Neuropsychiatric Sequelae of Traumatic Brain Injury

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ABSTRACT

The prevalence of traumatic brain injury (TBI) is increasing, particularly in the population of veterans. Many times, the motor and sensory consequences of TBI are addressed, but the post-TBI neuropsychiatric sequelae, which may be as, or even more devastating than the motor and sensory deficits, are left unattended. Cognitive, mood, anxiety, thought, impulse, and substance disorders, and a variety of personality disorders can be seen following TBI. The neuropsychiatric sequelae of TBI not only interfere with day-to-day function, but can severely impede rehabilitation efforts. To date, there have been few large-scale studies looking at the effectiveness of the various treatment modalities, including psychotherapeutic and pharmacological interventions.

KEYWORDS: Traumatic brain injury, concussion, neuropsychiatric sequelae, cognitive disorders, mood disorders, treatment

EPIDEMIOLOGY AND ETIOLOGY

Traumatic brain injury (TBI) is defined as traumatically induced physiological disruption of the brain, and is occurring with increasing frequency. The incidence is ~506 per 100,000 people.[1] Traumatic brain injury is being seen more often, particularly in patients injured in war. Many of the veterans with TBI whose other injuries would have been fatal in previous wars are now surviving because of improved protective gear.[2] The peak incidence is between the ages of 15 and 24 and older than the age of 64 years. Males are affected twice as often as females. In the civilian population, alcohol is involved in more than half the cases of TBI. People from lower socioeconomic groups are significantly more likely to be affected by TBI. Motor vehicle accidents (MVAs), particularly motorcycle accidents, account for the most frequent civilian cause of TBI. Falls are the next most common cause of head injury, with a high rate in the elderly. Recurrent head injury is common in patients with a history of alcohol abuse and individuals playing contact sports.[3] The estimated annual cost of TBI in the United States is $60 billion for treatment and lost productivity.

As significant as the epidemiology of TBI is, the prevalence of post-TBI syndromes is significant and includes post-traumatic stress disorder (PTSD), depression, mania, and aggression.[4] Post-TBI post-traumatic stress disorder occurs in up to 27%, including patients with no clear recall of the event.[5,6] Post-TBI depression has an incidence of 15 to 33% and prevalence of 18 to 42%.[7] Post-TBI mania occurs in <10% of patients with TBI.[8] Post-TBI aggression (agitation, disinhibition, personality changes) occurs in variable frequencies depending on criteria, ranging from 20 to 49%.[9,10] Although delusions and auditory hallucinations are common in the acute post-traumatic state, post-TBI psychosis occurs in <10% of the TBI population.[11,12]

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Table 1 Glasgow Coma Scale Scores

Eyes
Open spontaneously = 4
Open to verbal stimuli = 3
Open to pain = 2
Do not open = 1
Verbal
Spontaneous speech, oriented = 5
Spontaneous speech, disoriented = 4
Nonsense speech = 3
Sounds = 2
No speech at all = 1
Motor
Spontaneous movement = 6
Localizes pain = 5
Withdraws from pain = 4
Decorticate posturing = 3
Decerebrate posturing = 2
No movement at all = 1

The prognosis following TBI is related to the initial Glasgow Coma Scale (GCS) score[13,14] (Tables 1–3).

PATHOPHYSIOLOGY

The neuropathophysiology of TBI can be divided into biomechanical, biochemical, and biomolecular mechanisms. The acute injury results from primary (mechanical) physical disruption of the brain. Head injuries are divided into open, where there is a breach of the skull by fracture or penetrating injury, and closed, when the cranium is intact. Because of the brain's environment—floating in the cerebrospinal fluid (CSF) in the cranium—sudden acceleration, deceleration, or torsion injuries can cause the brain to strike the skull, causing injury. There are two basic types of brain injury: (1) direct trauma to the brain, causing contusions, hemorrhages, and lacerations; and (2) diffuse axonal injury, from stretch injuries to the deep white matter. Coup/contrecoup injuries occur when the brain is injured by a torsion injury of the head in which opposite sites in the brain are injured; for example, the left frontal and right parieto-occipital areas. The most commonly injured areas of the brain are the anterior poles of the frontal and temporal lobes, where they abut bony ridges of the skull.

Table 2 Severity Grading of Traumatic Brain Injury

	Glasgow Coma Scale Score	Loss of Consciousness (time)
Mild	13–15	Less than 30 min
Moderate	9–12	30 min to 1 wk
Severe	<9	More than 1 wk

Table 3 Prevalence and Prognostic Indicators for Traumatic Brain Injury[14]

Glasgow Coma Scale Score	Severity Percentage in Patients Admitted to Hospital (%)	Mortality (%)
Mild (13–15)	80	0
Moderate (9–12)	10	10
Severe (<9)	10	60

Because the brainstem is fixed to the base of the skull, it turns as the skull does, but the cerebrum does not. This causes axonal shearing injuries in the long white matter tracts in the parasagittal areas, the corpus callosum, and the upper brainstem. This injury may range from neurapraxia, with focal demyelination, to axonotmesis with complete severing of the axon. The severity of the injury to the axons determines whether there will eventually be resumption of function.

Secondary (delayed, nonmechanical) postinjury factors include excitotoxic amino acid release, including glutamate. Oxidant injury from free radical release may result in secondary injury. Secondary causes of injury following the immediate head injury include physiological and pathological responses, such as alterations in cerebral blood flow and cerebral perfusion pressure. Reperfusion injury may result. Seizures may occur, along with centrally mediated systemic effects, which may include shock, electrolyte imbalances, and hypothermia. Hypoxia, brain edema, increased intracranial pressure, hemorrhage, ischemia, and infection (with open head injuries) may occur.

COURSE OF ILLNESS: ACUTE, SUBACUTE, AND LONG TERM

Acute Phase: Emergency Management

Emergency management in the acute phase of TBI includes GCS classification, documenting clinical findings, monitoring fluid balance, and maintaining airway and oxygenation. Pharmacological, surgical, and invasive interventions are also part of acute TBI management; however, the emergency care of TBI is beyond the scope of this article and is not discussed.

Subacute Phase: Post-Traumatic Delirium and Amnesia

In the subacute phase, during the period immediately following regaining consciousness following a TBI, patients go through a state during which they are delirious and of which they are amnestic. Risk factors for more severe and more prolonged delirium include

older age,[15] hypoalbuminemia,[16] and prior neurological abnormalities.[17] As with delirium of other causes, there may be a fluctuating course with episodes of hyper- and hypoactivity. Patients with this condition demonstrate disorientation and impaired attention. Often they have a disrupted sleep-wake cycle, sleeping during the day and waking at night. The period of amnesia often outlasts the period of clear delirium. The duration of post-traumatic delirium varies with the number of lesions seen on computed tomography (CT) scan and fluid attenuated inversion recovery (FLAIR) sequence magnetic resonance imaging (MRI).[18] Magnetic resonance spectroscopy (MRS) shows decreased *N*-acetylaspartate and increased choline, which is due to the loss of neurons and increased glial cells.[19]

Treatment of the delirium includes treatment of any other contributing disorders such as metabolic or infectious disturbances. Providing orienting stimuli in the environment can help decrease confusion and disorientation. Atypical neuroleptics, except for clozapine, which lowers the seizure threshold and has significant anticholinergic properties, are the most useful pharmacological agents. There is some evidence that the typical neuroleptics may slow cognitive recovery.[20] The typical neuroleptics are more likely to cause extrapyramidal adverse effects, particularly in patients with TBI. Except when withdrawal from sedative-hypnotic medications is part of the cause of delirium, benzodiazepines should not be used because they worsen the delirium.

Long-Term Neuropsychiatric Sequelae

Once the patient is beyond the acute and subacute phases, many are left with neuropsychiatric sequelae of TBI. Underscoring the importance of addressing TBI sequelae, Robert Karol warns that treatment providers who attend "only to cognitive and physical deficits after brain injury and downplay emotional concerns are unlikely to ameliorate behavioral dyscontrol."[21] We divide the discussion of post-TBI issues into social/self, symptoms and syndromes.

Self/social issues include vocation/financial, physical skills, appearance, intelligence/thought, relationships, and sexual functioning. Post-TBI job loss results in loss of income, sometimes a supportive spouse, and a disability application. Physical skills lost sometimes include physical strength, speed, dexterity, athleticism, and difficulties with spasticity, paralysis, balance, visuospatial function, visual praxis, and adjusting to equipment. Issues associated with appearance include scars from injury and from surgery and verbal expression difficulty. Formerly high-functioning patients are sometimes devastated by the impact of mild TBI on their thinking and intelligence. Attention, reasoning, language, memory, planning, and tracking (executive functioning) all can be affected by TBI. A commonly overlooked area in TBI is the effect on relationships and sexual functioning. Family, friends, work, and community of faith may be estranged due to new frustrations or behaviors or bolstered as supports after TBI.

Common issues related to symptoms include behavioral outbursts, emotional adjustments, cognitive deficits, and physical concerns. The link between ability to adjust to TBI and the capacity to do so is complicated by a major factor. In addition to having to adjust to dysregulation in behavior, emotions, thinking, and physical challenges, persons with TBI must make these adjustments with a brain that processes information poorly. A person with limited coping skills may become frustrated with his or her mood variability or with limb weakness, and may as a result have outbursts. Trouble with attention, decreased ability to understand, and difficulty remembering things may impact an individual's ability to adjust to deficits. The patient may lose the information given at the doctor's office, or may forget to use the assistive device. He or she may have problems with perceiving situations or assign incorrect motives to other people's actions.

Common syndromes seen post-TBI include: behavioral disinhibition, depression/anxiety/psychosis, substance abuse, attention/cognitive disorders, and motor/sensory disorders. Given the lack of controlled treatment studies for post-TBI syndromes, the information provided here is from studies from the literature with the caveat that there currently are no U.S. Food and Drug Administration (FDA)-approved interventions for post-TBI neuropsychiatric syndromes. Key rules of thumb for these syndromes are to start lower and go slower. Brain injury confers increased sensitivity to the active agents of the central nervous system (CNS); therefore, treatment and side effects may be accentuated at lower doses in patients after TBI. Second, to systematically approach treatment in TBI beyond pharmacological interventions, three areas are important to keep in mind: (1) identification of target symptoms, (2) consideration of coexisting medical problems and iatrogenic contributions, and (3) implementation of nonpharmacological treatment.[22]

The initial steps of treatment include a comprehensive neuropsychiatric evaluation and testing. This may include neurological and psychiatric examination to document baseline deficits, diagnoses, and functioning. A neuropsychological battery documents the cognitive skills and limitations, and provides a baseline from which gains in cognitive rehabilitation can be benchmarked. Neurophysiological tests may show brain dysfunction and seizures.[23] When indicated, neuroimaging may be of benefit to show ischemia, hemorrhage, encephalomalacia, neuronal loss, and altered cerebral metabolism or perfusion[24] (Fig. 1; Table 4).

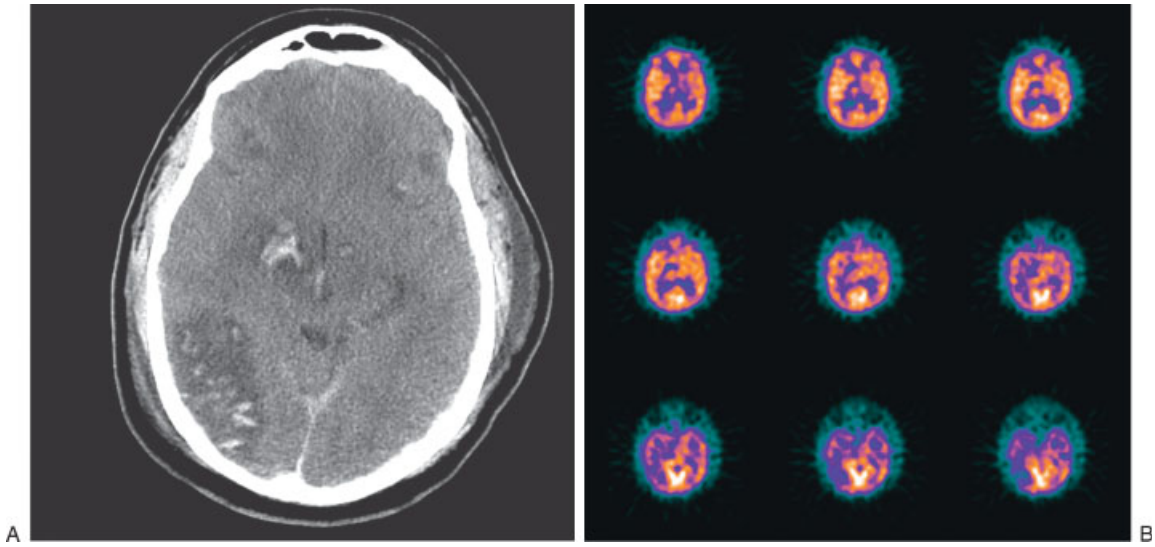

Figure 1 Neuroimaging in traumatic brain injury (TBI). Transaxial images from non-contrast head CT and single-photon emission computerized tomography (SPECT) images showing intraventricular hemorrhage and large parenchymal hematoma in right parieto-occipital area and hypoperfusion in the same area. (Image courtesy of Alan Siegel, Dartmouth Medical School, Nuclear Medicine.)

COGNITIVE DYSFUNCTION

The severity of post-traumatic cognitive disturbance depends on the degree of diffuse axonal injury[25] as well as the volume and location of focal injuries. Diffuse axonal injury is more often associated with generalized cognitive dysfunction, such as attention disorder, whereas focal injuries cause specific deficits, such as aphasia.

Patients with generalized cognitive dysfunction have difficulties following conversations. They tend to be perseverative but have problems maintaining their train of thought. Because of difficulties with selective and divided attention, patients with a history of TBI have difficulty with multitasking. Declarative memory for events is more affected than implicit memory. Working memory and prospective memory (remembering to pay one's bills) are impaired, particularly after damage to the frontal lobes. Functional magnetic resonance imaging (fMRI) shows altered patterns of activation of the brain during memory tasks in patients with TBI.[26]

Executive function involving the frontal lobe–basal ganglionic–thalamic circuits is responsible for establishing goals, planning, initiating, sequencing, and inhibiting responses.[27] Frontal lobe injuries impair executive function, conceptual reasoning, and decision making. Patients with frontal lobe damage have difficulty with self monitoring and regulation. These deficits may significantly interfere with a patient's ability to cooperate with any type of psychotherapy or behavioral therapy.

Small studies have shown cholinesterase inhibitors,[28] stimulants,[29] L-dopa,[30] tricyclic antidepressants,[31] and lamotrigine[32] to be helpful in treating cognitive deficits.

MOTIVATION

Motivation refers to how behavior is started, energized, and sustained. Abulia, or lack of motivation, is common following significant head injury. Orbitofrontal and medial frontal cortical injuries affect motivation as well as injuries to the ventral pallidum and ventral tegmentum.[33] The mildest degree of impairment of motivation sometimes is erroneously referred to as apathy. Apathy is defined as a lack of emotion or feeling. Apathy is sometimes manifested as abulia as a quantitative rather than a qualitative change in drive, characterized by diminished overt behavior, goal-related cognition, and emotional responses. On examination, psychomotor retardation may be observed in mild to moderate TBI. With abulia, the ability to plan and react is preserved, but diminished in force. A more extreme form of abulia is characterized by a poverty of behavior and speech, lack of initiative, loss of emotional responses, and severe psychomotor slowing. Akinetic mutism can be observed in TBI as an extreme form of a deficit of motivation in which the patient is awake and able to track visually with no other responses.

Treatment of amotivational syndromes involves both pharmacological treatment and behavioral interventions. Stimulants and dopaminergic medications, as well as activating antidepressants such as bupropion or monoamine oxidase inhibitors (MAOIs), may increase motivation. Selective serotonin reuptake inhibitors (SSRIs) and typical neuroleptics may worsen amotivational syndromes.[34] Nonpharmacological treatments include rewarding goal-directed behavior, psychological prostheses such as lists and prompting, behavior modification, and family intervention. Lack of motivation, as

Table 4 Ancillary Testing in Traumatic Brain Injury

1. Neuropsychological testing: cognitive functioning, language testing, tests of motivation and malingering, tests for premorbid functioning
   - Types of attention include selected, sustained, and divided
   - Types of memory disturbances can be anterograde, which is loss of the ability to lay down new memories, or retrograde, in which there is loss of previously acquired memories
   - Executive functions often affected by TBI include judgment, reasoning, concept formation, planning, organizing, set maintenance and flexibility, and impulse control
   - Language
   - Tests for motivation and malingering, required especially when litigation is potentially involved
   - Tests to determine the level of premorbid functioning
2. Electrophysiological: EEG and QEEG, evoked potentials including ERPs
   - EEG: used to assess for post-traumatic epilepsy or encephalopathy
   - QEEG: sometimes used, but is of questionable utility[23]
   - ERPs
3. Neuroimaging
   - CT: useful for examining blood and bone status
   - MRI: excellent resolution of structural lesions
   - fMRI: used in research presently; shows localization of task-specific operations
   - PET: shows level of cerebral metabolic activity; heterogeneous pattern may indicate TBI among other conditions in the differential diagnosis
   - SPECT: shows level of cerebral perfusion; heterogeneous pattern may indicate TBI among other conditions in the differential diagnosis
   - MRS: shows areas of cerebral neuronal loss
   - DTI/FT: shows cerebral white matter tracts

TBI, traumatic brain injury; EEG, electroencephalography; QEEG, quantitative EEG; ERPs, evoked response potentials; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; fMRI, Functional MRI; SPECT, single-photon emission computerized tomography; MRS, magnetic resonance spectroscopy; DTI/FT, diffusion tensor imaging and fiber tractography.

with cognitive deficits, can be a major obstacle to success in rehabilitation.

MOOD DISORDERS

Following TBI, up to 50% of patients have symptoms of depression, with 20% meeting *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) criteria for major depression. The incidence of depression in patients with TBI is approximately twice that of other patients who were as badly injured but without a head injury.[7] Patients with TBI have a significantly increased risk of suicide. There is controversy about whether the laterality of the injury makes a difference in the occurrence of depression, with some studies suggesting that right hemispheric lesions are more likely to be associated with depression, but neither left nor right-sided lesions consistently reveal associations.[35] Mania can occur in patients with TBI but is much less common and is usually of short duration. Anxiety disorders, discussed later, are also common, particularly in patients with depression.

The differential diagnosis includes apathy, emotional lability, PTSD, and pathological laughing and crying, which may be symptoms of pseudobulbar affect.

Tricyclic antidepressants (TCAs) may be of benefit in treating anxiety and depression,[36] but they should be limited to agents with the least anticholinergic activity, the least sedation, and the least effect on the seizure threshold. With their safety profile, low histamine, cholinergic, and α-adrenergic binding SSRIs are preferred for mood and anxiety; however, side effects of sexual dysfunction, dyspepsia, drowsiness, and irritability may limit their use in TBI. Stimulants, amantidine, and anticholinesterase drugs have been shown to be helpful in some studies.[37–39] Clonidine, carbamazepine, and divalproex are the drugs of choice for post-traumatic mania, with lithium being reserved for patients with a prior history of mania.[40] Pseudobulbar affect is treated with TCAs[41] and with combination dextromethorphan hydrobromide and quinidine sulfate.[42]

PSYCHOTIC DISORDERS

Approximately 1.5% of TBI patients develop psychotic symptoms. The onset is generally quite delayed following the injury, around 4 years.[43] The psychoses are characterized by hallucinations and delusions with retained insight. Although non-delirium associated hallucinations can occur post-TBI, the absence of Schneiderian first-rank symptoms—such as thought insertion and thought withdrawal—distinguishes TBI psychosis from schizophrenia. Other factors distinguishing TBI psychosis from schizophrenia include a later age of onset, less premorbid psychiatric disturbance, briefer duration, less common family history, better response to neuroleptics, less need for maintenance medication, and a better prognosis.[44] In some patients, post-TBI psychosis may be an ictal-related process. Post-TBI psychosis has the same features as interictal psychosis.

Treatment for post-TBI psychosis with neuroleptics should be initiated at one third to one half the usual doses because of potential adverse reactions.[45] There is some evidence that neuroleptics may impede cognitive recovery.[46] Atypical neuroleptics, except for clozapine, which is strongly anticholinergic and lowers the seizure threshold, are the drugs of choice. Benzodiazepines should be used sparingly, if at all.

POST-TRAUMATIC STRESS DISORDER AND OTHER ANXIETY DISORDERS

Patients who have suffered a TBI may have anxiety presenting as insomnia, inability to concentrate, free-floating anxiety, phobias, and panic attacks. Subthreshold PTSD symptoms are common in civilians,[47] and PTSD is now being seen increasingly in veterans who sustained TBI.[48] Patients may be particularly anxious in situations in which they know they cannot perform as well as they did before their injury. It is important that family members and coworkers realize and accept that the patient is not the same person they knew before the trauma. This is important not only to decrease the patient's performance anxiety, but also to help the patient realize and accept his or her limitations. Approximately 10% of patients with TBI suffer from a generalized anxiety disorder. Travel phobias are seen in 25% of patients with TBI who were injured in MVAs. Interestingly, PTSD is less common in patients who lost consciousness as a result of their injury.[6,49]

Treatment includes family therapy to help family members adjust to the "new" person in their lives. Behavior therapy, including desensitization, can be helpful. A short course of a short-acting benzodiazepine may help in an acute stress situation. Although SSRIs may be helpful, they may also exacerbate apathy and cause sexual dysfunction. Antiepileptic drugs (AEDs) may also be useful, particularly in patients who are aggressive. As noted earlier, neuroleptics are more likely to cause adverse reactions in patients with TBI and may slow down cognitive recovery.

SOMATOFORM DISORDERS

An understudied, but prevalent condition found in some patients with TBI is somatization. This may manifest itself with ill-defined symptoms, including dizziness, vertigo, gait instability, headache, fatigue, malaise, tinnitus, visual disturbances, cognitive "fogginess," non-neuroanatomical paresthesias, weakness, focal deficits, and nonepileptic events. Patients in this category are often classified as having "postconcussional syndrome."[50] Interestingly, 30% of patients with nonepileptic seizures report a prior history of TBI.[51,52] Treatments for somatoform disorders are lacking, but preliminary evidence in non-TBI populations shows benefits of cognitive behavior therapy (CBT).[53,54]

COGNITIVE DISORDERS

Cognitive impairments are among the most commonly occurring sequelae in TBI, and post-traumatic cholinergic deficits are thought to contribute to the development of post-traumatic cognitive impairments.[55] A randomized double-blind placebo-controlled study of a cholinesterase inhibitor in 157 post-TBI patients failed to show a difference from placebo on both primary cognitive and secondary outcome measures.[56]

PERSONALITY CHANGE DUE TO A MEDICAL CONDITION

The most disruptive consequences of TBI at 1, 5, and 15 years after the event are personality changes. Such changes may include lability, disinhibition, aggression, apathy, and paranoia. The personality changes are most often exaggerations of premorbid personality traits. The "pseudoborderline" personality is characterized by impulsivity, lack of empathy, loss of a sense of self, and inability to monitor one's own behavior. Patients who display mania, euphoria, and impulsivity are labeled as "pseudosociopathic." This syndrome is associated with damage to the orbitofrontal cortex. Medial frontal damage may cause a "pseudodepressed" personality disorder with severe apathy. Explosive personality disorders in which patients are irritable and subject to sudden rages and violence are commonly seen, particularly in patients who use alcohol.

Environmental management is essential for personality disorders, which can be affected by pain and fatigue. Management includes sleep hygiene; avoiding caffeine, alcohol, and illicit substances; avoiding chronic opiates for pain; and maintaining an exercise plan and stretches. Treatment of these various personality changes must include counseling. Pharmacological treatment with tricyclic and SSRI antidepressants may help with lability. Low-dose stimulants, L-dopa, and dopamine agonists have been shown in some studies to be helpful with impulsivity.[57]

AGGRESSIVE DISORDERS

In different studies, the incidence of aggression post-TBI is between 35 and 90%.[58,59] Agitation occurs commonly in the delirious subacute phase of recovery. Chronic irritability and aggression are seen in ~40 to 70% of patients with TBI. Aggression in patients with TBI is generally reactive without premeditation, and is nonpurposeful, explosive, periodic, and egodystonic; that is to say, the patients are genuinely remorseful after the event.[60] Damage to the limbic system, orbitofrontal cortex, left anteromedial frontal lobe, and anterior cingulate have been particularly associated with aggressive behavior.[61] Studies have found increased amounts of CSF norepinephrine[62] and decreased amounts of serotonin in violent patients.[63]

Behavior modification is probably the most effective treatment for these patients. Careful observation and documentation of the patient's aggressive outbursts may reveal triggers of and secondary gains from this behavior.

Levy et al provide an overview of pharmacological management of agitation in TBI,[64] and many of the agents used for agitation are also used for aggression. Antipsychotic medications do not help with chronic, nonpsychotic aggression. In fact, akathisia, a common adverse reaction to typical neuroleptics, may actually increase violent behavior. As noted previously,

neuroleptics have been shown to slow recovery from TBI. Benzodiazepines may cause a paradoxical response in TBI patients, as they do in children. Low-dose buspirone has been tried in some patients, but it may also cause a paradoxical reaction. Antipsychotic agents should be reserved for patients who are truly psychotic. Carbamazepine, valproic acid, gabapentin, and oxcarbazepine have been used successfully in some patients. Lithium is useful in patients who are clearly manic or who display cyclic violence. Antidepressant medications, including TCAs and SSRIs, have been shown to be helpful in small studies. High-dose propranolol, up to 12 mg/kg/d, has been very helpful in some patients.[65]

SUBSTANCE DISORDERS

A history of substance abuse predicts increased disability, poorer prognosis, and delayed recovery. Although consensus in the literature indicates that substance-abuse rates decline following injury, conflicting literature shows a significant history of brain injury in patients with addictions.[66] More recent literature reveals that when combined with difficulties in psychosocial adjustment and coping skills, cognitive impairments may increase the risk for chronic substance abuse in a subset of patients with TBI. Substance abuse significantly complicates TBI rehabilitation and recovery.

Traumatic Brain Injury and the Family

Patients who have suffered a TBI need a social support system to help them adapt to their new lives. The family is usually the source of this support; communities of faith and local or national brain injury support groups are also used. Daily structure is of benefit with vocational rehabilitation and volunteer programs if the patient is unable to return to work. Despite the TBI sequelae, it should be emphasized to the patient and the family that he or she must be able to behave appropriately within the family and social settings. The spouse has the double responsibility of not only caring for the patient, but also becoming the primary or only breadwinner. For the family, the patient with TBI is often a different person than the one they knew before the injury, even though they may look exactly the same. Unfortunately, these changes are usually for the worse. Often the patients are less caring, more irritable, and prone to violence as well as depressed, anxious, and withdrawn. The patient's lack of awareness or angry denial of any deficits or personality changes leads him or her to feel like people are picking on him. The patient may then become more angry and aggressive, further alienating the family members who may ultimately abandon the patient. It is important that the family realizes that the patient may struggle to control his or her behavior and fully function in the same manner as before the trauma.

This does not mean the family has to accept the behavior, but to deal with it by working to modify the behavior by emphasizing that it is the behavior that is wrong, not the person. "Time-outs" and rewarding good behavior may make a significant difference in the patient's actions and ease the tensions within the family. Individual and family therapy can address issues of limit setting, boundaries, and forgiveness. Clearly, alcohol and substance use, which further disinhibits patients, is discouraged and is a prescription for disaster. The safety of the family and the individual has to be ensured for the benefit of all in the support system.

CONCLUSION

Traumatic brain injury can cause not only focal deficits of motor activity or language, but also a variety of potentially disabling psychiatric symptoms and syndromes. These include mood and anxiety disorders; personality disturbances; aggression; and, occasionally, psychosis. Treatment is complicated by cognitive deficits, lack of motivation, and lack of awareness of deficits. Controlled treatment trials for TBI are lacking. Pharmacological treatment may include a wide range of medications, such as antidepressants, antipsychotics, mood stabilizers, and stimulants. Family and individual counseling is particularly important in helping the patient and the family reconcile themselves to the reality of the behavioral changes in the patient post-TBI.

REFERENCES

1. Ommaya AK, Dannenberg AL, Salazar AM. Causation, incidence, and costs of traumatic brain injury in the U.S. military medical system. J Trauma 1996;40(2):211–217
2. Warden D. Military TBI during the Iraq and Afghanistan wars. J Head Trauma Rehabil 2006;21(5):398–402
3. Centers for Disease Control and Prevention. Traumatic Brain Injury in the United States. Available at: http://www.cdc.gov/ncipc/pub-res/TBI_in_US_04/TBI%20in%20the%20US_Jan_2006.pdf. Accessed December 10, 2008
4. Kim E, Lauterbach EC, Reeve A, et al; ANPA Committee on Research. Neuropsychiatric complications of traumatic brain injury: a critical review of the literature (a report by the ANPA Committee on Research). J Neuropsychiatry Clin Neurosci 2007;19(2):106–127
5. Turnbull SJ, Campbell EA, Swann IJ. Post-traumatic stress disorder symptoms following a head injury: does amnesia for the event influence the development of symptoms? Brain Inj 2001;15(9):775–785
6. Bryant RA, Harvey AG. Relationship between acute stress disorder and posttraumatic stress disorder following mild traumatic brain injury. Am J Psychiatry 1998;155(5):625–629
7. Jorge RE, Robinson RG, Moser D, Tateno A, Crespo-Facorro B, Arndt S. Major depression following traumatic brain injury. Arch Gen Psychiatry 2004;61(1):42–50

8. Shukla S, Cook BL, Mukherjee S, Godwin C, Miller MG. Mania following head trauma. Am J Psychiatry 1987;144(1): 93–96
9. Rao V, Spiro JR, Handel S, Onyike CU. Clinical correlates of personality changes associated with traumatic brain injury. J Neuropsychiatry Clin Neurosci 2008;20(1):118–119
10. Max JE, Koele SL, Castillo CC, et al. Personality change disorder in children and adolescents following traumatic brain injury. J Int Neuropsychol Soc 2000;6(3):279–289
11. Thomsen IV. Late psychosocial outcome in severe traumatic brain injury. Preliminary results of a third follow-up study after 20 years. Scand J Rehabil Med Suppl 1992;26:142–152
12. Thomsen IV. Late outcome of very severe blunt head trauma: a 10-15 year second follow-up. J Neurol Neurosurg Psychiatry 1984;47(3):260–268
13. Dikmen SS, Temkin NR, Machamer JE, Holubkov AL, Fraser RT, Winn HR. Employment following traumatic head injuries. Arch Neurol 1994;51(2):177–186
14. MacKenzie EJ, Edelstein SL, Flynn JP. Hospitalized head-injured patients in Maryland: incidence and severity of injuries. Md Med J 1989;38(9):725–732
15. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. JAMA 1990;263(8):1097–1101
16. Trzepacz PT, Francis J. Low serum albumin levels and risk of delirium. Am J Psychiatry 1990;147(5):675
17. Trzepacz PT, Kennedy R. Delirium and posttraumatic amnesia. In: Silver JM, McAllister TW, Yudofsky SC, eds. Textbook of Traumatic Brain Injury. 1st ed. Washington, DC: American Psychiatric Publishing Inc; 2005:182
18. Wilson JT, Teasdale GM, Hadley DM, Wiedmann KD, Lang D. Post-traumatic amnesia: still a valuable yardstick. J Neurol Neurosurg Psychiatry 1994;57(2):198–201
19. Walz NC, Cecil KM, Wade SL, Michaud LJ. Late proton magnetic resonance spectroscopy following traumatic brain injury during early childhood: relationship with neurobehavioral outcomes. J Neurotrauma 2008;25(2):94–103
20. Rao N, Jellinek HM, Woolston DC. Agitation in closed head injury: haloperidol effects on rehabilitation outcome. Arch Phys Med Rehabil 1985;66(1):30–34
21. Karol RL. Neuropsychosocial Intervention: The Practical Treatment of Severe Behavioral Dyscontrol After Acquired Brain Injury. Chapter 3, The contribution of adjustment issues to behavioural dyscontrol. Boca Raton, FL: CRC Press; 2003:49–70
22. Karol RL. Neuropsychosocial Intervention: The Practical Treatment of Severe Behavioral Dyscontrol After Acquired Brain Injury. Chapter 6, The role of medications in behavioural management. Boca Raton, FL: CRC Press; 2003:133–154
23. Coburn KL, Lauterbach EC, Boutros NN, Black KJ, Arciniegas DB, Coffey CE. The value of quantitative electroencephalography in clinical psychiatry: a report by the Committee on Research of the American Neuropsychiatric Association. J Neuropsychiatry Clin Neurosci 2006;18(4):460–500
24. Borg J, Holm L, Cassidy JD, et al; WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. Diagnostic procedures in mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004;(43, Suppl):61–75
25. Scheid R, Walther K, Guthke T, Preul C, von Cramon DY. Cognitive sequelae of diffuse axonal injury. Arch Neurol 2006;63(3):418–424
26. Perlstein WM, Cole MA, Demery JA, et al. Parametric manipulation of working memory load in traumatic brain injury: behavioral and neural correlates. J Int Neuropsychol Soc 2004;10(5):724–741
27. Cummings JL. Frontal-subcortical circuits and human behavior. Arch Neurol 1993;50(8):873–880
28. Zhang L, Plotkin RC, Wang G, Sandel ME, Lee S. Cholinergic augmentation with donepezil enhances recovery in short-term memory and sustained attention after traumatic brain injury. Arch Phys Med Rehabil 2004;85(7):1050–1055
29. Whyte J, Vaccaro M, Grieb-Neff P, Hart T. Psychostimulant use in the rehabilitation of individuals with traumatic brain injury. J Head Trauma Rehabil 2002;17(4):284–299
30. Lal S, Merbtiz CP, Grip JC. Modification of function in head-injured patients with Sinemet. Brain Inj 1988;2(3):225–233
31. Reinhard DL, Whyte J, Sandel ME. Improved arousal and initiation following tricyclic antidepressant use in severe brain injury. Arch Phys Med Rehabil 1996;77(1):80–83
32. Pachet A, Friesen S, Winkelaar D, Gray S. Beneficial behavioural effects of lamotrigine in traumatic brain injury. Brain Inj 2003;17(8):715–722
33. Mega MS, Cummings JL. Frontal-subcortical circuits and neuropsychiatric disorders. J Neuropsychiatry Clin Neurosci 1994;6(4):358–370
34. Marin R, Chakravorty S. Disorders of diminished motivation. In: Silver JM, McAllister TW, Yudofsky SC, eds. Textbook of Traumatic Brain Injury. 1st ed. Washington, DC: American Psychiatric Pub; 2005:343
35. Jorge RE, Robinson RG, Starkstein SE, Arndt SV. Depression and anxiety following traumatic brain injury. J Neuropsychiatry Clin Neurosci 1993;5(4):369–374
36. Wroblewski BA, Joseph AB, Cornblatt RR. Antidepressant pharmacotherapy and the treatment of depression in patients with severe traumatic brain injury: a controlled, prospective study. J Clin Psychiatry 1996;57(12):582–587
37. Lee H, Kim SW, Kim JM, Shin IS, Yang SJ, Yoon JS. Comparing effects of methylphenidate, sertraline and placebo on neuropsychiatric sequelae in patients with traumatic brain injury. Hum Psychopharmacol 2005;20(2):97–104
38. Sawyer E, Mauro LS, Ohlinger MJ. Amantadine enhancement of arousal and cognition after traumatic brain injury. Ann Pharmacother 2008;42(2):247–252
39. Tenovuo O. Central acetylcholinesterase inhibitors in the treatment of chronic traumatic brain injury-clinical experience in 111 patients. Prog Neuropsychopharmacol Biol Psychiatry 2005;29(1):61–67
40. Pope HG Jr, McElroy SL, Satlin A, Hudson JI, Keck PE Jr, Kalish R. Head injury, bipolar disorder, and response to valproate. Compr Psychiatry 1988;29(1):34–38
41. Schiffer RB, Herndon RM, Rudick RA. Treatment of pathologic laughing and weeping with amitriptyline. N Engl J Med 1985;312(23):1480–1482
42. Schiffer R, Pope LE. Review of pseudobulbar affect including a novel and potential therapy. J Neuropsychiatry Clin Neurosci 2005;17(4):447–454
43. Fujii D, Ahmed I. Psychotic disorder following traumatic brain injury: a conceptual framework. Cogn Neuropsychiatry 2002;7(1):41–62
44. Sachdev P, Smith JS, Cathcart S. Schizophrenia-like psychosis following traumatic brain injury: a chart-based descriptive and case-control study. Psychol Med 2001;31(2): 231–239

45. McAllister TW, Ferrell RB. Evaluation and treatment of psychosis after traumatic brain injury. NeuroRehabilitation 2002;17(4):357–368
46. Hoffman AN, Cheng JP, Zafonte RD, Kline AE. Administration of haloperidol and risperidone after neurobehavioral testing hinders the recovery of traumatic brain injury-induced deficits. Life Sci 2008;83(17-18):602–607
47. Ohry A, Rattok J, Solomon Z. Post-traumatic stress disorder in brain injury patients. Brain Inj 1996;10(9):687–695
48. Schneiderman AI, Braver ER, Kang HK. Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder. Am J Epidemiol 2008;167(12):1446–1452
49. Williams WH, Evans JJ, Wilson BA, Needham P. Brief report: prevalence of post-traumatic stress disorder symptoms after severe traumatic brain injury in a representative community sample. Brain Inj 2002;16(8):673–679
50. Carroll LJ, Cassidy JD, Peloso PM, et al; WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004;(43, Suppl):84–105
51. Westbrook LE, Devinsky O, Geocadin R. Nonepileptic seizures after head injury. Epilepsia 1998;39(9):978–982
52. Hudak AM, Trivedi K, Harper CR, et al. Evaluation of seizure-like episodes in survivors of moderate and severe traumatic brain injury. J Head Trauma Rehabil 2004;19(4): 290–295
53. Barsky AJ, Ahern DK. Cognitive behavior therapy for hypochondriasis: a randomized controlled trial. JAMA 2004; 291(12):1464–1470
54. LaFrance WC Jr, Miller IW, Ryan CE, et al. Cognitive behavioral therapy for psychogenic nonepileptic seizures. Epilepsy Behav 2009;14(4):591–596
55. Arciniegas DB. The cholinergic hypothesis of cognitive impairment caused by traumatic brain injury. Curr Psychiatry Rep 2003;5(5):391–399
56. Silver JM, Koumaras B, Chen M, et al. Effects of rivastigmine on cognitive function in patients with traumatic brain injury. Neurology 2006;67(5):748–755
57. Gualtieri CT, Evans RW. Stimulant treatment for the neurobehavioural sequelae of traumatic brain injury. Brain Inj 1988;2(4):273–290
58. Tateno A, Jorge RE, Robinson RG. Clinical correlates of aggressive behavior after traumatic brain injury. J Neuropsychiatry Clin Neurosci 2003;15(2):155–160
59. Max JE, Robin DA, Lindgren SD, et al. Traumatic brain injury in children and adolescents: psychiatric disorders at two years. J Am Acad Child Adolesc Psychiatry 1997;36(9): 1278–1285
60. Silver JM, Yudofsky SC, Anderson KE. Aggressive disorders. In: Silver JM, McAllister TW, Yudofsky SC, eds. Textbook of Traumatic Brain Injury. 1st ed. Washington, DC: American Psychiatric Publishing Inc; 2005:261
61. Grafman J, Schwab K, Warden D, Pridgen A, Brown HR, Salazar AM. Frontal lobe injuries, violence, and aggression: a report of the Vietnam Head Injury Study. Neurology 1996;46(5):1231–1238
62. Brown GL, Goodwin FK, Ballenger JC, Goyer PF, Major LF. Aggression in humans correlates with cerebrospinal fluid amine metabolites. Psychiatry Res 1979;1(2):131–139
63. Linnoila VM, Virkkunen M. Aggression, suicidality, and serotonin. J Clin Psychiatry 1992;53(Suppl):46–51
64. Levy M, Berson A, Cook T, et al. Treatment of agitation following traumatic brain injury: a review of the literature. NeuroRehabilitation 2005;20(4):279–306
65. Warden DL, Gordon B, McAllister TW, et al; Neurobehavioral Guidelines Working Group. Guidelines for the pharmacologic treatment of neurobehavioral sequelae of traumatic brain injury. J Neurotrauma 2006;23(10):1468–1501
66. Graham DP, Cardon AL. An update on substance use and treatment following traumatic brain injury. Ann N Y Acad Sci 2008;1141:148–162