Behavioral and Psychiatric Comorbidities of TBI

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Abstract

Traumatic brain injury (TBI) is associated with a variety of behavioral consequences, including symptoms of depression, anxiety, aggression, and impulse control and overlaps with many of the symptoms of post-traumatic stress and post-traumatic stress disorder. There are many challenges to researchers and clinicians, including heterogeneity of the injury, distinguishing premorbid characteristics from the consequences of the TBI, lack of specificity in diagnostic criteria, and the absence of systematic therapeutic trials. In this chapter, we present an overview of the literature on psychiatric and behavioral consequences of TBI, highlighting those studies that investigate the incidence of these conditions, contribution of premorbid functioning to subsequent symptoms, and characteristics of mild TBI (frequently referred to as concussion) that provide clues to distinguishing it from other psychiatric comorbidities. Our analysis of the available literature suggests that in some, but not all cases, TBI may diminish inhibitory

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control over certain behaviors while in others, there may be an exacerbation of clinical expression of psychiatric symptoms. Treatment needs to consider whether there is a unique sensitivity to adverse events in patients who have suffered a TBI and prospective trials should be encouraged.

Keywords
Impulsive aggression • Post-concussion syndrome • Suicide • Post-traumatic stress disorder • Depression • Traumatic brain injury • Military • Veteran • Aggression

Introduction

An estimated 1.7 million Americans sustain a traumatic brain injury (TBI) each year (Faul et al. 2010) and over 5.3 million (2% of the US population) are currently living with a disability from TBI that requires assistance in activities of daily living (Brain Injury Association of America 2009). Men are 1.5 times more likely to sustain a TBI than women, and military activities increase the risk of TBI (Schwab et al. 2007). Approximately 35.2% of TBIs are caused by falls, 17.3% by motor vehicle accidents, 16.5% by being struck by something or striking one's head against something, and 10% by assaults (Faul et al. 2010). Among military personnel serving in a warzone, explosive blasts are the leading cause of TBI (Champion et al. 2009). TBI is associated with a variety of subsequent neurological disorders, including epilepsy, Alzheimer's disease, and Parkinson's disease (National Institute of Neurological Disorders and Stroke 2002). TBI has also been associated with a number of psychiatric and behavioral effects, including the development of mood and anxiety disorders, aggressive behavior, and post-traumatic stress (PTS) and post-traumatic stress disorder (PTSD).

TBI Psychiatric and Behavioral Comorbidities

Development of mood and anxiety disorders has been reported following TBI with anxiety and depression occurring most frequently in mild TBI (mTBI) (described below). Variation in the frequency of these disorders has been reported across studies. Some research suggests that depressive symptoms are more frequent than those associated with anxiety (Deb and Crownshaw 2004) though depression may be more likely to remit (Hibbard et al. 1998). An estimated 6–77% (as reported in Horner et al. 2008) of those with TBI report post-injury depression, although Levin et al. (2001) found that the prevalence of depression following TBI (17%) did not differ from that experienced following general trauma (6%). The wide range of prevalence estimates is believed to result from variation across studies in injury severity, method of diagnosis (for TBI and depression), and other methodological issues (Horner et al. 2008). The problem is further complicated by an overlap in symptoms between TBI and depression (e.g., sleep disturbance). Prevalence of anxiety after TBI has been reported as high as 70%, but a meta-analysis found the prevalence of anxiety disorders following TBI to be 29%, with 23% for mTBI (Moore et al. 2006). Levin et al. (2001) found that the prevalence of depression following TBI did not differ for mild (18%) and moderate (11%) TBI. Variation also occurs based on anxiety disorder (Deb and Crownshaw 2004; Fann et al. 1995). Substantial comorbidity may occur (Moore et al. 2006); for example, Hibbard et al. (1998) found that 44% of their sample with TBI reported two or more Axis I disorders an average of 8 years following injury. Among 1,560 adults who completed telephone interviews 1 year following TBI, approximately 40% reported clinically significant symptoms of mood or anxiety

disorders (Horner et al. 2008). Most work with the development of anxiety disorders involves PTSD, which is described in detail below.

The examination of co-occurring depression and TBI has been complicated by a variety of methodological factors, including variation across studies in sample characteristics, severity and definition of TBI and depression, and assessment instrument (Horner et al. 2008). Studies examining risk factors for depression after TBI have yielded mixed results (for discussion, see Levin et al. 2001; Rosenthal et al. 1998; Moldover et al. 2004); for example, some have found that older age (Levin et al. 2005) and female gender (Glenn et al. 2001) significantly predict post-injury depression, whereas others have reported that these were not significant predictors (Mooney et al. 2005; Seel et al. 2003; Hibbard et al. 2004; Rapoport et al. 2003). Although it is unclear what proportion of individuals with TBI have mood and anxiety disorders prior to their injury, in general, 6.7% of individuals over the age of 18 in the USA experience major depression and 18% experience an anxiety disorder each year (Kessler et al. 2005). With the exception of suicide-related TBI, it is unclear if psychiatric disorders pose a risk for TBI, though some studies have found that premorbid psychiatric disorders, such as alcohol abuse, anxiety, and depression, increase the risk of post-injury depression or anxiety (Horner et al. 2008; Hibbard et al. 1998; Jorge and Robinson 2002; Moldover et al. 2004). Depression following TBI has been associated with poorer cognitive functioning (Chamelian et al. 2006; Keiski et al. 2006) and poorer psychosocial functioning (Draper et al. 2007; Hibbard et al. 2004) than reported by those without depression. It has also been associated with a failure to recover as expected following TBI (Mooney et al. 2005).

That said, the etiology of these deficits is unclear; negative outcomes such as poor psychosocial functioning have been hypothesized to be the cause (Bay et al. 2008) and the consequence (Draper et al. 2007) of depression. It is also possible that for some individuals, depression following TBI may reflect an organic etiology (Levin et al. 2005) associated with the neurological issues associated with TBI; for example, lesions in the regions such as the left dorsofrontal cortex, left basal ganglia, or right posterior hemisphere have distinguished depressed and nondepressed patients with TBI (Rosenthal et al. 1998). Differentiating a diagnosis of depression from other issues following TBI is complicated (Jorge and Robinson 2002), as psychiatric symptoms following TBI, such as irritability and anger, are common to PTSD, depression, aggression, and some neuroanatomical lesions. It is also counterintuitive that symptoms of depression and anxiety are more common among those with mild than those with more severe injuries, though lack of awareness associated with severe TBI has been hypothesized as a possible explanation (Moldover et al. 2004). Taken together, this research suggests that the development of psychiatric issues following TBI may represent the developmental concept of *equifinality*, in which the same outcome (e.g., depression) may result from disparate causes and circumstances, such as premorbid dysfunction, poor psychosocial functioning after TBI, or nature and anatomic location of TBI.

Just as depression and other psychiatric conditions are associated with an increased risk of suicide in soldiers returning from combat deployments (Pietrzak et al. 2009; Tanielian and Jaycox 2008), a history of combat-related TBI must also be considered when assessing suicide risk of returning soldiers and veterans. In their review of the relation between TBI and suicidality, Simpson and Tate (2007) conclude that those recovering from TBI have a three- to fourfold increased risk of committing suicide relative to the general population, and that this increase appears to remain constant at least through the first 15 years post-injury. A recent Danish population-based study including nearly 150,000 subjects examined the relation between TBI severity and suicide risk (Teasdale and Engberg 2001). While those with severe TBI, as defined by the presence of cerebral contusions or intracranial hemorrhages, demonstrated the highest risk of suicide (i.e., 4.1 times increased risk) relative to the general population, those classified with a concussion still demonstrated an increased risk of suicide (i.e., three times increased risk). It has been suggested, however, that the increased

rates of suicide for mTBI are likely related to post-injury and/or concomitant psychosocial factors, whereas suicidality following severe TBI is likely related to the injury and subsequent sequelae (Simpson and Tate 2007). Given that the vast majority of combat-related TBIs from the current wars in Iraq and Afghanistan are classified as mild (Tanielian and Jaycox 2008), the relation between TBI severity and suicidality must be carefully considered in order to fully appreciate the potential implications for health management of returning military personnel and veterans. Although causal attribution cannot be drawn from correlational studies, the possibility that such an association exists between combat-related concussion and suicide has extremely important implications for mental health screening and suicide prevention efforts given the relatively high incidence of history of concussion in returning military personnel (estimated to be between 5 and 20% of service members in deployed units [Tanielian and Jaycox 2008]). Future attempts to further explicate the complex relation between concussion and suicide must take into account the various shared risk factors between TBI and suicidality (e.g., young age, male gender, substance abuse, aggression/impulsivity) to determine the extent to which concussion uniquely contributes to suicide risk (Wasserman et al. 2008).

Aggressive behavior following TBI complicates rehabilitation (Nott et al. 2006), is a concern for caregivers (Johnson and Balleny 1996), and has been associated with lower psychosocial functioning 10 years following injury (Draper et al. 2007). The prevalence of aggression following TBI differs based on definition/severity of TBI, definition and assessment of aggression, reporting period, reporter (self, caregiver, staff), sample, and timing of assessment. Aggression following TBI may be expressed as agitation (Kim 2002; Nott 2006), intimate partner violence (Arango-Lasprilla et al. 2008; Marsh and Martinovich 2006), suicide attempts (Oquendo 2004), sexual violence or sexual disinhibition (DelBello 1999; Kelly et al. 2008), verbal aggression (Dyer et al. 2006), or physical aggression (Alderman 2007). As in the general population, verbal aggression typically is more frequent than physical aggression (Kelly et al. 2008; Dyer et al. 2006). The frequency of aggression following TBI has ranged from 11 to 96% based on the form of violence and the assessment instrument used (as reported in Tateno et al. 2003). Using the Overt Aggressive Scale (OAS, Yudofsky et al. 1986), Tateno et al. (2003) found that 33.7% of patients with TBI compared to 11.5% of patients without TBI reported aggressive acts in the 6 months following their injury. The frequency also varies based on the sample, severity of TBI, and duration of time since injury, with more agitation and aggression reported soon after the injury (Nott et al. 2006). For example, using the Overt Aggression Scale—Modified for Neurorehabilitation (OAS-MNR, Alderman et al. 1997), Alderman (2007) reported 5,548 episodes of aggression perpetrated by 108 patients with severe neurological damage over 14 days on an inpatient unit. The authors noted that the episodes were triggered by staff prompts or erupted with no apparent provocation. Using the OAS, Baguley et al. (2006) reported that rates of aggression among patients with moderate to severe TBI fluctuated over the 5 years following injury, but that at any given time approximately 25% of patients with TBI were expressing "severe" aggression. Johnson and Balleny (1996) reported that among individuals who survived severe TBI and were followed for 3 years, 55% of those whose injury occurred more than 18 months ago compared to 13% of those whose injury occurred less than 18 months ago had verbal or physical aggression as reported by family members; however, severity of behavioral problems (aggression and other problems) was not significantly correlated with the severity of head injury. Using the Buss Perry Aggression Scale (BPAQ, Buss and Perry 1992), Dyer et al. (2006) compared a sample of participants with TBI to those with spinal cord injury (SCI), and those without injury on measures of anger, aggression, and impulsivity 10 years following injury. Participants with TBI (severity not specified) reported more impulsivity, anger, and verbal aggression than those with SCI. When caregiver's reports were used, participants with TBI were also rated as more verbally aggressive than those with SCI. TBI has also been associated with anger and aggression among forensic samples. Slaughter et al. (2003) randomly selected 69 inmates

of a county jail of whom 87% (67% mild, 33% moderate/severe) reported a lifetime history of TBI and 36% (80% mild, 20% moderate/severe TBI) reported a TBI in the past year. Based on the Brief Anger and Aggression Questionnaire (BAAQ, Maiuro et al. 1987), more extreme anger and aggression were reported by those with TBI than those without. Similarly, using the index offense of record, Brewer-Smyth et al. (2004) found that women incarcerated for a violent crime had more traumatic brain injuries with loss of consciousness in their lifetimes than those incarcerated for a nonviolent crime; however, only one participant convicted of a violent crime reported severe brain injury.

TBI and aggression has been examined among military samples; Vietnam veterans with TBI from penetrating brain wounds reported more aggression and violence than those without TBI (Grafman et al. 1996). At the time this chapter was written, the association between TBI and aggression had not been examined systematically among military personnel serving in Operation Enduring Freedom and Operation Iraqi Freedom, but the consequences of TBI are a concern given the proliferation of improvised explosive devices (IEDs) used in these conflicts. Among the personnel serving in Iraq, it is estimated that approximately 11% meet the criteria for mild TBI through surveys (MHAT V 2008). In a similar vein among a sample of 2,525 Army infantry soldiers serving in Iraq, Hoge et al. (2008) reported that 4.9% reported loss of consciousness and 10.3% reported altered mental status. Although survey data provides clues about the possible scope of the problem, survey reports of TBI symptoms and criteria are not necessarily confirmed by a clinical assessment and, therefore, may not accurately estimate prevalence.

Aggression following TBI often co-occurs with other post-injury psychiatric and psychosocial issues, such as anger (Dyer et al. 2006), hostility (Oquedo et al. 2004), impulsivity (Dyer et al. 2006), depression (Baguley et al. 2006), PTS, PTSD (Bryant 2001), and substance abuse (Draper et al. 2007). Though premorbid factors such as alcohol use may influence the presence (TBI vs. no TBI, Oquedo et al. 2004) and etiology (i.e., whether due to violent or nonviolent causes, Schopp et al. 2006) of TBI, these factors seem to be less predictive of post-injury aggression than the other post-injury psychosocial issues. For example, in a 5-year follow-up study, age and depressive symptoms, as rated with the Beck Depression Inventory (Beck 1988), were the only factors that predicted aggression at 6-, 24-, and 60-month follow-up (Baguley et al. 2006). The disorders and symptoms co-occurring with aggression following TBI are similar to those in non-TBI samples: Anger and hostility have been associated with PTSD (Orth and Wieland 2006) and irritability and aggressive outbursts have been observed among depressed patients (Haller and Kruk 2006). Impulsivity and substance use, specifically alcohol use, have been associated with a variety of violent acts, and are thought to be associated via shared biological substrates or altered social information processing (Hoaken and Steward 2003; Moeller et al. 2001). The comorbidity may also be an artifact of the diagnostic criteria for Axis I and Axis II disorders, which may include irritability, anger, impulsivity, and aggression (APA 2000). Given these similarities, it is unclear what distinguishes TBI aggression from that observed among non-injured individuals and consequently what novel aspects for TBI-aggression treatment would need to be considered. Because TBI involves lesions to the brain, usually in the frontal lobes, it is possible that specific executive function deficits experienced by individuals with TBI and aggression may provide clues to understanding the phenomenology and treatment of this behavioral problem. Group differences on executive deficits have been examined among individuals with TBI based on the etiology of their injury (violent vs. nonviolent), with results suggesting that premorbid factors, and not the nature of injury, influence the outcome following TBI (Machamer et al. 2003; Schopp et al. 2006). In a study of sex differences in executive functions among individuals with TBI, women outperformed men on neuropsychological assessments, but premorbid factors and factors related to the injury were most predictive of neuropsychological functioning among men and women (Niemeier et al. 2007). When comparing men with and without TBI who were receiving court-ordered treatment for intimate

partner violence, men with TBI had poorer executive functioning and lower post-injury IQ than the non-TBI batterers (March and Martinovich 2006). Underscoring the importance of considering premorbid differences, these studies do not yet definitively establish how executive functions may be associated with aggression post-TBI.

Among aggressive individuals without TBI, studies of executive deficits have primarily involved examining neuropsychological differences between those with impulsive versus premeditated subtypes of aggressive behavior. Impulsive aggression is characterized as a hair-trigger response to a threat with a behavioral loss of control, and premeditated aggression is a planned act usually carried out for a specific purpose or goal (Barratt et al. 1991; Barratt et al. 1997b; Stanford et al. 2003). The neuropsychological correlates of impulsive aggression include specific language and executive function deficits, particularly verbal performance that involves more complex analyses (Villemarette-Pittman et al. 2003; Miller et al. 2008). Trauma survivors with impulsive aggression also evidenced alexithymia, which is an inability to recognize and articulate one's emotional experience, suggesting that verbal deficits may also be associated with emotional awareness deficits (Teten et al. 2008). The pattern of executive function deficits and other characteristics, such as similar neuroanatomical lesions (Greve et al. 2002), lack of self-awareness (Dyer et al. 2006), and language difficulties (Wood et al. 2006), suggests that post-TBI aggression is likely to be the impulsive subtype of aggression. Moreover, impulsive aggression is overrepresented among veterans with PTSD such that in one study over 70% of male veterans with PTSD compared to 29% of those without PTSD reported impulsive aggression (Teten et al. 2010). The frequent co-occurrence of PTSD and TBI (described below) may provide further evidence that post-TBI aggression is primarily impulsive aggression. Characterizing this problematic behavior would provide a framework for conceptualizing aggressive behaviors co-occurring with TBI and introduce novel approaches to treatment, such as anticonvulsants (Stanford et al. 2005) and cognitive behavioral therapy (McCloskey et al. 2008).

Orbitofrontal regions have been associated with alterations in behavior including impulse control since reports of the prototypical patient with frontal injury (Damasio et al. 1994; Stein and Moeller 2005). Studies specifically of impulsive aggression among individuals with TBI suggest associations with lesions of the ventromedial prefrontal cortex (Greve et al. 2002) using neuropsychological testing sensitive to this region (e.g., Revised Strategy Application Test). One difficulty in generalizing subtypes of aggression and their relationship to neuroanatomical underpinnings from the extensive literature on aggression in TBI is that impulsivity and impulsive aggression are often equated, whereas, at least in highly impulsive individuals with antisocial behavior, the degree of impulsivity does not itself distinguish those with predatory vs. impulsive aggression, but the existence of language impairments and parietal electrophysiological processing differences did distinguish them (Barratt et al. 1997a). This research suggests that impulsivity alone is not sufficient to cause an individual to become impulsively aggressive and it is likely that additional deficits that may be associated with TBI are important to this condition. Initial work in long-term survivors of severe TBI with impulsive aggression did not demonstrate these specific neuropsychological abnormalities, suggesting that there may be alternative pathways to impulsive aggression (Greve et al. 2001). However, in this study, premorbid functioning was associated with impulsive aggression, suggesting that it may be difficult retrospectively to delineate the specific contribution of the TBI to the behaviors of interest.

The Relationship Between Mild TBI and PTSD

There is considerable interest in the potential relationship between mTBI and PTSD given the context in which both occur during military deployment. To better understand this issue, a background on mTBI is provided with an emphasis on those

characteristics that complicate the separation of the consequences of mTBI from PTSD.

Epidemiology and Classification of mTBI with a Focus on Symptoms

Approximately 70–90% of head injuries are classified as mild in nature (Kraus and Nourjah 1988; Sosin et al. 1996). Incidence rates of mTBI in the civilian population, however, are widely considered to be underestimated since approximately 25% of individuals suffering an mTBI do not seek medical attention (Centers for Disease Control and Prevention 2003). As with moderate to severe TBI, the rate of mTBI is greatest in males and young adults and the most common mechanisms include motor vehicle accidents and falls (Cassidy et al. 2004). Similar to the civilian population, the majority of military TBIs are mild. In fact, the incidence of mTBI in contemporary warfare may be on the rise due to the prevalent use of explosive munitions (i.e., IEDs and mines). In one study, 22.8% of soldiers returning from the Iraq War were noted to have a history of at least one mTBI during deployment, most of which were mild in nature (Terrio et al. 2009). It is estimated that by 2008 as many as 300,000 soldiers had suffered an mTBI in the wars in Iraq and Afghanistan (Tanielian and Jaycox 2008), although this may be an inflated estimate based on the lack of validity of the diagnostic criteria used to derive the approximation (Hoge et al. 2009). These issues are important to address as the definitions and context affect our understanding of the psychological and psychiatric effects of TBI.

Characterization of the personal and economic impact of mTBI is complicated by the lack of uniformity in the definition (Centers for Disease Control and Prevention 2003). The diagnosis of mTBI is based on the assessment of acute injury severity characteristics immediately following an injury to the head resulting from blunt trauma and/or acceleration or deceleration forces. Most contemporary mTBI classification schemes require a period of impaired consciousness (including loss of consciousness), memory dysfunction for a period of time surrounding the injury (i.e., retrograde or post-traumatic amnesia), or neurological or physiological dysfunction (e.g., seizures, lethargy, and vomiting) proximal to the time of injury. A consensus group associated with the American Congress of Rehabilitation Medicine (ACRM) defined mTBI as any one of the following: any period of loss of consciousness, any loss of memory for events before or after the accident, any alteration in mental state at the time of the accident, or any focal neurological deficits that may or may not be transient (ACRM 1993). Historically, this was an important departure from previously held notions that an observed loss of consciousness was required to establish a history of mTBI (Ruff 2005), although it should be noted that other diagnostic systems may require a loss of consciousness to establish a history of mTBI (Diagnostic and Statistical Manual of Mental Disorders-IV-TR 2000). In order to create a clearer boundary between those with mild versus those with moderate to severe TBI, the ACRM consensus group suggested that those with mTBI experience a loss of consciousness of no greater than 30 min, experience a post-traumatic amnesia of no greater than 24 h, and should have a Glasgow Coma Scale (GCS) score of 13 or greater within 30 min after their injury. The ACRM definition of mTBI has gained traction in the research and clinical community over the last 15 years and has been adapted by other health agencies (Centers for Disease Control and Prevention 2003).

Various subclassifications of mTBI have been also proposed which take into account the length of loss of consciousness or altered mental status as in the case of sports-related concussion (American Academy of Neurology 1997) or the presence or absence of positive neuroimaging findings (Levin et al. 1987). The American Academy of Neurology classification system specifies three grades of concussion: Grade 1 being defined by transient confusion, no loss of consciousness, and concussion symptoms or mental status abnormalities that resolve in less than 15 min; Grade 2 being defined by transient confusion, no loss of consciousness, and concussion symptoms or mental status abnormalities lasting more than 15 min; and Grade 3 being

defined by any loss of consciousness. In the context of sports, the American Academy of Neurology recommends that only those players experiencing a Grade 1 concussion who demonstrate a normal sideline assessment (while at rest and with exertion) should return to play the same day. Players with persisting symptoms after a Grade 1 concussion and those with Grade 2 or 3 concussions should not return to play on the same day. In order to determine readiness to return to play and overall neurologic status after a concussion, the American Academy of Neurology also advocates for repeated observation and assessment over the course of recovery (American Academy of Neurology 1997).

Although general consensus has been reached regarding the diagnostic criteria for mTBI, several shortcomings of the diagnostic system have been identified. Without direct observation from trained bystanders or emergency medical technicians, there is no way to verify that the minimal criteria for mTBI were present at the time of the injury (i.e., brief period of altered mental status). Despite the apparent fallibility of relying on retrospective, self-reported changes in mental status to establish a history of mTBI, this is considered standard practice in diagnosing mTBI (Alexander 1995; Ruff 2005) and has been recommended by the Centers for Disease Control in cases of non-medically attended TBI (Centers for Disease Control and Prevention 2003). Additionally, alcohol and recreational drugs present at the time of injury or therapeutic drugs administered in the immediate post-injury period can cause alterations in consciousness and perturbations in autobiographic memory, all of which can be mistaken for injury-related alterations in mental status (Ruff 2005).

Diagnosing a history of combat-related mTBI presents even greater challenges. First, a brief period of altered mental status may go unreported in the midst of life-threatening events like close proximity to a detonated IED, an event that has been exceedingly common during the Iraq and Afghanistan conflicts (Gondusky and Reiter 2005; Terrio et al. 2009). Second, symptoms related to mTBI may be overlooked in the presence of other combat-related injuries that require immediate medical attention (e.g., traumatic amputations, lacerations, and burns). These first two diagnostic issues would result in an underidentification of a history of mTBI. Third, common diagnostic criteria with reasonable specificity in the civilian population, such as feeling dazed or confused, may result in insufficient levels of specificity when applied to injuries incurred during combat deployments. Conversely, a brief period of confusion or disorientation may represent a psychological reaction to an unexpected, highly stressful event rather than a manifestation of underlying brain injury. The third diagnostic issue would, thus, result in an overidentification of a history of mTBI.

Although there is a rich literature evaluating the sequelae of TBI and a general sense of agreement in terms of outcomes following moderate to severe TBI, there is less consensus in terms of outcomes following mTBI. Many studies evaluating the impact of mTBI have had widely different findings (e.g., Binder et al. 1997; Rimel et al. 1981) and this, in turn, is likely related to the inherent methodological difficulties in studying this population. For example, many people do not seek treatment following mTBI as there is likely perception that mTBI will have few meaningful consequences. This sharply contrasts against the established and adverse consequences that are associated with moderate to severe TBIs. For those patients that do seek emergent care, a GCS may be obtained, but this instrument is not suited to assess the more subtle cognitive changes that are likely to occur following an mTBI (Lezak et al. 2004). Historically, the lack of agreement about the mTBI classification has made comparisons between studies difficult and has the potential to skew data in a variety of ways. In both clinical and research settings, comprehensive neuropsychological evaluations in the period following mTBI are typically not undertaken and even fewer evaluations are likely to occur at more distal time points. For this reason, comparatively less is known about the impact that mTBI has on neuropsychological functioning relative to moderate to severe head injuries. Even the most promising prospective studies are often hampered by significant selection biases (i.e., oversampling

from emergent care settings and attrition in longitudinal designs), less effective use of appropriate controls, and not controlling for potential confounds (Carroll et al. 1994). Despite these limitations regarding mTBI, there are several tenets that can be drawn from the literature and we address these below.

Tenet 1: Injury Severity is Related to Outcome

In a series of widely recognized studies (Dikmen et al. 1995a, b), it was demonstrated that both cognitive and functional outcomes following head injury are related to severity of TBI, with mTBI having better outcomes and severe TBI having the worst outcomes. The strength of these studies is that a large number of patients ($N=436$), with various injury severities, completed assessments at 1 month and 12 months post-injury with minimal attrition. In addition to the within-subjects comparisons, their patients were also compared to a matched trauma control sample ($N=132$) also evaluated at 1 month and 1 year post-injury. Patients with a history of TBI increasing in severity from moderate to severe, as measured by increased time to follow commands (the motor score from the GCS), had an incrementally greater chance of having more widespread and persisting neuropsychological and functional impairments 1 year post-injury. Among patients with a history of mild head injury (TFC < 1 h), however, baseline performance on neuropsychological testing was similar to trauma controls at 1 month (Dikmen et al. 1995a) and the vast majority were noted to experience good psychosocial outcomes 1 year post-injury (Dikmen et al. 1995b).

mTBI can occur in the context of other factors such as positive CT findings (e.g., "complicated mTBI" [focal brain lesion, skull fracture, etc.]) and this may further cause difficulties in recovery. In keeping with the inverse relationship between injury severity and outcome, patients with a history of complicated mTBI appear to have poorer cognitive function within the first month following mTBI (Williams et al. 1990). Kwok et al. (2008) evaluated complicated mTBI patients ($N=31$) with GCS scores ranging from 13 to 15 with abnormal CT scans (skull fractures, hematomas, subarachnoid hemorrhage) and found persisting impairments in attention at 3 months. The performance of patients with a history of complicated mTBI has also been compared to the performance of patients with a history of moderate TBI. In this study, patients with a history of complicated mTBI ($N=102$) and moderate TBI ($N=127$) underwent neuropsychological testing at discharge from a rehabilitation facility and after 1 year. At both time points, there were noteworthy similarities between the mTBI and moderate TBI groups, with mTBI patients evidencing less severely impaired cognitive processing speed. Both groups were also noted to have incomplete recovery in functional status at the 1 year follow-up, with no differences found between the groups (Kashluba et al. 2008). There remains some debate as to whether complicated and uncomplicated mTBI patients should be pooled together in studies, or if those with complications should be viewed as a separate diagnostic group.

Tenet 2: Symptoms Immediately Following an mTBI Are Varied and May Occur Across Cognitive, Physical, and Affective Domains

Self-report symptom inventories (e.g., Rivermead Post-Concussion Symptoms Questionnaire [RPQ], Standardized Assessment of Concussion [SAC], etc.) have been utilized in the period following mTBI and in a variety of different settings (Potter et al. 2006; McCrea et al. 2000; see Alla et al. 2009 for review of various inventories). The most frequent subjective complaints following mTBI include headache, dizziness, irritability, poor concentration, fatigue, and memory loss, with the majority of symptoms resolving within 1 month (Ryan and Warden 2003; McCrea 2008). Across multiple factor analytical studies, these varied symptoms have been noted to load onto cognitive, physical, and affective clusters, although there is some debate as to whether a single factor that some label "concussion" better accounts for the symptoms (Potter et al. 2006; Smith-Seemiller et al. 2003; Piland et al. 2006).

A similar pattern of symptoms has also been described in the sports concussion literature, with headache, dizziness, sensitivity to light, and cognitive difficulties (e.g., slowed cognitive processing speed, memory difficulty) reported in the period following mTBI (McCrea 2008). In a large sample of college football players prospectively evaluated prior to mTBI and at several time points post-injury, more severe symptoms were noted immediately following the mTBI and patterns of symptom recovery emerged as early as 3 h post-injury (McCrea et al. 2003). Within 7 days post-injury, there were no differences relative to baseline scores or matched controls. It is important to note that there are noteworthy differences between the general population and athletes evaluated in the sports concussion literature, as "motivation to return to play" in the latter may result in underreporting of mTBI symptoms. This likely explains the interesting finding that athletes report faster resolution of symptoms relative to those in the general population, as 85% of athletes reported full symptom recovery within 1 week and fewer than 3% reported symptoms beyond 1 month (see NCAA Concussion Study; McCrea et al. 2003) in contrast to an appreciably higher proportion reported in the non-sports concussion literature (e.g., 8–33%; Lees-Haley et al. 2001; Ryan and Warden 2003; Rimel et al. 1981).

Tenet 3: The Vast Majority of mTBI Patients Will Experience Full Cognitive Recovery Within 3 Months

It is generally accepted that among patients sustaining an mTBI the majority of symptoms resolve during the first week following the injury, with nearly complete resolution of most symptoms for most patients occurring within the first 3 months following the injury (e.g., Dikmen et al. 1986; Levin et al. 1987; Schretlen and Shapiro 2003). Consistent with this, the World Health Organization (WHO) has concluded the best evidence suggesting: "there are no mTBI-attributable, objectively measured, cognitive deficits beyond 1–3 months' post-injury in the majority of cases" (Carroll et al. 1994). The WHO based their conclusions on a critical review of the literature and parallels the findings from meta-analytic studies evaluating patient performance on cognitive testing following mTBI. Binder et al. (1997) included studies evaluating the cognitive functioning in adults (11 studies, 314 patients, 308 controls) at least 30 days following mTBI. The overall effect size was significant, but small ($d = 0.18$), although a more conservative g statistic was notably smaller and not significant ($g = 0.07$). Patient performance on cognitive testing was further analyzed using neuropsychological domains of attention, memory acquisition, and performance skills (only three domains were examined across enough of the studies to allow for meaningful analyses). Among these three, only attention emerged as impaired following mTBI with a small effect size ($g = 0.17$). The authors also found it worthwhile to determine the positive and negative predictive values (PPV and NPV) of neuropsychological testing in patients with mTBI in the reviewed studies, as the detection of more subtle cognitive difficulties is more difficult than obvious neurological impairments. Given the low prevalence of persisting attention impairments based on their data (5%), the likelihood of accurately classifying mTBI with abnormal performance on cognitive measures, even with unrealistic sensitivity and specificity for the cognitive instruments (e.g., 0.9), was small at 0.32, and with smaller sensitivity and specificity test values the PPVs continued to decrease. In contrast, the NPV of these cognitive measures was consistently high at all sensitivity and specificity levels (>0.98), suggesting much higher accuracy when diagnosing no persisting brain injury following mTBI based on neuropsychological measures.

More pronounced impairments in attention following mTBI have been reported in recent prospective studies (e.g., Kwok et al. 2008; Landre et al. 2006). Landre et al. (2006) found mTBI patients ($N = 37$) to perform worse on measures of vigilance, attention, and memory relative to trauma patients ($N = 32$) approximately 5 days post-injury. The effect sizes for these group differences were in the moderate to large range. Interestingly, both mTBI and the trauma controls reported few concussion symptoms following

their injury and pain levels were controlled for and found not to be associated with cognitive performance in either group. That more pronounced cognitive impairments are found in some studies (e.g., Landre et al. 2006) but not others (e.g., Binder et al. 1997) may, in part, be related to the timing of neuropsychological evaluations relative to the onset of the head injury. For example, in the Binder et al. (1997) meta-analysis, only studies evaluating cognitive performance 3 months post-injury, or later, were included, whereas other studies may focus on patient cognitive performance within the first or second week following mTBI. Consistent with this, Schretlen and Shapiro (2003) examined the effect of mTBI on cognitive performance across different time points post-injury. In their meta-analysis, cognitive performance varied as a function of time, with a significant medium effect size reported among patients tested during the first 6 days post-injury ($d = 0.41$, mTBI patients performing at the 33rd percentile of matched controls) and a smaller but significant effect size reported among patients tested 7–29 days post-injury ($d = 0.29$). Patients tested 1–3 months post-injury, and after 3 months post-injury, demonstrated no differences from controls. Belanger et al. (2005) demonstrated a similar finding, with small performance declines across seven of eight cognitive domains for mTBI patients evaluated acutely (<90 days) relative to those mTBI patients evaluated post-acutely (≥90 days). Interestingly, in this meta-analysis, there was variability in performance across domains for those mTBI patients evaluated acutely, with the most pronounced effects of mTBI for delayed memory and verbal fluency.

Tenet 4: A Significant Minority of Patients Will Experience Persisting Post-concussive Syndrome Symptoms

It is important to note that individual patients may experience variability, both in terms of rate of recovery during this time period as well as between various symptom clusters (Dikmen et al. 1995b; McCrea 2008). For a "significant minority," there may be mTBI symptoms that extend beyond the expected 3-month recovery period (Belanger et al. 2005; Binder et al. 1997). The persistence of symptoms following mTBI is known as post-concussion syndrome (PCS) (e.g., PCS, typically greater than 3 months post-injury), although the nature and reasons for persistence of these symptoms is the source of much debate. The relationship between reported symptoms immediately following mTBI and persistence of post-concussion symptoms remains unclear, in part because there are few studies consistently and systematically evaluating these factors in the literature (Carroll et al. 1994).

There is limited evidence to suggest that headache and dizziness in the ER, and dizziness 2 weeks post-injury, may be predictive of persisting concussion symptoms (De Kruijk et al. 2002; Yang et al. 2009). However, it is also important to note that many symptoms associated with concussion are also endorsed at high rates in other populations. Headache, fatigue, forgetfulness, frustration, irritability, concentration difficulty, and sleep disturbance are among many overlapping symptoms reported at high rates and varying severity in college (Wang et al. 2006), claimant (Lees-Haley et al. 2001), adult control (Paniak et al. 2002a), and chronic pain populations (Iverson and McCracken 1997; Smith-Seemiller et al. 2003), although typically at lesser severity levels than those with mTBI within the first month post-injury (Carroll et al. 1994). In a landmark study that supports a cognitive-behavioral conceptualization for PCS etiology and informs current mTBI treatments, Mittenberg et al. (1992) suggest that patients have pre-injury *expectations* about mTBI symptoms and these, in turn, have the potential to become self-fulfilling. This was based on their finding that healthy adults endorsed symptoms they would expect to have 6 months following an mTBI at similar levels to patients with PCS (i.e., both reported similar levels of anxiety, depression, irritability, fatigue, memory difficulty). Additionally, when PCS patients were asked to estimate the same symptoms prior to their own injuries, compared to a healthy adult sample rating current symptoms, the PCS patients consistently reported fewer pre-injury problems. Thus, it is hypothesized that PCS patients have expectations regarding TBI which have the potential to form internal representations about

outcomes. These representations have the potential to become self-fulfilling and may augment perceived intensity and frequency of PCS symptoms (Miller and Mittenberg 1998).

While post-concussion symptoms have been weakly linked to prognosis, multiple studies have demonstrated that compensation-seeking behavior is associated with persistence and severity of impairments as well as a delayed return to work and slowed recovery following mTBI (Binder and Rohling 1996; Carroll et al. 1994; Paniak et al. 2002b). Belanger et al. (2005) found that across studies, clinic-based samples including patients engaged in litigation were likely to have greater cognitive sequelae ($d = 0.74$ after 3 months) and that litigation was negatively associated with improvement of cognitive functioning over time. Conclusions related to the nature of this relationship are not addressed by correlative studies; the association could plausibly reflect more severe impairment independently leading to compensation seeking. Other moderating factors that have been less reliably related to PCS include being female, off work due to injury, and history of psychiatric illness. Prior psychiatric illness has also been identified as a risk factor for acute stress disorder following a motor vehicle collision and this is, in turn, a predictor of the later development of PTSD (Carroll et al. 1994).

Complicated Comorbidity: Mild TBI and PTSD

Exposure to trauma, such as the potentially life-threatening events often associated with an mTBI (e.g., motor vehicle accidents and combat), places individuals at risk for various psychiatric disorders, most notably PTSD. As defined by the American Psychiatric Association, PTSD is a constellation of symptoms including reexperiencing the event, avoidance of reminders of the event, and chronic hyperarousal that persist 3 months or more after exposure to a life-threatening trauma (APA 2000). Physical injury to the body and brain associated with a life-threatening trauma has been shown to further increase the likelihood of developing PTSD. Given the increased risk of both trauma and TBI in combat, the recent wars in Iraq and Afghanistan have highlighted the complications associated with identifying TBI in the context of PTSD and vice versa. In a sample of 100 soldiers with similar combat experience, 16.7% of those who incurred a bodily injury during combat met the criteria for PTSD after deployment, while only 2.5% of those without injury were diagnosed with PTSD (Koren et al. 2005). The association between injury and later development of PTSD appears to be even greater in the case of mTBI relative to other bodily injuries. Hoge et al. (2008) noted a strong association between combat-related mTBI and screening positive for PTSD. In a stratified sample of soldiers who reported a history of no injury, non-brain injury, mTBI with altered mental status, and mTBI with loss of consciousness, the rate of positive post-deployment PTSD screens rose steadily from 9.1% in the non-brain injury group to 43.9% in the mTBI with loss of consciousness group. What remains unclear is if this relation between PTSD and history of mTBI would be changed if more stringent diagnostic standards for PTSD and mTBI (i.e., clinician-confirmed diagnosis) were employed. This frequent occurrence of PTSD symptomatology after mTBI is not unique to military populations. Estimated rates of PTSD following mTBI have ranged from 17 to 33% in civilians with TBI (Bryant and Harvey 1995, 1998; Middelboe et al. 1991; Ohry et al. 1996), a rate of PTSD considerably higher than 7.8% lifetime prevalence rate noted in the civilian population (Kessler et al. 1995).

The topic of PTSD following mTBI has caused considerable controversy for two reasons. First, the development of PTSD is assumed to stem from intense psychological trauma wherein the perceived potential for loss of life is present. From this perceived threat at the time of the traumatic event, the individual subsequently "cannot forget" the trauma as evidenced through reexperiencing the trauma, avoiding situations that serve as reminders of the trauma, and hypervigilance towards perceived threats. It has been questioned whether this psychological response to a trau-

matic event can occur in the context of a TBI associated with loss of memory for the event.

An early study on this topic appeared to validate the logical conclusion that mTBI should serve as a protective factor against later PTSD (Sbordone and Liter 1995). Of the 70 patients with either PTSD or a history of mTBI included in this study, none of the patients with a history of TBI reported any reexperiencing symptoms, consistent with the expectation that an amnestic state associated with an mTBI would preclude later recall of the event. Of note, the majority of patients in this study either reported loss of consciousness or amnesia for the event (i.e., 85.7% reported a positive loss of consciousness and 96.4% reported amnesia for the event), suggesting that this sample may have included a disproportionate number of patients with somewhat more significant mTBIs. Contemporary diagnostic standards now require only a period of disorientation or confusion to denote the presence of an mTBI (ACRM 1993), indicating that many individuals in the general population who are diagnosed with mTBI do not suffer loss of consciousness or amnesia for the event. A more recent study exploring the association between memory for the traumatic event and later development of PTSD suggested that those patients with mTBI without amnesia for the event were at increased risk of developing PTSD relative to those patients without memory for the event (Gil et al. 2005). The representativeness of the 120 patients in this study has also been called into question, however, since all the patients required hospitalization for observation.

Other studies, however, have failed to support the hypothesis that amnesia for the traumatic event surrounding the mTBI reduces the likelihood of developing PTSD. A large-scale study of consecutively evaluated civilians indicated that a history of mTBI with loss of consciousness does appear to be a risk factor for development of PTSD (Mayou et al. 2000). In this study, individuals with a definite loss of consciousness secondary to mTBI were more likely to be diagnosed with PTSD 3 months post-injury than those patients without a clear loss of consciousness. In a smaller but well-designed study of consecutively admitted patients with an average of 9 h of post-traumatic amnesia, Bryant and Harvey (1998) also found an elevated rate of PTSD at 6 months post-injury. King (2008) offered three explanations for the paradoxical appearance of PTSD (especially reexperiencing symptoms) following an mTBI with apparent loss of consciousness or post-traumatic amnesia proximal to the traumatic event. First, it is possible that islands of memory persist during the period of apparent amnesia. Second, an implicit fear response may still be evoked when a person is exposed to stimuli reminiscent of the traumatic event even if there was a clear loss of consciousness. Lastly, individuals without memory for the traumatic event may develop imagined or reconstructed memories based on information provided by others.

Although some consensus regarding the occurrence of PTSD following mTBI has been reached, a second problem concerns the considerable overlap in PTSD and PCS. Symptoms common to both disorders include sleep disturbance, irritability, memory and concentration difficulties, reduced speed of processing, depression, fatigue, headaches, and nausea (King 2008). As might be expected, the presence of PTSD following mTBI is associated with increased post-concussion symptoms' report, and PTSD symptoms are correlated with post-concussion symptoms. In a sample of 105 motor vehicle collision survivors with and without mTBI, the frequency of reported post-concussion symptoms was greatest in individuals who sustained an mTBI and had been diagnosed with PTSD and overall report of PTSD symptoms was significantly correlated with the report of post-concussion symptoms (Bryant and Harvey 1999).

In the context of combat-related mTBI, the controversy of mTBI as a risk factor for PTSD is different. Unlike the civilian population where a single event is theorized to precipitate both the mTBI and subsequent PTSD, the traumatic event that is associated with a combat-related mTBI often represents perhaps one in a series of psychologically traumatic events taking place over several months. A study of soldiers returning from the wars in Afghanistan and Iraq showed that a history of mTBI is associated with multiple injuries and exposure to heighted combat intensity (Hoge et al. 2008). In this context,

a diagnosis of mTBI simply serves as a proxy indicating a likely history of exposure to repeated, traumatic events, any of which could have contributed to the later development of PTSD. In a theater of combat, the relationship between mTBI and PTSD is extremely complex. Although further research is needed to better delineate the interplay between these two disorders, it could be hypothesized that an mTBI occurring in the context of acute stress disorder or PTSD has the potential to worsen the anxiety disorder through a temporary reduction in cognitive resources used to process the ongoing trauma. Conversely, chronic stress associated with the presence of acute stress disorder or PTSD could impede or otherwise alter the trajectory of the course of spontaneous recovery of cognitive functioning following mTBI. Further research is needed to determine what other physical and psychological comorbidities (i.e., chronic pain, depression, etc.) may share in this complex interplay. Needless to say, the considerable symptom overlap and the high rates of PTSD and mTBI comorbidity in returning combatants from Afghanistan and Iraq present diagnostic challenges even to highly trained specialists (Kennedy et al. 2007).

Treatment of Behavioral Disorders Following TBI

Treatment of behavioral problems following TBI, including impulsive aggression (IA), a hair-trigger response to a threat with a behavioral loss of control (Barratt et al. 1991), has been recently reviewed by Warden et al. (2006). This and earlier reviews of therapy (e.g., Silver and Yudofsky 1995) demonstrate a paucity of large randomized trials that address behavioral outcomes. While there is little in the way of large randomized, long-term trials specifically in TBI patients to recommend most therapies, promising research implicates certain pharmacological approaches, such as beta-adrenergic receptor blocking agents. Other potential agents, in which most work has involved aggression in other conditions but with some support following TBI, include anticonvulsant agents such as carbamazepine and valproic acid (Silver and Yudofsky 1995). Our own work with phenytoin shows a very specific benefit in reducing the severity and frequency of IA acts (Barratt et al. 1991, 1997), although this work was in patients with no evidence of past symptomatic TBI and with normal EEG. It remains to be studied whether this work will translate to patients post-TBI. As with all of these agents, a thorough understanding of their side effects is necessary to individual assessments of risk and benefits.

Treatment recommendations of behavioral disorders in TBI patients generally involve targeting symptoms, such as attention, mood, and psychotic symptoms. Evidence on effectiveness in the treatment of other psychiatric disorders occurring in the TBI patients is similarly limited, but general treatment recommendations include agents shown to be beneficial in these conditions in non-TBI patients including selective serotonin reuptake inhibitors and anticonvulsants as well as non-pharmacological, behavioral therapies (Deb and Crownshaw 2004; Warden et al. 2006). There is currently great interest in the possibility of treatment of PTSD in combat veterans using the adrenergic agent, prazosin (Raskin 2003). Benefit for nightmares was particularly noted, while improvement in other symptoms is also being investigated in an ongoing clinical trial.

There are several reviews addressing the efficacy of treatment for persistent PCS symptoms of mTBI (e.g., Borg et al. 2004; Comper et al. 2005; Snell et al. 2009), although there are few well-designed studies. Treatments following mTBI vary depending on factors, such as time since injury and the symptoms experienced following the event. In general, mTBI treatments can be viewed as falling into one or more of the following four categories: cognitive behavioral therapy, cognitive remediation, pharmacotherapy for symptom-based management, and education and support, depending upon the symptoms present. We present a basic treatment algorithm (see Fig. 13.1) that describes mTBI interventions, both for symptom reduction and prevention of PCS, for military personnel and veterans at various time points post-injury. This model assumes the presence of unit and military medical personnel who are familiar enough with injury severity

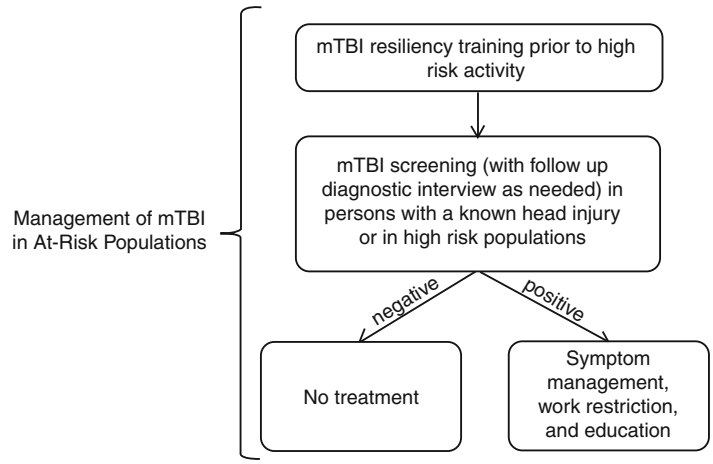

Fig. 13.1 Management of mTBI during acute recovery. The treatment algorithm for the management of mTBI during acute recovery is based on earlier work by Mittenberg et al. (1996), Paniak et al (1998), and others who have demonstrated the effectiveness of brief interventions for reducing the severity of symptoms following mTBI

characteristics to assist in classifying a suspected mTBI (see Fig. 13.1 level b).

Individual- and population-based mTBI screening instruments, such as the Standardized Assessment of Concussion (McCrea et al. 1998) upon which the more recent Military Acute Concussion Evaluation is based (Knuth et al. 2005) and the Brief Traumatic Brain Injury Screen (Schwab et al. 2007), have shown promise, although verification of the diagnosis through follow-up clinical interview is still necessary due to false-positive errors. As described earlier in this chapter, consensus criteria for concussion/mTBI are available to improve diagnostic accuracy (American Academy of Neurology 1997; ACRM 1993). Once the diagnosis has been verified and the specific symptoms have been detailed through clinical interview, symptom management and work restrictions should be considered, with the goals being to maximize functional recovery (Jaffee et al. 2009). While these first two aspects of treatment are meant to reduce the immediate impact of mTBI, the third component of treatment is aimed at reducing the subsequent development of PCS. It is during this period of time shortly following mTBI that psycho-education has been determined to be the most effective for the purpose of reducing subsequent PCS (Borg et al. 2004). However, it is important to note that in the WHO review of mTBI interventions, no treatments were found to provide clinically important effects on symptoms or disability, although there was some evidence to suggest that early education and limited support (e.g., information about common complaints and the likelihood for a good outcome) as to the effects of mTBI may reduce future symptom complaints (Borg et al. 2004). This approach of intervening after exposure to a trauma in order to reduce the likelihood of future maladjustment has also met with success in the management of PTS symptoms in military personnel following combat deployment (Adler et al. 2009).

Based upon their research regarding misappraisal of symptoms in mTBI patients (see above), Mittenberg et al. (1996) developed an effective, brief 1-h educational intervention. The effectiveness of this intervention in decreasing later post-concussive symptoms was demonstrated in 58 consecutive mTBI hospital admissions (GCS ≥ 13, Galveston Orientation and Amnesia Test score >75, no significant extracranial injuries). Half of the patients were randomized into a treatment arm during which time they met with a therapist to discuss symptoms for approximately 1 h and were provided with educational materials. The other patients received routine care and were provided with written discharge instructions that were verbally reviewed by a nurse. Six months after admission, mTBI patients in the treatment arm reported reduced symptom duration (33 days vs. 51 days) and a lower number of post-concussive symptoms (1.6 symptoms vs. 3.1) relative to the patients who received the standard

of care (Mittenberg et al. 1996; Miller and Mittenberg 1998). More recently, psycho-education and support provided via telephone calls (four calls at 2, 4, 8, and 12 weeks post-injury) were also shown to be effective at reducing post-concussive symptoms 6 months post-mTBI relative to standard emergency room care (e.g., instruction handout) (Bell et al. 2008). The relative benefit of the follow-up telephone calls is difficult to determine due to the design of the study, although the results of other mTBI intervention studies indicate that more than one treatment session may not have an added benefit (Paniak et al. 1998, 2000).

Diagnostic criteria have also been developed to identify those individuals who experience an abnormal persistence of post-concussion symptoms following mTBI, otherwise known as PCS. The International Classification of Diseases, Tenth Revision, criteria include a history of TBI and the presence of three or more of the following eight symptoms: headache, dizziness, fatigue, irritability, insomnia, concentration difficulty, memory difficulty, and intolerance of stress, emotion, or alcohol (World Health Organization 1993). Proposed criteria for the diagnosis of post-concussional disorder have also been put forth for further research in the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition—Text Revision (American Psychiatric Association 2000). These criteria are as follows: (A) history of TBI causing "significant cerebral concussion;" (B) cognitive deficit in attention and/or memory; (C) presence of at least three of the following symptoms, e.g., fatigue, sleep disturbance, headache, dizziness, irritability, affective disturbance, personality change, and apathy, that appear after injury and persist for ≥3 months; (D) symptoms begin or worsen after injury; (E) symptoms interfere with social role functioning; and (F) exclusion of dementia due to head trauma and other disorders that better account for the symptoms. Boake et al. (2005) noted that the prevalence of diagnosed PCS was higher 3 months post-injury using the ICD-10 criteria (64%) relative to the DSM-IV-TR criteria (11%) in a sample of 178 adults with mild-to-moderate TBI, although both criteria showed poor specificity when tested with a control sample of 104 adults with extracranial injuries. The authors note that the relatively limited ICD-10 PCS criteria likely contributed to the higher diagnostic rates using that classification scheme, while the lack of specificity demonstrated by both classification schemes was due to the frequent endorsement of symptoms by patients without cranial injuries.

For military personnel who subsequently develop PCS, the Department of Veterans Affairs and Department of Defense recommend a combination of both psycho-education and symptom management (see Fig. 13.2) (Department of Veterans Affairs and Department of Defense 2009). The effectiveness of this treatment paradigm, especially the provision of psycho-education to veterans who may be several years post-injury, has yet to be determined. From a theoretical standpoint, it may be possible that allowing PCS to develop without early education allows patients to develop resistance to subsequent attempts at reducing PCS through education. That is, once erroneous expectations about consequences of mTBI are left unchecked for many months or years post-injury, patients may be reticent to consider other causes of their symptoms. Lastly, we also believe that there may be some benefit to early psycho-educational intervention for military personnel prior to deployment in that education at this level may provide resiliency in terms of subsequent development of PCS following mTBI. At present, there are no studies addressing the effectiveness of pre-deployment resiliency training. We believe, however, that this is a natural extension of the literature and is meant to augment, rather than replace, psycho-educational interventions that should occur immediately after a soldier sustains an mTBI.

Conclusion: Behavioral and Psychiatric Comorbidities of TBI

Extensive evidence associates TBI with psychiatric and behavioral sequelae. While the design of these studies makes it often difficult to differentiate symptoms based on severity of injury,

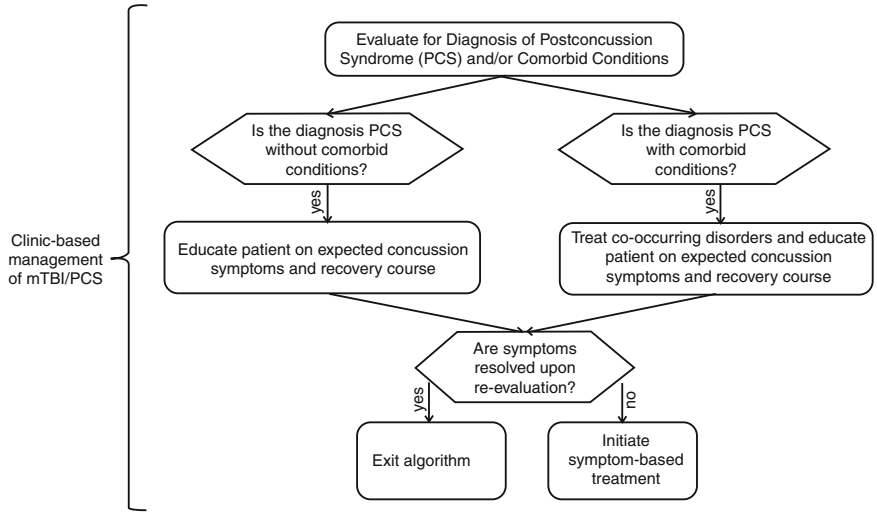

Fig. 13.2 Management of PCS. The treatment algorithm for the management of PCS is designed in part after the treatment recommendations offered by the Department of Veterans Affairs and Department of Defense (2009)

premorbid deficits, and functioning from the contribution of the TBI, it seems very likely that at the minimum, TBI is a risk for accentuating premorbid behaviors (Greve et al. 2001), and individual cases indicate the potential for profound behavioral change (Damasio et al. 1994). The mechanism of these effects has not been examined, although changes in self-regulation and social information processing may result from neurological insult, psychiatric symptoms, or substance use. On the other hand, it is also conceivable that psychiatric disorder and TBI become difficult to distinguish from an epidemiological perspective given that circumstances may put an individual at risk for both (Hoge et al. 2008). In this case, prospective studies and treatment interventions will be needed to identify the salient underlying disorders. Several research groups are pursuing a variety of imaging, neuropsychological, and treatment studies to identify characteristics that would contribute to this distinction. In the interim, it is important from a patient care perspective to identify treatable behaviors that are causing distress to the patients or those around them. While definitive evidence for efficacy is in many cases lacking, a number of reasonable suggestions or extrapolations from other conditions have been reported that provide a starting point to develop a treatment plan. However, lack of definitive evidence for efficacy or the possibility of a unique sensitivity to adverse events affecting TBI patients suggests that treatment should be approached with an appreciation for potential difficulties.

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