared with the initial (first 12-24 h) head CT scan, the follow-up CT scan may better reveal small hemorrhages, which coalesce to form a brain contusion.
  o CT scanning can depict acute hemorrhages, skull fractures, cerebral edema, and cerebral herniation. An acute subdural hematoma is approximately 3 times more common than an epidural hematoma in sports-related head injuries.
• MRI of the head is more sensitive than CT scanning for detecting subtle changes such as small hemorrhages, edema, and diffuse axonal injury (DAI).
  o MRI should not be ordered in emergency situations because CT scanning is faster than MRI and has the advantages listed above.
  o The advantages of MRI compared with CT scanning include the ability of MRI to better depict subtle edema, small hemorrhages, arteriovenous malformations, and DAI.
DAI is seen in severe head injuries and is thought to result from the shearing of multiple axons. DAI is represented on MRIs as diffuse, high-signal intensity specks in the white matter.

MRI should be ordered if the patient's symptoms persist and CT scanning results are normal or if the symptoms are atypical or worsen despite normal or stable CT scan findings.

Other Tests

Neuropsychologic testing

- This is an in-depth examination of the injured athlete's thought processes and is considered the criterion standard for the initial and follow-up assessment of concussion patients, especially those with SIS.
- A neuropsychologist certified by the American Board of Professional Psychology is the best resource for these assessments, and a consultative approach is preferred, as opposed to merely a description of test data.
- A range of cognitive and behavioral tests are used, based on the preferences of the neuropsychologist, the severity of the injury, the specific clinical issue at hand (e.g., return to school, return to work, manage finances), the educational and cultural background of the examinee, and the time post injury.
- The occurrence of multiple concussions is associated with reduced cognitive performance on neuropsychologic tests.
- Hinton-Bayre et al showed that impaired performance on psychometric tests continued even after the athletes (professional rugby players) were symptom free.\(^\text{[71]}\)

- Electroencephalography (EEG)
  - EEG yields conflicting and typically nonspecific results. Most of the research with EEG has involved boxers.
  - Busse and Silverman showed that 37% of abnormal EEG findings occurred in boxers who have had a concussion.\(^\text{[72]}\)
  - Kaplan and Browder studied 1400 electroencephalograms in boxers and found that 34% of the athletes had normal EEG findings.\(^\text{[73]}\) The authors concluded that fighters with a lower ring rating had a higher percentage of disorganized EEG findings.
  - Johnson used EEG to evaluate retired professional boxers and found chronic brain damage in 12 of 15 of these individuals 22 years after their careers had ended.\(^\text{[15]}\)
  - Other studies show abnormal EEG findings in 20-30% of boxers.
  - However, early studies by Beaussart and Beaussart-Boulengé did not find any correlation between EEG changes and the severity of postconcussion syndrome in 3100 cases.\(^\text{[14]}\)

- Dynamic imaging
o Single-photon emission computed tomography (SPECT) scanning and positron emission tomography (PET) scanning have high sensitivity, but the specificity of these modalities is unclear and the clinical correlation is limited. At present, these tests are used primarily for research activities.

o In addition, these examinations are expensive and not easily available to most clinicians.

o Results from these tests may be overinterpreted or underinterpreted in medicolegal settings; the use for these types of activities should be discouraged until further definitive research is performed and has undergone peer review.

Procedures

- ICP monitoring may help in severe TBI, but it has limited usefulness in patients with mild TBI.
- Patients with an ICP greater than 25 mm Hg generally have more unfavorable outcomes than those with lower ICP measurements

Acute Phase

Rehabilitation Program

Physical Therapy

The goal of all therapy is to maximize the patient's strength and functional independence.

Athletes who have had severe head injuries may require rehabilitation for a prolonged period. In most patients, mild brain injuries do not require extensive rehabilitation, but they do require focal medical and rehabilitation care based on the individual's clinical evaluation and diagnostic test results.

Physical therapy is helpful in patients with increased tone, motor deficits, or mobility problems after a brain injury. Range-of-motion exercises are helpful in managing spasticity and preventing contractures.

Occupational Therapy

Occupational therapy is helpful in patients with brain injuries who may have motor and/or cognitive processing deficits and who may need to improve their ability to perform activities of daily living. The use of assistive devices can also be addressed.
**Speech Therapy**

Speech therapy is often useful in detecting subtle changes in the patient's thought processes and speech patterns. A speech therapist can help a patient with brain injury overcome barriers related to these changes.

**Recreational Therapy**

Recreational therapy is helpful in achieving community reintegration of the patient. Neuropsychologic measures may be good indicators of residual injury, and repeated testing may reveal when the athlete reaches a plateau.

**Medical Issues/Complications**

Medical issues in patients with brain injuries include the following:

- **Homeostatic abnormalities:** Loss of autonomic control of blood pressure or respiration and cardiac abnormalities may occur.
- **Endocrine abnormalities:** The syndrome of inappropriate antidiuretic hormone (SIADH) and diabetes insipidus are common problems.
- **Behavioral issues:** The patient may become uninhibited, impulsive, or agitated. Aggressive treatment with behavioral programs, counseling, and short-term medication usage is most effective. Medication usage (mood stabilizers, atypical antipsychotics) should be instituted carefully and with full knowledge of the indicators of clinical success, duration of treatment, and potential adverse effects.
- **Deep venous thrombosis:** Cifu et al showed that approximately 20% of patients admitted to a brain-injury rehabilitation unit had deep venous thrombosis.\(^{[74]}\)
- **Pulmonary embolus:** This is a rare condition, but if it is suspected, emergent treatment is indicated.
- **Complications of severe brain injury:** Brainstem herniation, rebleeding, and death may occur.

Minor issues in patients with brain injuries include the following:

- **Dizziness:** Most commonly, this is due to limitations in neck movement (pain) and peripheral trauma to the vestibular/labyrinthine system. Rarely, it is due to injury to the brainstem (central) balance coordinating structures. Dizziness is treated with medications and therapy.
- **Insomnia:** This is commonly related to issues of pain, dizziness, behavioral problems, nightmares/flashbacks, altered physical activity levels, or idiopathic reasons. Insomnia is best treated with a rapid return to activity, treatment of secondary issues, and short-term nonaddictive sleep aides.
Behavioral issues: Behavior may vary from excessive (see above) or depressed. Normalizing sleep-wake cycles, controlling pain, reactivating physical skills, and reassurance help most individuals. Individualized psychotherapy is also highly effective.

Photophobia/hyperacusis: These conditions are rarely significant long-term issues. They should be treated aggressively initially with dark glasses/white-noise generators and then a rapid weaning program. Sustained difficulties may suggest an undetected injury or secondary psychologic issues.

Surgical Intervention

Evacuation is required for epidural hematomas, significant subdural hematomas, and large intracerebral hematomas that cause mass effect. Ventriculostomy may be required for significant edema and/or possible herniation.

Recovery Phase

Rehabilitation Program

Physical Therapy

In the case of a severe head injury, many of the aforementioned therapies can be continued in an outpatient setting, but most of the rehabilitation process is focused on reintegrating patients with brain injuries into their home environment and community.

Maintenance Phase

Rehabilitation Program

Physical Therapy

Patients with TBI may require educational or neuropsychologic support for an extended period, depending on the severity of the head injury.

Occupational Therapy
See Acute Phase, Rehabilitation Program, Occupational Therapy.

Speech Therapy
See Acute Phase, Rehabilitation Program, Speech Therapy.

Recreational Therapy
See Acute Phase, Rehabilitation Program, Recreational Therapy.

Medication Summary

Care should be used when instituting therapy with medications that potentially have sedating effects, because sedation may complicate the monitoring of a patient with a brain injury. Some medications that can have significant sedating effects on such patients include H2 blockers (eg,
ranitidine, famotidine), diphenhydramine, narcotic pain relievers, nonsteroidal anti-
inflammatory drugs (NSAIDs), benzodiazepines, antipsychotics, and seizure medications.

Some medications may improve the patient's focus and alertness. A few of these medications are discussed below. In addition to the agents that may enhance thinking skills, aggressive management of specific symptoms is also warranted, including insomnia (trazodone), headaches (butalbital, aspirin, and caffeine [Fiorinal]; isometheptene mucate, dichloralphenazone, and acetaminophen [Midrin]; acetaminophen; NSAIDs; local agents), dizziness (meclizine, buspirone, vestibular programs, liberatory technique), and depression (cognitive behavioral therapy, selective serotonin reuptake inhibitors [SSRIs]).

**CNS Stimulants**

**Class Summary**
Central nervous system (CNS) stimulants are used to treat the hypoarousal and poor initiative often seen in patients with brain injuries.

**Methylphenidate (Ritalin, Ritalin SR)**

Although most notably used in children with attention-deficit/hyperactivity disorder (ADHD), this agent often helps with hypoarousal. Frequently the first drug used in patients with brain injury.

Not used as often in children with brain injury; when used, administer as in children with ADHD. Administered in morning and at noon before a therapy session to facilitate stimulant effect and increase attention to tasks. If no response is achieved, can be discontinued and another medication can be used.

**Anti-Parkinson Agents**

**Class Summary**
Anti-Parkinson medications have been useful in patients with brain injuries because these drugs increase their arousal and attention to tasks.

**Amantadine (Symmetrel)**

Unknown mechanism of action; may release dopamine from remaining dopaminergic terminals in patients with Parkinson disease or from other central sites. Less effective than levodopa in treating Parkinson disease; slightly more effective than anticholinergic agents.

**Carbidopa/levodopa (Sinemet)**

May increase alertness and attention to task in patients with brain injury.

**Central Nervous System Stimulant, Nonamphetamine**

**Class Summary**
Nonamphetamine CNS agents have actions that are similar to sympathomimetic agents.
Modafinil (Provigil)
May exert stimulant effects by decreasing GABA-mediated neurotransmission. Has wake-promoting actions similar to sympathomimetic agents. Improves wakefulness in patients with excessive daytime hypersomnolence. Has been used in narcolepsy and primary hypersomnia. Mechanism of action is unclear.

Return to Play

No good parameters have been proposed for repetitive head injury. As a result, most physicians use the parameters for concussion. The following systems present 2 options for concussion management, although many options are available. Note that in the following descriptions, asymptomatic means that the patient is symptom free at rest and with exertion.

Concussion Scales With Return-to-Play Criteria

Cantu system
The Cantu system grading is as follows:

- Grade I – No loss of consciousness, or posttraumatic amnesia for less than 30 minutes
  - First concussion – Return to play if patient is asymptomatic for 1 week
  - Second concussion – Return to play if patient is asymptomatic for 2 weeks
  - Third concussion – Terminate season
- Grade II – Loss of consciousness for less than 5 minutes, or posttraumatic amnesia for 30 minutes to 24 hours
  - First concussion – Return to play if patient is asymptomatic for 1 week
  - Second concussion – Return to play if, after at least 1 month, patient asymptomatic for 1 week
  - Third concussion – Terminate season
- Grade III – Loss of consciousness for more than 5 minutes, or posttraumatic amnesia for longer than 24 hours
  - First concussion – Return to play if, after at least 1 month, patient asymptomatic for 1 week
  - Second concussion – Terminate season

Kelly system
The Kelly system grading is as follows:

- Grade I – No loss of consciousness, transient confusion for less than 15 minutes
  - First concussion – Return to play if patient is asymptomatic within 15 minutes
  - Second concussion in same contest – Remove from play
  - After fourth concussion in season – Terminate season
- Grade II – No loss of consciousness, transient confusion for longer than 15 minutes
  - First concussion – Return to play if patient is asymptomatic for 1 week
Second concussion – Return to play if patient is asymptomatic for 2 weeks
Third concussion – Terminate season
- Grade III – Loss of consciousness, brief (seconds) or prolonged (minutes)
  - First concussion with brief loss of consciousness – Return to play if patient is asymptomatic for 1 week
  - First concussion with prolonged loss of consciousness – Return to play if patient is asymptomatic for 2 weeks
  - Second concussion – Return to play if patient is asymptomatic for 1 month

Complications
The most common complication at follow-up is further head injury and/or cognitive decline. Matser et al found that concussion is specifically associated with impaired performance in memory and planning functions.\textsuperscript{[16]}

Prevention
Equipment and rule changes have significantly reduced the number and severity of head injuries in American football over the last 25 years. The dramatic difference seen in football has sparked debate about equipment and rule changes in soccer because a significant number of concussions are now known to occur when players hit the ball with their head.
In preventing SIS, the recognition of a concussion is the key factor. Preventing an athlete from returning to play while he or she still has symptoms from a concussion and following the guidelines for concussion management may help avert a catastrophic outcome.

The American Academy of Neurology (AAN) has issued a brief position statement on sports concussion. The AAN recommends caution and protection first: If an athlete is suspected of having a concussion or closed head injury, then first remove the athlete from practice or competition, and do not allow return to play until he or she is evaluated by a physician with experience in treating concussions and cleared for return.\textsuperscript{[79]}

Prognosis
The prognosis varies with the severity of the injury. By definition, repetitive head injury is worse than a single minor concussion; neuropsychologic test results are worse in patients with repetitive minor concussions. Regarding SIS, rapid transport to a medical facility with neurosurgical specialists may prevent or limit the rapid decline often seen with SIS.

Education
Educate athletes, coaches, and healthcare professionals about the potentially catastrophic effects of SIS. Coaches and healthcare professionals need to know how to prevent SIS by not allowing the athlete to return to play while he or she is still recovering from a previous head injury.
References


