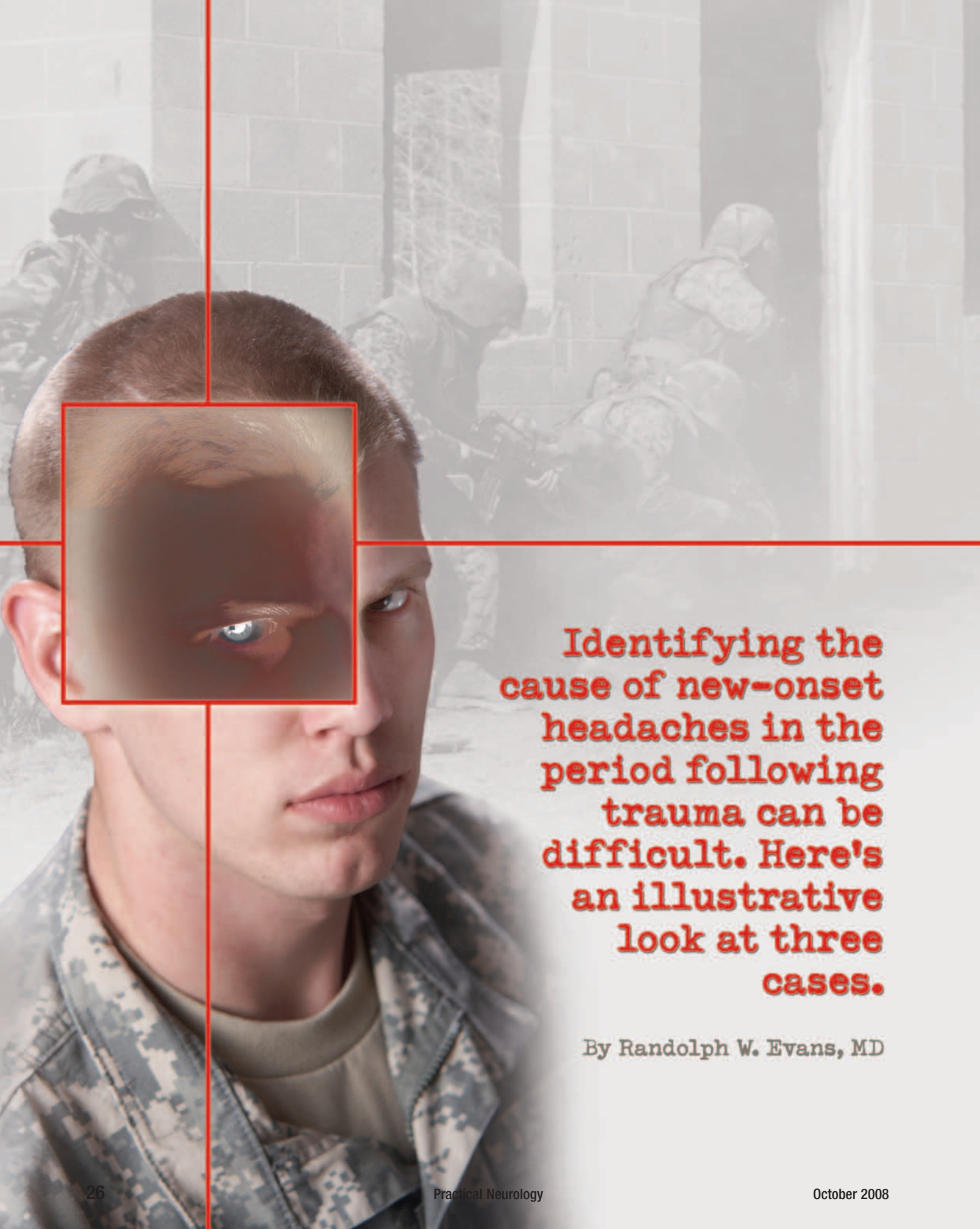

Identifying the cause of new-onset headaches in the period following trauma can be difficult. Here's an illustrative look at three cases.

By Randolph W. Evans, MD

Since the start of military operations in 2001, more than 1.6 million United States military personnel have been deployed to Afghanistan and Iraq. Although common, the precise number of soldiers with mild closed head injury is not known. In a retrospective survey of 2,525 Army infantry soldiers performed three to four months after returning from a one-year deployment in Iraq in 2006 to assess the prevalence of mild traumatic brain injury, 4.9 percent reported injuries with loss of consciousness and 10.3 percent reported injuries with altered consciousness.[1]

In another survey of 2,235 US military personnel returning from deployment in Iraq and Afghanistan by September, 2004, about 12 percent reported a history consistent with mild traumatic brain injury.[2] In the 2006 study, the mechanisms of injury (which were not mutually exclusive) were as follows: blasts or explosions, 75 percent; falls, 29 percent; vehicle accidents, 22 percent; fragment or shrapnel, 21 percent; and bullets, two percent. Headaches during the prior month, although not further described, were more common in the mildly head injured as follows: no injury, 8.4 percent; altered mental status, 17.7 percent; and loss of consciousness, 32.2 percent. Little has been published about these posttraumatic headaches. Three active duty Army soldiers I recently evaluated may exemplify the posttraumatic headaches and associated disorders.

Cases

Case 1. This 39-year-old man was seen in April 2008 with a chief complaint of posttraumatic headaches. In November 2006, while wearing his Kevlar helmet, body armor, and a head muffler, he was standing outside of his truck in eastern Afghanistan when three rocket-propelled grenades hit the truck. He was thrown 25-30 feet by the explosion. He believes that he was unconscious for three to four minutes. When he woke up, he was confused. All sounds were initially muffled. As he sat up, he heard gunshots of the Taliban shooting at him. He sustained shrapnel wounds to both legs, the left hand, and the right side of the face. He was able to get back to his base and was treated by a physician's assistant who cleaned his wounds. He went back out the next day and was in a firefight two days later. He completed his tour and returned to the United States in March 2007.

He had a mild headache right after the injuries, and developed severe headaches two days later. The severe headaches initially occurred two to three times per week, then became daily in September of 2007. They have now decreased to one to two times per week for the last couple of months since starting amitriptyline 50mg at bedtime, which he has tolerated without side effects. The headaches are a right-sided, especially frontoparietal throbbing with an intensity ranging from 3/10 to 10/10, with nausea, light, and noise sensitivity, and, about 40 percent of the time, vomiting but no aura. He takes

almotriptan 12.5mg without side effects, and the headache goes away in about 40 minutes. Without the medication, the headache could last 24 hours. The headaches can be triggered by weightlifting and doing stomach crunches. Topiramate did not prevent the headaches.

Shortly after his injuries, the patient started having dizzy spells that would initially last 10 minutes at a time but now last 20-30 seconds. He has a sensation of light-headedness or spinning occurring two to three times per week. He reported no hearing or visual symptoms but has some intermittent ringing in his right ear. He has persistent complaints of difficulty with short-term memory and concentration.

A magnetic resonance imaging (MRI) scan of the brain in November 2007 was normal. He underwent psychological testing in December 2007 and was administered the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Form B and was reported as showing deficits in delayed memory, attention, language, and visuospatial/construction consistent with a traumatic brain injury. However, full neuropsychological assessment in April 2008 produced invalid results atypical for acquired brain injury. He also reported multiple symptoms of re-experiencing (nightmares, flashbacks, and stressful reaction when reminded), sleep difficulty, and hyperarousal consistent with posttraumatic stress disorder (PTSD). There was a past medical history of hypertension on metoprolol 50mg bid since 2002 but no prior history of headaches or head trauma. There was a family history of his sister with migraines.

Neurological examination was normal. To try to further decrease the frequency of headache and treat PTSD, I increased the dose of amitriptyline to 75mg at bedtime.

In civilian studies, headaches are variably estimated as occurring in 30-90 percent of persons symptomatic following mild head injury, which can range from mild to severe in intensity and have a variable frequency of occasional to daily.

Case 2. This 41-year-old man was seen in April 2008 with a chief complaint of posttraumatic headaches. In April 2005, while he was wearing a helmet and body armor, his unit was ambushed north of Baghdad, Iraq and hit by multiple rocket-propelled grenades. He was knocked down and was dazed and confused and had blood coming from his nose, sustaining shrapnel wounds in the legs, hands, and buttocks. He was in the middle of combat and had to continue fighting and kill five enemy combatants at close range. He developed a headache right afterward and ringing in the ears. His first medical attention was a month later when he saw two doctors and was found to have a healed perforation of the left tympanic membrane and an infected perforation of the right tympanic membrane, which was treated and then eventually healed without surgery. He returned to the United States in July 2005 and saw two otolaryngologists later that year. A computerized axial tomography (CAT) scan of the brain was negative. An audiogram showed decreased hearing in both ears. He has had constant ringing in both ears, occasional lightheadedness, and feels off balance when he is standing on one leg.

Symptoms of hypervigilance, sleep disturbance, and reacting strongly to experiences that remind him of stressful combat experiences resulted in a psychiatrist diagnosing PTSD. In February 2008, the RBANS was normal. Neuropsychological testing in April 2008 was normal except for two tests that showed emotional interference. Since the injuries, he has had almost daily headaches that are a behind-the-eyes and top-of-the-head dull pain with an intensity ranging from 3/10 to 8/10, with an average of 4/10. Headaches typically start about noon to 1pm and last the rest of the day. He has no nausea or visual symptoms but has light and noise sensitivity all the time. He occasionally takes an oxycodone and acetaminophen combination tablet, which dulls the pain, but he usually takes no medication. He has not had any change in smell or taste but has trouble falling and staying asleep, short-

term memory problems, and difficulty with concentration, which is improving. He has had daily neck pain for 10 years since neck injuries in training with an intensity ranging from 5/10 to 6/10—worse since the 2005 injury. He has more numbness of the right than the left upper extremity, going into all of the fingers of the hands. He has had a cervical spine MRI study in the past without neural compression. He saw a pain specialist the previous day who started pregabalin 50mg bid and continued prescriptions for meloxicam and lidocaine 5% patches.

There was a history of headaches since his 20s, occurring about once a month and sometimes triggered by heat, described as a bitemporal aching and throbbing with an intensity of 5/10 associated with light and noise sensitivity but no nausea or aura. The headaches would resolve in a couple of hours after taking aspirin or acetaminophen. Previously he had been exposed to blasts in training in deployment in Bosnia and Iraq without any sequelae. Past medical history was otherwise negative. He was also taking citalopram for PTSD. Family history was positive for his father and brother with migraine. On examination, there was bilateral mid-superior nuchal line tenderness with digital pressure reproducing the headache and bilateral cervical paraspinal tenderness. Neurological examination was normal. Bilateral occipital nerve blocks were performed by injection of 3cc each of 1% lidocaine. He was also placed on cyclobenzaprine 5mg three times daily as necessary.

Case 3. This 24-year-old man was seen in April 2008 with a chief complaint of posttraumatic headaches. In July 2006, while he was wearing a helmet, ear plugs, and body armor, his vehicle was hit by an improvised explosive device in Baghdad, Iraq. He remained in the vehicle, was thrown against the roof, and hit his head twice. There was no loss of consciousness, but he was dazed and confused and sustained shrapnel wounds to his right upper extremity and right knee. He saw a doctor that day. He returned to patrols later that day and returned to the United States in October 2006. The headaches started within one month after the injury (he could not be more precise) and were daily until the prior two or three weeks when they decreased to every other day. He described a behind-the-left-eye and bilateral nuchal-occipital pressure, aching and sharp pain with an intensity ranging from 2/10 to 10/10 with an average of 5/10-6/10 associated with nausea and noise sensitivity but no vomiting. Light sensitivity was present all of the time. About twice a month, the headache was a 10/10. About 20 minutes before the headache, two to four times per month, he would see halos or fuzziness around the vision, lasting 45 minutes to two hours, persisting during the headache. The headaches would last anywhere from 45 minutes to two to three days with an average of two to three hours. He did not have any neck pain. An isomethptene combination would relieve the milder headaches and dull the severe headaches, naproxen sodium did not help, and an aspirin, acetaminophen, and caffeine combination would dull the pain. He had trouble falling and staying asleep but denied any nightmares or flashbacks. He reported both short-term and long-term memory problems, difficulty with concentration, and depression.

A psychiatrist had just started duloxetine and quetiapine. He had dizziness on a daily basis since the injury, with a sensation of lightheadedness, lasting seconds a few times per day. He has no hearing complaints, spinning sensation, change in taste or smell, or visual complaints.

In February 2008, the RBANS was reported as showing mild memory abnormalities consistent with a traumatic brain injury. A psychologist diagnosed PTSD. In April 2008, full neuropsychological assessment was normal and dramatically improved from the prior study, suggesting that the prior test results were not valid measures of his true cognitive status. There was no prior history of significant head trauma or headaches. He was in a vehicle in April 2006 when an improvised explosive device went off, but he did not sustain any injury. Past medical history was negative except for a history of alcohol abuse upon returning from Iraq treated in an alcohol abuse unit. There was no family history of migraine. On general physical examination, suboccipital digital pressure did not reproduce the headache. Neurological examination was normal. After discussion with his psychiatrist, the duloxetine was discontinued and he was started on venlafaxine for treatment of depression, PTSD, and prevention of headaches.

Questions

What are the classifications of the headaches and how do they compare with posttraumatic headaches in civilians? What treatments are available? Do the patients have post-concussion syndrome or could PTSD be responsible for many of the other symptoms?

All three of these patients sustained mild head injuries in blast trauma, two from rocket-propelled grenades and one from an improvised explosive device, which is the most common mechanism of mild head injury in Iraq. There are three types of blast injuries. A primary blast injury is the direct result of blast wave-induced changes in atmospheric pressure (barotrauma). A secondary blast injury results from objects put in motion by the blast hitting people (ballistic trauma). A tertiary blast injury involves people being forcefully placed in motion by the blast. Compare the civilian population of the United States where 75 percent or more of the head injuries are mild, and estimates of the relative causes of head trauma are as follows: motor vehicle accidents 45 percent, falls 30 percent, occupational accidents 10 percent, recreational accidents 10 percent, and assaults 5 percent.[3]

What are the classifications for the headaches? According to the criteria of the International Classification of Headache Disorders-2 (ICHD-2), Cases 1 and 2 meet the criteria for chronic posttraumatic headache attributed to mild head injury as follows: either no loss of consciousness, or loss of consciousness of <30 minutes' duration; Glasgow Coma Scale (GCS) 13; symptoms and/or signs diagnostic of concussion; headache develops within seven days after head trauma; and headache persists for more than months after head trauma with the exception of the GCS score, which is not available.[4]

However, Case 3 does not meet the criteria of onset within seven days after head trauma because the patient's best recollection is onset within one month.

Are the headaches due to trauma? The seven-day latency is arbitrary, particularly since the etiology of posttraumatic headaches is not understood but was chosen to include those patients with a high likelihood of having posttraumatic and not incidental new onset primary or other secondary headaches or preexisting headaches. However, in a male patient such as in Case 3 with no prior history of headaches, the probability of developing new daily persistent headaches in a one-month period is extremely low. Consider posttraumatic migraine where it would not be surprising if there was a latency of weeks or months for onset akin to posttraumatic epilepsy. Conversely, since migraine is a rather common disorder, the longer the latency between the trauma and onset, the more likely that the trauma may not have been causative. Case 3 does meet ICHD-2 for chronic migraine without aura and with aura.

What were his chances of developing migraine unrelated to the blast injury? The incidence of migraine in males under the age of 30 is 0.25 percent per year or, in this case, 0.021 percent per one month. Was the new onset migraine due to the mild head injury or coincidence? Three months seems a more reasonable latency for onset than does seven days.[5] Using ICHD-2 criteria, we further classify the headache types of Cases 1 and 2. Case 1 meets the criteria for episodic migraine without aura. Case 2 meets the criteria for chronic tension-type headache (you can argue that the constant photo- and phonophobia, which would exclude tension-type headache, are due to another disorder, postconcussion syndrome). Although Case 2 does not meet the ICHD-2 criteria for occipital neuralgia ("a paroxysmal jabbing pain in the distribution of the greater or lesser occipital nerves or of the third occipital nerve, sometimes accompanied by diminished sensation or dysaesthesia in the affected area"), on examination, he was found to have marked tenderness over bilateral greater occipital nerves. I administered bilateral greater occipital nerve blocks with lidocaine as part of his treatment based upon benefit reported in uncontrolled case series[6] and my own similar extensive experience. It is not certain whether the addition of a corticosteroid has additional benefit (there is no additional benefit to adding a corticosteroid when treating transformed migraine7). Case 2 was also taking oxycodone on an occasional basis for a neck injury. Many patients will also develop chronic pain from neck or other injuries, which may be treated with daily opiates.

Little is known about the prevalence, types, duration, and risk factors for posttraumatic headaches in US soldiers injured in Iraq and Afghanistan. In civilian studies, headaches are variably estimated as occurring in 30-90 percent of persons symptomatic following mild head injury,[8] which can range from mild to severe in intensity and have a variable frequency of occasional to daily. Paradoxically, headache prevalence and lifetime duration are greater in those with mild head injury compared with those with more severe trauma.[9] Posttraumatic headaches are more common in those with a history of headache,[10] which may be greater in Army personnel. In a recent survey with responses from 2,726 United States Army soldiers just returned from a one-year combat tour in Iraq, 17.4 percent of males and 34.9 percent of females reported a history consistent with migraine during the prior year.[11] This prevalence is much greater than the gender and age-matched population (six percent males, 20 percent females), which Theeler et al attribute to the psychological and physical stresses of a combat environment triggering migraine in susceptible individuals.

About 85 percent of posttraumatic headaches are of the tension type.[12] Temporomandibular joint injury and greater and lesser occipital neuralgia can be present independently or concurrently with another headache type. Pain referred from an injured C2-3 facet joint (which is innervated by the third occipital nerve), third occipital headache,[13] may produce a headache similar to occipital neuralgia. Tenderness over the C2-3 facet joint is suggestive of the diagnosis, which can be established by an anesthetic block. Neck injuries commonly accompany head trauma and can produce headaches. Recurring de novo attacks of migraine with and without aura can result from mild head injury, or preexisting migraine can be exacerbated. Many patients have more than one type of headache or have headaches with tension and migraine features. Rarely, mild head injuries can cause headaches due to subdural and epidural hematomas, low cerebrospinal fluid pressure (due to a cerebrospinal fluid leak through a dural root sleeve tear or a cribiform plate fracture),[14] hemorrhagic cortical contusions (due to subarachnoid hemorrhage), and carotid and vertebral artery dissections. There are rare reports attributing trauma to the onset of cluster headaches,[15] hemicrania continua,[16] short-lasting unilateral neuralgiform headache attacks with conjunctival injection, tearing, sweating, and rhinorrhea (SUNCT),[17] short-lasting unilateral headache with cranial autonomic symptoms (SUNA),[18] and

chronic paroxysmal hemicrania.[19] Supraorbital and infraorbital neuralgia can result from trauma around the orbit. Finally, in the presence or absence of a laceration, an aching, soreness, tingling, or shooting pain over the site of the original trauma can develop[20] that may persist for weeks or months but rarely for more than one year. All three of our military patients had chronic headaches present for at least 1.5 years.

How commonly do headaches persist in civilian studies? The percentage of patients with persistent headaches after the injury is as high as 78 percent[21] after three months, 35 percent after one year,[22] 24 percent after two years,[23] and 24 percent after four years.[24] There are few studies evaluating specific drug treatments for posttraumatic headaches.[25] The headaches are treated as the primary type along with physical therapy, biofeedback, and counseling as appropriate.[26] Medication overuse or rebound should be avoided, although the level of evidence demonstrating medication overuse headache in the post- traumatic population is anecdotal. Posttraumatic headaches can be especially resistant to treatment; population-based treatment studies are not available. As noted, the headaches are commonly co-morbid with PTSD, which is often treated with selective serotonin reuptake inhibitors (SSRIs). However, venlefaxine is also effective for PTSD[27] and may be more effective for prevention of posttraumatic headaches than SSRIs. While SSRIs are generally not effective for primary headache prevention, venlefaxine may be and has fewer side effects than amitriptyline.[28,29] Alternatively, amitriptyline may also be effective for the prevention of headaches and can be somewhat effective for PTSD.[30]

Although not studied for prevention of posttraumatic headaches, topiramate is an option since it is effective for prevention of episodic and chronic migraine and may also be effective for prevention of chronic tension-type headache.[31]

The Post-Concussion Syndrome and Controversy

The Quality Standards Subcommittee of the American Academy of Neurology defines concussion as a trauma-induced alteration in mental status that may or may not involve loss of consciousness.[32] The post-concussion syndrome usually follows mild head injury and comprises one or more of the following symptoms and signs: headaches, dizziness, vertigo, tinnitus, hearing loss, blurred vision, diplopia,

convergence insufficiency, light and noise sensitivity, diminished taste and smell, irritability, anxiety, depression, personality change, fatigue, sleep disturbance, decreased libido, decreased appetite, memory dysfunction, impaired concentration and attention, slowing of reaction time, and slowing of information processing speed.[12] Rare sequelae of mild head injury include subdural and epidural hematomas, seizures, transient global amnesia, tremor, and dystonia. The most common complaints are headaches, dizziness, fatigue, irritability, anxiety, insomnia, loss of concentration and memory, and noise sensitivity.[8,23] Loss of consciousness does not have to occur for the post-concussion syndrome to develop. Over 50 percent of patients with mild head injury will develop the post-concussion syndrome.[33]

Possible substrates for impairment following mild traumatic brain injury include diffuse axonal injury and release of the putative excitatory neurotransmitters acetylcholine, glutamate, and aspartate.[34] The pathophysiology of brain injury with blast trauma is not certain.[35-37] One controversial hypothesis is the transfer of kinetic blast energy through the vascular system to the brain. A subdivision into an early post-concussion syndrome and a late or persistent post-concussion syndrome when symptoms and signs persist for more than six months can be useful.[38] In the late group, psychologic factors and compensation issues may contribute to persisting symptoms. These patients are very similar to those with chronic pain syndromes and may have the interaction of chronic headaches and depression.[39] The post-concussion syndrome has been recognized for at least the last few hundred years and has been controversial for over 144 years.[40-42] For the minority of patients with persistent post-concussion symptoms, a variety of nonorganic explanations have been advanced including the following: psychogenic disorders (stress and pre-morbid neurosis, depression, and other types of personality and psychiatric disorders);[43] psychosocial problems;[44] chronic pain;[38] PTSD;[45] expectation of chronic symptoms;[46] base rate phenomenon (since many of the post-concussion symptoms are common in the general population, the base rate phenomena are misattributions of symptoms as due to the injury);[47] malingering;[48] and secondary gain due to litigation.[49]

Posttraumatic stress disorder, diagnosed in all three of these cases, commonly occurs following mild closed head injury and has some symptoms similar to the post-concussion syndrome. In a study of civilian patients with posttraumatic headache present for more than three months, nearly 30 percent were diagnosed with PTSD.[50] In Hoge et al's survey of US infantry soldiers returning from Iraq, of those reporting loss of consciousness, 43.9 percent met criteria for PTSD, as compared with 27.3 percent of those reporting altered mental status, 16.2 percent with other injuries, and 9.1 percent with no injury.[1] Their analyses suggest that the high rates of physical health problems reported by soldiers with mild traumatic brain injury three to four months after deployment are mediated largely by PTSD or depression but that mild traumatic brain injury was associated with headache among those who had lost consciousness.

When asked about their medical problems, all three of the patients told me that they had "TBI." Cases 1 and 3 were diagnosed with mild traumatic brain injury based upon the results of the RBANS but, in both cases, comprehensive neuropsychological assessment showed no evidence of cognitive impairment. The Army is starting to use the Automated Neuropsychological Assessment Metric for screening.[51] However, there is the potential for misdiagnosis of cognitive impairment of traumatic brain injury on screening batteries and comprehensive assessments due to numerous factors, including the materials used, cooperation and motivation of the patient, patient's personal reactions to their altered functioning (eg, the level of anxiety, depression, and anger), and the skill and clinical sensitivity of the examiner.[52]

Case 3 also had a history of alcohol abuse, which is common among returning soldiers following combat,[53] is co-morbid with PTSD, and may confound diagnoses of post-concussion syndrome. Soldiers should not be given an iatrogenic disease based upon misdiagnosis of a permanent brain injury with the expectation of poor recovery.[1,45] Even when cognitive impairment is present after the injury, rapid improvement to a normal level of neurobehavioral functioning typically occurs within three months of injury and persistent cognitive impairment is the exception.[54] Patients with multiple concussions over time may have some degree of subtle cognitive impairment.[55] The complaints of many soldiers with persistent posttraumatic headaches and other legitimate symptoms of post-concussion symptoms may be inappropriately minimized by health care professionals, fellow soldiers, their superiors, family members, and civilian employers. They may have sustained a mild head injury with minimal if any external trauma and seem "fine."

One possible explanation for this skepticism is that for many people, their knowledge of the sequelae of head injuries is entirely the product of "movie magic," what I have termed the "Hollywood head injury myth."[56] In detective, boxing, martial arts, combat, westerns, and action stories, kicks, punches, blows, and blasts (which in reality would be fatal or near fatal) are delivered to the face and head in rapid succession and then brushed off by the combatants after eliciting only a grimace and a grunt. Actors appear in the next scene with no symptoms and maybe a bandage over their eye. Not only is head trauma not taken seriously in cartoons and slapstick routines in movies of any vintage; it is considered funny (consider the Road Runner and the Three Stooges).

Our actual experience is miniscule compared with the thousands of simulated head injuries the average person wit-

nesses in the movies and on television. Soldiers themselves might buy into this mythology and think of themselves as invincible Rambos. Thus, education about mild traumatic brain injury and headaches is an important part of the treatment. Physicians can also use the increasingly familiar examples from sports (such as boxing, football, and hockey and well-known athletes who had to retire due to post-concussion syndrome such as Troy Aikman and Pat La Fontaine) which, ironically, may have a certain credibility from the media reports and the fascination with elite athletes.

Future Directions

Prospective series of soldiers with posttraumatic headaches would be helpful to determine whether the onset, type, and persistence of headaches are any different from those seen in civilians. In addition to the uncertain risk of late post-concussion syndrome and the risk of PTSD, it is not certain if or how headaches may differ in those who sustain mild traumatic brain injury from blast trauma. It will be difficult in many cases to determine what types and whether posttraumatic headaches are due to primary blast injuries alone or attributable to the additional trauma sustained in secondary and/or tertiary blast injuries. Prospective studies of treatment of all types of posttraumatic headaches and studies of medication overuse headache are needed to add to the dearth of information. Additional information about the impact of the headaches (which likely have a sizeable effect on troop readiness, return to civilian work and study, and quality of life) would also be of great interest. Certainly, basic science research is essential to better understand mechanisms of brain and psychological trauma and to improve treatment in the future. Recognizing the magnitude of the problem, the US Congress provided the Department of Defense with $150 million for research on traumatic brain injury and $151 million for research on PTSD during fiscal year 2007 (the abstracts of funded research programs are available at cdmrp.army.mil/phtbi/default.htm).[35] Currently, the Department of Veteran's Affairs recognizes that resources are inadequate to deal with the number of patients with sequelae of traumatic brain injuries.[57]

Given the great number of patients with posttraumatic headaches and the likelihood of chronicity in some, growing

numbers will be seen by civilian physicians in the years to come as the soldiers are discharged and enter civilian life and some seek care outside of veteran's facilities.[51] In 1962, speaking to the Army's 1st Armored Division, which had been secretly moved into position during the Cuban missile crisis, President Kennedy read a poem that, according to legend, was found many years previously in a sentry box in Gibraltar: "God and the soldier/all men adore/In time of danger/and not before./When the danger is passed/ and all things righted/God is forgotten/ and the soldier slighted."[58]

Hopefully, Congress and the Departments of Defense and Veteran's Affairs will continue to recognize the urgency of providing for the medical needs of our soldiers and veterans which include posttraumatic headaches. **PN**

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