

LEARNING OBJECTIVE: Readers will evaluate and treat concussion in the context of current guidelines and refer patients to specialty clinics as appropriate

ALEXANDRA STILLMAN, MD

Director of Concussion, Traumatic Brain Injury and Neurorehabilitation, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center; Instructor of Neurology, Harvard Medical School, Boston, MA

NANCY MADIGAN, PhD

Concussion Clinic, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center; Instructor of Neurology, Harvard Medical School, Boston, MA

MICHAEL ALEXANDER, MD

Concussion Clinic, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center; Professor of Neurology, Harvard Medical School, Boston, MA

ALVARO PASCUAL-LEONE MD, PhD

Chief of Cognitive Neurology, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center; Professor of Neurology, Harvard Medical School, Boston, MA

REBEKAH MANNIX, MD

The Micheli Center for Sports Injury Prevention, Waltham, MA; Sports Concussion Clinic, Division of Sports Medicine, Boston Children's Hospital; Brain Injury Center, Boston Children's Hospital; Division of Emergency Medicine, Boston Children's Hospital; Associate Professor of Pediatrics and Emergency Medicine, Harvard Medical School, Boston, MA

WILLIAM P. MEEHAN III, MD

Director, Micheli Center for Sports İnjury Prevention, Waltham, MA; Director of Research, Brain Injury Center, Boston Children's Hospital; Associate Professor of Pediatrics and Orthopaedics, Harvard Medical School, Boston, MA

Concussion: Evaluation and management

ABSTRACT

Concussion is a common problem often managed by nonneurologists. It is often accompanied by headaches, dizziness, sleep disturbance, psychiatric symptoms, and cognitive issues. Here, we outline how to evaluate and manage concussion, including treatment of the most common symptoms.

KEY POINTS

Concussion results from a traumatic acceleration of the brain that leads to a metabolic mismatch, with an increased demand for adenosine triphosphate but decreased blood flow to the brain. This "energy crisis" results in variable signs and symptoms, most commonly headache, dizziness, sleep disturbance, cognitive problems, and emotional difficulties.

Initial therapy involves several days of cognitive and physical rest, followed by a gradual return to physical and cognitive activities.

There is no direct treatment for the physiology of concussion, but early treatment of symptoms and education about recovery and accommodations aids functional recovery.

Dr. Pascual-Leone serves on the scientific advisory boards for Constant Therapy, Neosync, Neuro-electrics, NovaVision, and Starlab.

Dr. Meehan has disclosed holding intellectual property rights with ABC-Clio Publishing Company, Springer International Publishing, and Wolters-Kluwer; receiving grant funding from the Football Players Health Study at Harvard, which is funded through the NFL Players Association; and receiving philanthropic support from the National Hockey League Alumni Association through the Corey C. Griffin Pro-Am Tournament.

doi:10.3949/ccjm.84a.16013

ONCUSSION, also known as mild traumatic brain injury, affects more than 600 adults per 100,000 each year and is commonly treated by nonneurologists. Public attention to concussion has been increasing, particularly to concussion sustained during sports. Coincident with this increased attention, the diagnosis of concussion continues to increase in the outpatient setting. Thus, a review of the topic is timely.

ACCELERATION OF THE BRAIN DUE TO TRAUMA

The definition of concussion has changed considerably over the years. It is currently defined as a pathophysiologic process that results from an acceleration or deceleration of the brain induced by trauma.² It is largely a temporary, functional problem, as opposed to a gross structural injury.^{2–5}

The acceleration of the brain that results in a concussion is usually initiated by a direct blow to the head, although direct impact is not required.⁶ As the brain rotates, different areas accelerate at different rates, resulting in a shear strain imparted to the parenchyma.

This shear strain causes deformation of axonal membranes and opening of membrane-associated sodium-potassium channels. This in turn leads to release of excitatory neurotransmitters, ultimately culminating in a wave of neuronal depolarization and a spreading depression-like phenomenon that may mediate the loss of consciousness, posttraumatic amnesia, confusion, and many of the other immediate signs and symptoms associated with concussion.

TABLE 1

Signs and symptoms of concussion

Symptoms

Headache

Dizziness

Balance problems

Unsteadiness

Light sensitivity

Vision changes

Nausea

Drowsiness

Amnesia

Sensitivity to noise

Tinnitus

Irritability

Feeling slowed down or "in a fog"

Difficulty concentrating

Difficulty remembering

Low energy, drowsiness

Sleep disturbance

Increased emotionality

Signs

Loss of consciousness

Amnesia

Confusion

Disorientation

Appearing dazed

Eye-movement abnormality

Inappropriate emotionality

Physical incoordination

Imbalance

Seizure

Slowed verbal responses

Based on information in reference 8

The sudden metabolic demand created by the massive excitatory phenomena triggers an increased utilization of glucose to restore cellular homeostasis. At the same time, cerebral blood flow decreases after concussion, which, in the setting of increased glucose demand, leads to an "energy crisis": an increased need for adenosine triphosphate with a concomitant decreased delivery of glucose. This mismatch between energy demand and supply is thought to underlie the most common signs and symptoms of concussion.

ASSESSMENT

History

The history of present illness is essential to a diagnosis of concussion. In the classic scenario, an otherwise asymptomatic person sustains some trauma to the head that is followed immediately by the signs and symptoms of concussion.

The most obvious sign of a concussion is loss of consciousness or a period of confusion with subsequent amnesia (also known as posttraumatic amnesia). However, a variety of symptoms may occur, such as headache, drowsiness, poor balance, and slowed verbal output (Table 1).

Many of these signs and symptoms are nonspecific and may occur without concussion or other trauma.^{8,9} Thus, the diagnosis of concussion cannot be made on the basis of symptoms alone, but only in the overall context of history, physical examination, and, at times, additional clinical assessments.

The symptoms of concussion should gradually improve. While they may be exacerbated by certain activities or stimuli, the overall trend should be one of symptom improvement. If symptoms are worsening over time, alternative explanations for the patient's symptoms should be considered.

Physical examination

A thorough neurologic examination should be conducted in all patients with suspected concussion and include the following.

A mental status examination should include assessment of attention, memory, and recall. Orientation is normal except in the most acute examinations.

Cranial nerve examination must include

A mismatch between energy demand and supply is thought to underlie the signs and symptoms of concussion careful assessment of eye-movement control, including smooth pursuit and saccades. However, even in patients with prominent subjective dizziness, considerable experience may be needed to actually demonstrate abnormalities.

Balance testing. Balance demands careful assessment and, especially for young athletes, this testing should be more difficult than the tandem gait and eyes-closed, feet-together tests.

Standard strength, sensory, reflex, and coordination testing is usually normal.

Any focal neurologic findings should prompt consideration of other causes or of a more serious injury and should lead to further evaluation, including brain imaging.

Diagnostic tests

Current clinical brain imaging cannot diagnose a concussion. The purpose of neuroimaging is to assess for other etiologies or injuries, such as hemorrhage or contusion, that may cause similar symptoms but require different management.

Several guidelines are available to assess the need for imaging in the setting of recent trauma, of which 2 are typically used^{10–12}:

The Canadian CT Head Rule¹⁰ states that computed tomography (CT) is indicated in any of the following situations:

- The patient fails to reach a Glasgow Coma Scale score of 15—on a scale of 3 (worst) to 15 (best)—within 2 hours
- There is a suspected open skull fracture
- There is any sign of basal skull fracture
- The patient has 2 or more episodes of vomiting
- The patient is 65 or older
- The patient has retrograde amnesia (ie, cannot remember events that occurred before the injury) for 30 minutes or more
- The mechanism of injury was dangerous (eg, a pedestrian was struck by a motor vehicle, or the patient fell from > 3 feet or > 5 stairs).

The New Orleans Criteria¹¹ state that a patient warrants CT of the head if any of the following is present:

- Severe headache
- Vomiting
- Age over 60

- Drug or alcohol intoxication
- Deficit in short-term memory
- Physical evidence of trauma above the clavicles
- Seizure.

Caveats: these imaging guidelines apply to adults; those for pediatric patients differ. ¹² Also, because they were designed for use in an emergency department, their utility in clinical practice outside the emergency department is unclear.

Electroencephalography is not necessary in the evaluation of concussion unless a seizure disorder is believed to be the cause of the injury.

Concussion in athletes

Athletes who participate in contact and collision sports are at higher risk of concussion than the nonathletic population. Therefore, specific assessments of symptoms, balance, oculomotor function, cognitive function, and reaction time have been developed for athletes.

Ideally, these measures are taken at preseason baseline, so that they are available for comparison with postinjury assessments after a known or suspected concussion. These assessments can be used to help make the diagnosis of concussion in cases that are unclear and to help monitor recovery. Objective measures of injury are especially useful for athletes who may be reluctant to report symptoms in order to return to play.

Like most medical tests, these assessments need to be properly interpreted in the overall context of the medical history and physical examination by those who know how to administer them. It is important to remember that the natural history of concussion recovery differs between sport-related concussion and concussion that occurs outside of sports.⁸

MANAGEMENT

The symptoms and signs after concussion are so variable and multidimensional that they make a generally applicable treatment hard to define.

Rest: Physical and cognitive

Treatment depends on the specifics of the injury, but there are common recommendations

If symptoms worsen over time, alternative explanations should be considered for the acute days after injury. Lacking hard data, the consensus among experts is that patients should undergo a period of physical and cognitive rest.^{13,14} Exactly what "rest" means and how long it should last are unknown, leading to a wide variation in its application.

Rest aids recovery but also may have adverse effects: fatigue, diurnal sleep disruption, reactive depression, anxiety, and physiologic deconditioning. Many guidelines recommend physical and cognitive rest until symptoms resolve, the but this is likely too cautious. Even without a concussion, inactivity is associated with many of the nonspecific symptoms also associated with concussion. As recovery progresses, the somatic symptoms of concussion improve, while emotional symptoms worsen, likely in part due to prolonged rest. 17

We recommend a period of rest lasting 3 to 5 days after injury, followed by a gradual resumption of both physical and cognitive activities as tolerated, remaining below the level at which symptoms are exacerbated.

Not surprisingly, many guidelines for returning to physical activity are focused on athletes. Yet the same principles apply to management of concussion in the general population who exercise: light physical activity (typically walking or stationary bicycling), followed by more vigorous aerobic activity, followed by some resistance activities. Mild aerobic exercise (to below the threshold of symptoms) may speed recovery from refractive postconcussion syndrome, even in those who did not exercise before the injury.¹⁸

Athletes require specific and strict instructions to avoid increased trauma to the head during the gradual increase of physical activities. The National Collegiate Athletic Association has published an algorithm for a gradual return to sport-specific training that is echoed in recent consensus statements on concussion. Once aerobic reconditioning produces no symptoms, then noncontact, sport-specific activities are begun, followed by contact activities. We have patients return to the clinic once they are symptom-free for repeat evaluation before clearing them for high-risk activities (eg, skiing, bicycling) or contact sports (eg, basketball, soccer, football, ice hockey).

Specific assessments have been developed for athletes

Cognitive rest

While physical rest is fairly straightforward, cognitive rest is more challenging. The concept of cognitive rest is hard to define and even harder to enforce. Patients are often told to minimize any activities that require attention or concentration. This often includes, but is not limited to, avoiding reading, texting, playing video games, and using computers.¹³

In the modern world, full avoidance of these activities is difficult and can be profoundly socially isolating. Further, complete cognitive rest may be associated with symptoms of its own. 15,16,20 Still, some reasonable limitation of cognitive activities, at least initially, is likely beneficial. 21 For patients engaged in school or academic work, often the daily schedule needs to be adjusted and accommodations made to help them return to a full academic schedule and level of activity. It is reasonable to have patients return gradually to work or school rather than attempt to immediately return to their preinjury level.

With these interventions, most patients have full resolution of their symptoms and return to preinjury levels of performance.

■ TREATING SOMATIC SYMPTOMS

Posttraumatic headache

Posttraumatic headache is the most common sequela of concussion.²² Surprisingly, it is more common after concussion than after moderate or severe traumatic brain injury.²³ A prior history of headache, particularly migraine, is a known risk factor for development of post-traumatic headache.²⁴

Posttraumatic headache is usually further defined by headache type using the International Classification of Headache Disorders criteria (www.ichd-3.org). Migraine or probable migraine is the most common type of posttraumatic headache; tension headache is less common.²⁵

Analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) are often used initially by patients to treat posttraumatic headache. One study found that 70% of patients used acetaminophen or an NSAID.²⁶

Treating early with effective therapy is the most important tenet of posttraumatic headache treatment, since 80% of those who self-

treat have incomplete relief, and almost all of them are using over-the-counter products.²⁷ Overuse of over-the-counter abortive medications can lead to medication overuse headache, also known as rebound headache, thus complicating the treatment of posttraumatic headache.²⁶

Earlier treatment with a preventive medication can often limit the need for and overuse of over-the-counter analgesics and can minimize the occurrence of subsequent medication overuse headache. However, in pediatric populations, nonpharmacologic interventions such as rest and sleep hygiene are typically used first, then medications after 4 to 6 weeks if this is ineffective.

A number of medications have been studied for prophylactic treatment of posttraumatic headache, including topiramate, amitriptyline, and divalproex sodium, ^{28–30} but there is little compelling evidence for use of one over the other. If posttraumatic headache is migrainous, beta-blockers, calcium-channel blockers, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibtors, and gabapentin are other prophylactic medication options under the appropriate circumstances.^{27,31,32} In adults, we have clinically had success with nortriptyline 20 mg or gabapentin 300 mg at night as an initial prophylactic headache medication, increasing as tolerated or until pain is controlled, though there are no high-quality data to guide this decision.

The ideal prophylactic medication depends on headache type, patient tolerance, comorbidities, allergies, and medication sensitivities. Gabapentin, amitriptyline, and nortriptyline can produce sedation, which can help those suffering from sleep disturbance.

If a provider is not comfortable prescribing these medications or doesn't prescribe them regularly, the patient should be referred to a concussion or headache specialist more familiar with their use.

In some patients, even some athletes, headache may be related to a cervical strain injury—whiplash—that should be treated with an NSAID (or acetaminophen), perhaps with a short course of a muscle relaxant in adults, and with physical therapy.³²

Some patients have chronic headache despite oral medications. Therefore, alternatives to oral medications and complementary therapies should be considered. Especially for protracted cases requiring more complicated headache management or injectable treatments, patients should be referred to a pain clinic, headache specialist, or concussion specialist.

Dizziness

Dizziness is also common after concussion. But what the patient means by dizziness requires a little probing. Some have paroxysms of vertigo. This typically represents a peripheral vestibular injury, usually benign paroxysmal positional vertigo. The latter can be elicited with a Hallpike maneuver and treated in the office with the Epley maneuver.³³

Usually, dizziness is a subjective sense of poor coordination, gait instability, or dysequilibrium. Patients may also complain of associated nausea and motion sensitivity. This may all be secondary to a mechanism in the middle or inner ear or the brain. Patients should be encouraged to begin movement—gradually and safely—to help the vestibular system accommodate, which it will do with gradual stimulation. It usually resolves spontaneously.

Specific treatment is unfortunately limited. There is no established benefit from vestibular suppressants such as meclizine. Vestibular rehabilitation may accelerate improvement and decrease symptoms.³³ Referral for a comprehensive balance assessment or to vestibular therapy (a subset of physical therapy) should be considered and is something we typically undertake in our clinic if there is no recovery from dizziness 4 to 6 weeks after the concussion.

Visual symptoms can contribute to dizziness. Convergence spasm or convergence insufficiency (both related to muscle spasm of the eye) can occur after concussion, with some studies estimating that up to 69% of patients have these symptoms.³⁴ This can interfere with visual tracking and contribute to a feeling of dysequilibrium.³⁴ Referral to a concussion specialist or vestibular rehabilitation physical therapist can be helpful in treating this issue if it does not resolve spontaneously.

Orthostasis and lightheadedness also contribute to dizziness and are associated with cerebrovascular autoregulation. Available

Rest benefits recovery, but it may also have adverse effects data suggest that dysregulation of neurovascular coupling, cerebral vasoreactivity, and cerebral autoregulation contribute to some of the chronic symptoms of concussion, including dizziness. A gradual return to exercise may help regulate cerebral blood flow and improve this type of dizziness.³⁵

Sleep disturbance

Sleep disturbance is common after concussion, but the form is variable: insomnia, excessive daytime somnolence, and alteration of the sleep-wake cycle are all seen and may themselves affect recovery.³⁶

Sleep hygiene education should be the first intervention for postconcussive sleep issues. For example, the patient should be encouraged to do the following:

- Minimize "screen time" an hour before going to bed: cell phone, tablet, and computer screens emit a wavelength of light that suppresses endogenous melatonin release^{37,38}
- Go to bed and wake up at the same time each day
- Minimize or avoid caffeine, nicotine, and alcohol
- Avoid naps.³⁹

Melatonin is a safe and effective treatment that could be added. ⁴⁰ In addition, some studies suggest that melatonin may improve recovery from traumatic brain injury. ^{41,42}

Mild exercise (to below the threshold of causing or exacerbating symptoms) may also improve sleep quality.

Amitriptyline or nortriptyline may reduce headache frequency and intensity and also help treat insomnia.

Trazodone is recommended by some as a first-line agent,³⁹ but we usually reserve it for protracted insomnia refractory to the above treatments.

Benzodiazepines should be avoided, as they reduce arousal, impair cognition, and exacerbate motor impairments.⁴³

Emotional symptoms

Acute-onset anxiety or depression often occurs after concussion. 44,45 There is abundant evidence that emotional effects of injury may be the most significant factor in recovery. 46 A preinjury history of anxiety may be a prognostic factor. Patients with a history of anxiety

or depression are more likely to develop emotional symptoms after a concussion, but emotional problems may develop in any patient after a concussion.^{47,48}

The circumstances under which an injury is sustained may be traumatic (eg, car accident, assault), leading to an acute stress reaction or disorder and, if untreated, may result in a more chronic condition—posttraumatic stress disorder. Moreover, the injury and subsequent symptoms may have repercussions in many aspects of the patient's life, leading to further psychologic stress (eg, loss of wages or the inability to handle normal work, school, and family responsibilities).

Referral to a therapist trained in skills-based psychotherapy (eg, cognitive-behavioral therapy, exposure-based treatment) is often helpful.

Pharmacologic treatment can be a useful adjunct. Several studies have shown that selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants may improve depression after concussion.⁴⁹ The prescription of antidepressants, however, is best left to providers with experience in treating anxiety and depression.

As with sleep disorders after concussion, benzodiazepines should be avoided, as they can impair cognition.⁴³

Cognitive problems

Cognitive problems are also common after concussion. Patients complain about every-day experiences of forgetfulness, distractibility, loss of concentration, and mental fatigue. Although patients often subjectively perceive these symptoms as quite limiting, the impairments can be difficult to demonstrate in office testing.

A program of gradual increase in mental activity, parallel to recovery of physical capacity, should be undertaken. Most patients make a gradual recovery within a few weeks.⁵⁰

When cognitive symptoms cause significant school or vocational problems or become persistent, patients should be referred to a specialty clinic. As with most of the consequences of concussion, there are few established treatments. When cognitive difficulties persist, it is important to consider the complications of

We recommend that patients rest 3–5 days, then gradually resume physical and cognitive activities as tolerated concussion mentioned above: headache, pain, sleep disturbance, and anxiety, all of which may cause subjective cognitive problems and are treatable.

If cognitive symptoms are prolonged despite improvement of other issues like headache and sleep disturbance, a low-dose stimulant medication such as amphetamine salts or methylphenidate may be useful for symptoms of poor attention. ⁴⁹ They should be only a temporary measure after concussion to carry the patient through a cognitively challenging period, unless there was a history of attention-deficit disorder before the injury. A variety of other agents, including amantadine, ⁵¹ have been proposed based on limited studies; all are off-label uses. Before considering these types of interventions, referral to a specialist or a specialty program would be appropriate.

■ IF SYMPTOMS PERSIST

With the interventions suggested above, most patients with concussion have a resolution of symptoms and can return to preinjury levels of performance. But some have prolonged symptoms and sequelae. Approximately 10% of athletes have persistent signs and symptoms of concussion beyond 2 weeks. If concussion is not sport-related, most patients recover completely within the first 3 months, but up to 33% may have symptoms beyond that.⁵²

Four types of patients have persistent symptoms:

Patients who sustained a high-force mechanism of injury. These patients simply need more time and accommodation.

REFERENCES

- Cassidy JD, Carroll LJ, Peloso PM, et al; WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; (suppl):28–60.
- Shaw NA. The neurophysiology of concussion. Prog Neurobiol 2002; 67:281–344.
- Denny-Brown DE, Russell WR. Experimental concussion: (section of neurology). Proc R Soc Med 1941; 34:691–692.
- Ommaya AK, Gennarelli TA. Cerebral concussion and traumatic unconsciousness. Correlation of experimental and clinical observations of blunt head injuries. Brain 1974; 97:633–654.
- Houlburn AHS, Edin MA. Mechanics of head injuries. Lancet 1943; 242:438–441.
- Gennarelli TA, Adams JH, Graham DI. Acceleration induced head injury in the monkey. I. The model, its mechanical and physiological correlates. Acta Neuropathol Suppl 1981; 7:23–25.

Patients who sustained multiple concussions. These patients may also need more time and accommodation.

Patients with an underlying neurologic condition, recognized prior to injury or not, may have delayed or incomplete recovery. Even aging may be an "underlying condition" in concussion.

Patients whose symptoms from an apparently single mild concussion do not resolve despite appropriate treatments may have identifiable factors, but intractable pain (usually headache) or significant emotional disturbance or both are common. Once established and persistent, this is difficult to treat. Referral to a specialty practice is appropriate, but even in that setting effective treatment may be elusive.

PATIENT EDUCATION

Most important for patient education is reassurance. Ultimately, concussion is a self-limited phenomenon, and reinforcing this is helpful for patients. If concussion is not sport-related, most patients recover completely within 3 months.

The next important tenet in patient education is that they should rest for 3 to 5 days, then resume gradual physical and cognitive activities. If resuming activities too soon results in symptoms, then they should rest for a day and gradually resume activity. If their recovery is prolonged (ie, longer than 6 weeks), they likely need to be referred to a concussion specialist.

- Giza CC, Hovda DA. The neurometabolic cascade of concussion. J Athl Train 2001; 36:228–235.
- 8. Meehan WP 3rd, Bachur RG. Sport-related concussion. Pediatrics 2009; 123:114–123.
- Iverson GL, Silverberg ND, Mannix R, et al. Factors associated with concussion-like symptom reporting in high school athletes. JAMA Pediatr 2015; 169:1132–1140.
- Stiell IG, Wells GA, Vandemheen K. et al. The Canadian CT head rule for patients with minor head injury. Lancet 2001; 357:1391–1396.
- Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E, DeBlieux PMC. Indications for computed tomography in patients with minor head injury. N Engl J Med 2000; 343:100–105.
- Kuppermann N, Holmes JF, Dayan PS, et al; Pediatric Emergency Care Applied Research Network (PECARN). Identification of children at very low risk of clinically important brain injuries after head trauma: a prospective cohort study. Lancet 2009; 374:1160–1170.
- McCrory P, Meeuwisse W, Johnston K, et al. Consensus Statement on Concussion in Sport: the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. Br J Sports Med

- 2009; 43(suppl 1):i76-i90.
- DeMatteo C, Stazyk K, Singh SK, et al; Ontario Neurotrauma Foundation. Development of a conservative protocol to return children and youth to activity following concussive injury. Clin Pediatr (Phila) 2015; 54:152–163.
- Willer B, Leddy JJ. Management of concussion and post-concussion syndrome. Curr Treat Options Neurol 2006; 8:415–426.
- DiFazio M, Silverberg ND, Kirkwood MW, Bernier R, Iverson GL. Prolonged activity restriction after concussion: are we worsening outcomes? Clin Pediatr (Phila) 2016; 55:443–451.
- Thomas DG, Apps JN, Hoffmann RG, McCrea M, Hammeke T. Benefits of strict rest after acute concussion: a randomized controlled trial. Pediatrics 2015; 135:213–223.
- Leddy JJ, Kozlowski K, Donnelly JP, Pendergast DR, Epstein LH, Willer B. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. Clin J Sport Med 2010; 20:21–27.
- McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. Br J Sports Med 2013; 47:250–258.
- Buckley TA, Munkasy BA, Clouse BP. Acute cognitive and physical rest may not improve concussion recovery time. J Head Trauma Rehabil 2016; 31:233–241.
- Brown NJ, Mannix RC, O'Brien MJ, Gostine D, Collins MW, Meehan WP 3rd. Effect of cognitive activity level on duration of post-concussion symptoms. Pediatrics 2014; 133:e299–e304.
- 22. Packard RC. Epidemiology and pathogenesis of posttraumatic headache. J Head Trauma Rehabil 1999; 14:9–21.
- Couch JR, Bearss C. Chronic daily headache in the posttrauma syndrome: relation to extent of head injury. Headache 2001; 41:559–564.
- Lucas S, Hoffman JM, Bell KR, Dikmen S. A prospective study of prevalence and characterization of headache following mild traumatic brain injury. Cephalalgia 2014; 34:93–102.
- Lucas S, Hoffman JM, Bell KR, Walker W, Dikmen S. Characterization of headache after traumatic brain injury. Cephalalgia 2012; 32:600–606.
- DiTommaso C, Hoffman JM, Lucas S, Dikmen S, Temkin N, Bell KR. Medication usage patterns for headache treatment after mild traumatic brain injury. Headache 2014; 54:511–519.
- Lucas S. Characterization and management of headache after mild traumatic brain injury. In: Kobeissy FH, ed. Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects. Boca Raton, FL: CRC Press/Taylor & Franis Group; 2015:145–154.
- Erickson JC. Treatment outcomes of chronic post-traumatic headaches after mild head trauma in US soldiers: an observational study. Headache 2011; 51:932–944.
- Tyler GS, McNeely HE, Dick ML. Treatment of post-traumatic headache with amitriptyline. Headache 1980; 20:213–216.
- Packard RC. Treatment of chronic daily posttraumatic headache with divalproex sodium. Headache 2000; 40:736–739.
- Kacperski J, Arthur T. Management of post-traumatic headaches in children and adolescents. Headache 2016; 56:36–48.
- Lenaerts ME, Couch JR, Couch JR. Posttraumatic headache. Curr Treat Options Neurol 2004; 6:507–517.
- Valovich McLeod TC, Hale TD. Vestibular and balance issues following sport-related concussion. Brain Inj 2015; 29:175–184.
- Master CL, Cheiman M, Gallaway M, et al. Vision diagnoses are common after concussion in adolescents. Clin Pediatr (Phila) 2016; 55:260–267.

- Tan CO, Meehan WP 3rd, Iverson GL, Taylor JA. Cerebrovascular regulation, exercise and mild traumatic brain injury. Neurology 2014; 83:1665–1672.
- Mahmood O, Rapport LJ, Hanks RA, Fichtenberg NL. Neuropsychological performance and sleep disturbance following traumatic brain injury. J Head Trauma Rehabil 2004; 19:378–390.
- Lewy AJ, Wehr TA, Goodwin FK, Newsome DA, Markey SP. Light suppresses melatonin secretion in humans. Science 1980; 210:1267– 1269.
- Figueiro MG, Wood B, Plitnick B, Rea MS. The impact of light from computer monitors on melatonin levels in college students. Neuro Endocrinol Lett 2011; 32:158–163.
- Rao V, Rollings P. Sleep disturbances following traumatic brain injury. Curr Treat Options Neurol 2002; 4:77–87.
- Samantaray S, Das A, Thakore NP, et al. Therapeutic potential of melatonin in traumatic central nervous system injury. J Pineal Res 2009; 47:134–142.
- 41. **Ding K, Xu J, Wang H, Zhang L, Wu Y, Li T**. Melatonin protects the brain from apoptosis by enhancement of autophagy after traumatic brain injury in mice. Neurochem Int 2015; 91:46–54.
- Babaee A, Eftekhar-Vaghefi SH, Asadi-Shekaari M, et al. Melatonin treatment reduces astrogliosis and apoptosis in rats with traumatic brain injury. Iran J Basic Med Sci 2015; 18:867–872.
- Arciniegas DB, Anderson CA, Topkoff J, McAllister TW. Mild traumatic brain injury: a neuropsychiatric approach to diagnosis, evaluation, and treatment. Neuropsychiatr Dis Treat 2005; 1:311–327.
- 44. O'Donnell ML, Creamer M, Pattison P, Atkin C. Psychiatric morbidity following injury. Am J Psychiatry 2004; 161:507–514.
- Dikmen SS, Bombardier CH, Machamer JE, Fann JR, Temkin NR. Natural history of depression in traumatic brain injury. Arch Phys Med Rehabil 2004; 85:1457–1464.
- Massey JS, Meares S, Batchelor J, Bryant RA. An exploratory study of the association of acute posttraumatic stress, depression, and pain to cognitive functioning in mild traumatic brain injury. Neuropsychology 2015; 29:530–542.
- Meares S, Shores EA, Taylor AJ, et al. The prospective course of postconcussion syndrome: the role of mild traumatic brain injury. Neuropsychology 2011; 25:454–465.
- Solomon GS, Kuhn AW, Zuckerman SL. Depression as a modifying factor in sport-related concussion: a critical review of the literature. Phys Sportsmed 2016; 44:14–19.
- Neurobehavioral Guidelines Working Group; Warden DL, Gordon B, McAllister TW, et al. Guidelines for the pharmacologic treatment of neurobehavioral sequelae of traumatic brain injury. J Neurotrauma 2006; 23:1468–1501.
- Dikmen S, McLean A, Temkin N. Neuropsychological and psychosocial consequences of minor head injury. J Neurol Neurosurg Psychiatry 1986; 49:1227–1232.
- Reddy CC, Collins M, Lovell M, Kontos AP. Efficacy of amantadine treatment on symptoms and neurocognitive performance among adolescents following sports-related concussion. J Head Trauma Rehabil 2013: 28:260–265.
- Leddy JJ, Sandhu H, Sodhi V, Baker JG, Willer B. Rehabilitation of concussion and post-concussion syndrome. Sports Health 2012; 4:147–154.

ADDRESS: William P. Meehan III, MD, Director, Mitchell Center for Sports Injury Prevention, 9 Hope Avenue, Suite 100, Waltham, MA 02453; William.Meehan@childrens.harvard.edu