Head trauma: neurobehavioral aspects

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Synonyms
Posttraumatic syndrome

Key points
• Head trauma can be associated with a diversity of neurobehavioral manifestations, including cognitive impairments and neuropsychiatric disorders.
• Acute concussion syndrome is a brain dysfunction without any macroscopic structural damage induced by an acute mechanical force and potentially associated with attention deficits, amnesia, loss of consciousness and a diversity of cognitive defects.
• Specific neuropsychiatric syndromes include depression, mania, psychosis, aggressive behavior, and personality changes.

Historical note and nomenclature
The ancient Egyptians and Greeks wrote on the neurobehavioral effects of traumatic brain injury. Over the centuries, the study of war wounds, particularly penetrating injuries, made a major contribution to our understanding of brain-behavior relationships. During the 20th century, traumatic brain injury and its consequences became an epidemic, primarily due to the widespread use of motor vehicles. In recent years, investigators have demonstrated that even mild traumatic brain injury can result in neurobehavioral changes.

Clinical manifestations
Most traumatic brain injuries are nonpenetrating and mild. Although classification schemes differ, 1 method of grading traumatic brain injury is as follows: mild traumatic brain injury is loss of consciousness for 5 minutes or less, an initial Glasgow Coma Scale score of 13 to 15, or a posttraumatic amnesia of less than 1 hour (Williams et al 1990; Brown et al 1994). Posttraumatic amnesia is a confusional state with prominent ongoing difficulty laying down new memories. Posttraumatic amnesia may be the best way to monitor the impact and
course of traumatic brain injury (Ellenberg et al 1996). Moderate traumatic brain injury is loss of consciousness for greater than 5 minutes but less than 6 hours, an initial Glasgow Coma Scale score of 9 to 12, or posttraumatic amnesia of 1 hour to 24 hours. Severe traumatic brain injury is loss of consciousness of 6 hours or more, an initial Glasgow Coma Scale score of 3 to 8, or posttraumatic amnesia for more than 24 hours.

The specific neurobehavioral aspects of traumatic brain injury include (1) acute concussional syndrome, (2) the postconcussional disorder, (3) diffuse traumatic brain injury, (4) focal traumatic brain injury, (5) secondary complications of acute traumatic brain injury, (6) delayed deterioration, (7) posttraumatic dementia, and (8) posttraumatic neuropsychiatric disorders. Some acute concussional or postconcussional symptoms occur in most traumatic brain injury patients, and the other neurobehavioral changes occur in about 10% of mild, 67% of moderate, and 100% of severe traumatic brain injury cases (Sorenson and Kraus 1991).

Acute concussion syndrome is brain dysfunction without any macroscopic structural damage induced by an acute mechanical force. The symptoms of concussion are variable. They range from mild attention deficits or confusion to delirium, amnesia, and loss of consciousness. In addition, dizziness, vertigo, and autonomic instability may be manifestations of an acute concussion. Delirium may be characterized by disorientation, confusion, agitation, emotional lability, hallucinations, and confabulation. As this delirium subsides, there may be continued amnesia. The ongoing memory difficulty of posttraumatic amnesia begins at the moment of injury and ends when normal continuous memories have resumed. A period of retrograde amnesia begins with the last clear memory from before the injury and ends at the moment of injury. As the patient improves, the duration of the retrograde amnesia shrinks to within a few minutes or seconds before the brain injury. Patients with mild head injury demonstrate deficits in attention, nonverbal fluency, and verbal memory. They also present slower visual and tactile reaction times (Mathias et al 2004). Heitger and colleagues demonstrated the presence of oculomotor and visuomotor deficits following mild head injury (Heitger et al 2004).

The postconcussional disorder is a constellation of symptoms that follows an acute concussion. This disorder may occur after even mild traumatic brain injury. Postconcussional symptoms occur in 80% to 100% of patients in the first month after injury and may persist after 1 year in a small percentage of patients (Bohnen et al 1992). Disturbances in somatic, affective, and cognitive spheres are present. Somatic symptoms include headaches, fatigue, disordered sleep, and dizziness; affective symptoms include anxiety, depression, emotional lability, irritability, or aggressive spells (Levin et al 1987b; Szymanski and Linn 1992; Milders et al 2003). The main cognitive deficits in memory are in information processing speed, attention, and concentration (Leininger et al 1990). The most common symptom may be difficulty with concentration. It has been further suggested that apparent cognitive defects are indeed the consequence of 2 related deficits: (1) a speed processing defect and (2) a deficit of the central executive system of working memory (Ciaramelli et al 2006). A noteworthy observation is that prefrontal dysfunction is invariably associated with the postconcussional syndrome (Datta et al 2009).

No formal criteria for postconcussional disorder exist, but research criteria have been suggested (Brown et al 1994). The research criteria, however, emphasize documented attention or memory deficits and the presence of symptoms for at least 3 months. Umile and colleagues suggest that the high frequency of temporal lobe abnormalities (which occur in about 75% of the cases), presumably involving
the hippocampus and related structures, may explain the frequent finding of memory disorders in this population (Umile et al 2002).

Diffuse traumatic brain injury may result in permanent neurobehavioral changes (Bond 1986; Salmond and Sahakian 2005). The more severe the head injury, the more likely that there will be residual deficits. The most prominent neuropsychological changes are in 4 areas: (1) information processing speed, (2) attention and concentration, (3) memory, and (4) frontal functions (Bond 1986; Fork et al 2005). Compared to controls, mild traumatic brain injury patients and those who had a severe injury have decreased processing speed on choice reaction time measures and on the Paced Auditory Serial Addition Test (PASAT).

Because of this slowing, performance IQs may be impaired compared to verbal IQs. Severe brain injury leaves patients with a residual subclinical motor slowing as well (Gray et al 1998). The most disturbed attention problem is in divided attention (splitting and shifting among tasks) rather than focused or sustained attention (Stuss et al 1989; Szymanski and Linn 1992). Persistent memory complaints in mild traumatic brain injury may result from these attention difficulties. On memory tests, severe traumatic brain injury patients have poor short-term verbal and nonverbal recall with encoding and retrieval deficits and relatively preserved procedural and remote memories (Crosson et al 1988). After severe brain injury, patients may experience difficulty retrieving autobiographical or historical knowledge and information specifically related to living objects. On frontal-executive functions, traumatic brain injury patients may have impaired judgment, abstraction, reasoning, planning, organizing, mental flexibility, follow-through, impulse control, coping, and anticipatory behavior (Fortin et al 2003; Krpan et al 2007). Even mild traumatic brain injury patients may perform worse than controls on some tests of reasoning (Leininger et al 1990; Borgaro et al 2003). Some patients have decreased word finding and verbal fluency (Crawford et al 2007), impaired comprehension of complex commands and affective content, decreased cohesive discourse, signs of interhemispheric disconnection such as left-sided apraxia and agraphia (Rubens et al 1977), and impaired awareness (Morton and Barker 2010).

Head injury sequelae in children are similar to sequelae observed in adult patients. They include psychomotor speed, memory, attention, and executive functioning defects; sometimes deficits are cumulative over time (Sans et al 2009). Long-term cognitive defects depend on age at the time of the injury (Anderson et al 2009), and injuries at earlier ages usually result in longstanding cognitive defects (Barker et al 2010).

Long-term follow-up of head injury is not frequently reported. In general, impairments can be found in different cognitive measures many years after the injury (Draper and Ponsford 2008; Ruttan et al 2008), whereas physical recovery is usually significant, cognitive and emotional disturbances have a poorer prognosis (deGuise et al 2008). Campbell and colleagues (Campbell et al 2004) followed 41 children with moderate or severe head injury within 16 to 38 months post injury. They found that the initial Glasgow Coma Scale was the best predictor of mortality and cognitive outcome. An improvement in intelligence and memory functioning was observed, with the group's mean performance on these cognitive measures falling within the average range. However, a considerable variability in the outcomes was found. Whitnall and colleagues followed up on 475 head-injured individuals 5 to 7 years after injury and compared their results with their outcome 1 year after injury. They found that 24% of the participants died between the first and the seventh year. In survivors, disability remained frequent in 53% (compared with 57% at one year). Some participants had improved (29%) but others had deteriorated (25%). Disability was significantly associated with
depression, anxiety, and low self-esteem (Whitnall et al 2006). Himanen and colleagues followed up 61 head-injured patients an average of 30 years after an initial evaluation. A slight general cognitive decline was observed with some improvement in semantic memory. Decline was observed only in men, whereas women maintained their cognitive level. Age was negatively associated with cognitive improvement (Himanen et al 2006). The researchers found that reductions in hippocampal volumes and lateral ventricular enlargement were significantly associated with disturbances in memory and executive functions. They proposed that the degree of damage leading to atrophic changes is more important for prognosis than the initial severity of the injury (Himanen et al 2005).

Focal traumatic brain injury results from frontotemporal contusions, coup-contrecoup contusions, or penetrating injuries. Contusions are usually accompanied by deficits from diffuse traumatic brain injury changes; however, they may occur independently. The most common and severe focal traumatic brain injury effects result from bilateral injuries to the basolateral and median frontal cortex and the temporal lobes (Pearl 1998; Schroeter et al 2010). Even more than severe diffuse traumatic brain injury, prominent frontotemporal contusions disrupt frontal functions (such as planning and organization) and temporal functions (such as learning and recent memory). PET and SPECT studies support the assumption that head injury impairs a frontal brain circuit involved in cognitive control (Wilson 2005). Using regional cerebral metabolism measures, Nakayama and colleagues observed bilateral hypometabolism in the medial prefrontal regions, the medial frontobasal regions, the cingulate gyrus, and the thalamus in a group of 52 patients with traumatic diffuse brain injury during the chronic stage (Nakayama et al 2006). Frontal injury may also cause patients to be disinhibited, inappropriate in their behavior, irritable, explosive, prone to aggression and substance abuse, and to have difficulties with sexual expression (Mazaux et al 1997). Conversely, some traumatic brain injury patients with frontotemporal contusions become withdrawn and apathetic. Coup-contrecoup lesions produce focal deficits such as aphasias and agnosias depending on the site of injury. Penetrating traumatic brain injuries have brain damage along the missile tract; this can cause extensive injury without producing loss of consciousness or posttraumatic epilepsy.

Secondary acute complications of traumatic brain injury result from other than direct traumatic effects on neuronal structures. The most important are vascular, such as intracerebral hemorrhages, infarctions from traumatic occlusions or tears of intracranial vessels, subdural hematomas, and epidural hematomas. Subdural hematomas in particular may present with an initial lucid interval with subsequent mental deterioration. Other secondary complications are metabolic, including hypoxia, edema, hyponatremia, and hormonal changes such as the syndrome of inappropriate antidiuretic hormone.

Delayed neurobehavioral deterioration may occur after traumatic brain injuries (McCrorry and Berkovic 1998). Some specific disturbances, such as conceptual difficulties and mood changes, may worsen over time (Lippert-Gruner et al 2006). As noted above, most patients who appear to have a lucid period after the head injury and have a subsequent deterioration have intracranial hematomas. Rarely, patients deteriorate from diffuse cerebral swelling. The etiology of this swelling is unclear, but it may result from disturbed vascular autoregulation. Patients with this usually fatal condition tend to be teenage males who sustain mild, sports-related head injuries. Investigators have proposed that diffuse cerebral swelling occurs when an athlete who has sustained an initial head injury sustains a second head injury before symptoms associated with the first have fully cleared (Cantu
1998; Echemendia and Julian 2001). Other research does not establish a role for this "second impact syndrome" in the causation of diffuse cerebral edema (McCorry and Berkovic 1998). In addition, a delayed decline in cognition may result from the gradual development of obstructive hydrocephalus due to damage to arachnoid villae and a decreased rate of cerebrospinal reabsorption.

Dementia may result from traumatic brain injuries. Early-onset dementia in particular is frequently associated with head injury history (McMurtray et al 2006). Dementia after a single traumatic brain injury follows considerable axonal injury and multiple contusions. In some patients, cognitive impairment progressively worsens after a severe traumatic brain injury and may ultimately result in dementia years later (Fisher 1985; Bond 1986). An association between the probability of developing dementia and ApoE genotype has been observed. Isoniemi and colleagues analyzed the genotype of 61 individuals who had suffered a brain injury more than 30 years earlier (Isoniemi et al 2006). A significantly lower cognitive performance in different neuropsychological testing was observed in individuals with the ApoE epsilon4 allele when compared with those without this allele. Some participants with the ApoE epsilon4 allele had developed a dementia syndrome, whereas most of the ApoE epsilon2-3-positive patients showed no significant intellectual decline.

Dementia also follows repeated blows to the head. Up to 50% of professional boxers develop dementia pugilistica, particularly if they started fighting in their teens, boxed for more than 10 years, accumulated more than 150 fights, and were known to "take a punch" (Roberts et al 1990; Erlanger et al 1999). Besides the usual cognitive and behavioral changes of severe traumatic brain injury, the clinical picture of dementia pugilistica includes psychomotor retardation, paranoia, belligerence, euphoria, depression, alcohol intolerance, dysarthria, scanning speech, ataxia, decreased coordination, parkinsonism, and pyramidal tract signs (Roberts et al 1990). MR and diffusion-weighted imaging show that microstructural damage of the brain associated with chronic traumatic brain injury in boxers may elevate whole-brain diffusion (Zhang 2003). This global elevation can exist even when routine MR findings are normal.

Specific neuropsychiatric syndromes include depression, anxiety, mania, substance disorders, psychosis, aggressive behavior, and personality changes (Nicholl and LaFrance 2009). The prevalence of significant and prolonged depression is 20% to 50% with all traumatic brain injuries (Gualtieri and Cox 1991; Silver et al 1991; Fann et al 1995), 6% to 39% with mild traumatic brain injuries (Schoenhuber and Gentilini 1988), and 10% to 77% with severe traumatic brain injuries (Varney et al 1987). The depression correlates more with the degree of neuropsychological impairment than with the severity of the traumatic brain injury (Bornstein et al 1989; Alexander 1992). Most patients have major depression, about half become depressed 6 months or more after their traumatic brain injury, and many have an increased risk of suicide (Varney et al 1987; Jorge et al 1993). Although rarer than depression, mania or hypomania can occur up to 12 years after traumatic brain injury (Wright et al 1997). Bipolar illness can appear immediately after traumatic brain injury or after a delay of months or longer and appears to occur in patients with an inherited vulnerability and predominant right hemisphere lesions. There is a greater than expected incidence of schizophrenia-like psychosis after traumatic brain injury (Davison and Bagley 1969). These patients often have symptoms similar to paranoid schizophrenia or fixed delusions, such as the belief that they have been sexually betrayed or are dead (Young et al 1992). Aggressive, violent, irritable behavior is another common mental syndrome that may persist years after severe traumatic brain injury (Thomsen 1984; Schoenhuber and Gentilini 1988; Turkstra 2003).
Other posttraumatic neurobehavioral changes include anxiety, emotional lability, nonepileptic seizures, and even obsessive-compulsive behaviors (Thomsen 1984; Jenike and Brandon 1988; Schoenhuber and Gentilini 1988; Thurber 1998). In children, severe traumatic brain injury can also result in phobias, rage attacks, and episodic depression (Basson et al 1991). Finally, appetite changes, frequent hyposexuality, rare hypersexuality, the Kluver-Bucy syndrome, and the Klein-Levin syndrome may occur after severe traumatic brain injury (Will et al 1988; Kreutzer and Zasler 1989; Gorman and Cummings 1992; Lewin and Sumners 1992).

One final clinical consideration is the presence of associated neurologic symptoms. Posttraumatic epilepsy may result in behavioral consequences including depression and a pervasive sense of losing control. Other reports note the occurrence of motor tics, vocal tics, and even akathisia after closed head trauma, even without definite focal abnormalities on neuroimaging (Kraus and Jankovic 1997).

Clinical vignette

A 37-year-old, right-handed male apparently was ejected from his vehicle. He was found about 20 feet from his car. His initial Glasgow Coma Scale at the scene was 3. He underwent CT scans that identified multiple hemorrhagic contusions. Evidence of punctuate hemorrhages in the brain stem, thalamus, and both frontal and parietal regions were reported. Multiple vertebral fractures were also observed.

He remained in coma for more than 1 week. One month later, he could follow simple commands, produce isolated words, and seemed to recognize family members. After being discharged from the hospital, he attended a rehabilitation program for a couple of months but, as a result of some inappropriate behaviors, was removed from the therapy program. His family reported significant personality changes. The patient frequently acted in an impulsive way. Verbal aggression, irritability, and lack of interest toward his family were noted.

Two neuropsychological tests were performed 3 months and 10 months after the head injury. The patient was cooperative throughout the evaluations and followed instructions. His social skills and general behavior were appropriate. He had no obvious visual or hearing impairments. He reported a 5-month total retrograde amnesia and 1-month total anterograde amnesia. He denied any significant depression. He mentioned that he was all right and was eager to return to his previous job but pointed out that he could not “control [his] impulses.”

Comparing the first (3-month) and second (10-month) evaluation (See Table 1), significant improvement was observed in most cognitive domains: language, memory, visuoconstructive abilities, and executive functions. Nonetheless, behavioral changes remained virtually the same between the first and the second testing. As a matter of fact, the behavioral changes were more disruptive to his social and working activities than were the cognitive impairments.

**Table 1. Patient’s Performance on Standard Neuropsychological Tests**

<table>
<thead>
<tr>
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<th>First testing (at 3 months)</th>
<th>Second testing (at 10 months)</th>
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<tbody>
<tr>
<td>General cognitive level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mini-mental state exam (MMSE)</td>
<td>21/30</td>
<td>28/30</td>
</tr>
<tr>
<td>• Neuropsi</td>
<td>77/130</td>
<td>97/130</td>
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</tbody>
</table>
### WAIS-III
- **Information**  SS=4  SS=6
- **Picture completion**  SS=4  SS=5
- **Digits**  SS=11  SS=11
- **Matrix reasoning**  SS=4  SS=7
- **Letter number sequencing**  SS=6  SS=7

### Multilingual aphasia examination
- **Token test**  20th percentile  50th percentile
- **Sentence repetition**  50th percentile  50th percentile

### Controlled word association
- **Letter F**  7  11
- **Animals**  12  20

### Rey-Osterrieth complex figure
- **Copy**  1st percentile  20th percentile
- **Delayed recall**  1st percentile  20th percentile

### Wechsler memory scale--R: logical memory
- **Immediate recall**  1st percentile  10th percentile
- **Delayed recall**  1st percentile  10th percentile

### Boston naming test
- **43/60**  53/60

### Hooper visual organization test
- **5th percentile**  40th percentile

### Trail-making test
- **Part A**  10th percentile  20th percentile
- **Part B**  10th percentile  10th percentile

### Stroop test
- **1st percentile**  15th percentile

### Etiology
Most traumatic brain injuries are nonpenetrating and result from motor vehicle accidents (50%), falls (21%), violence (12%), and sports or recreational injuries (10%) (Department of Health and Human Services 1989). Nonpenetrating traumatic brain injury is caused by linear acceleration or rotational acceleration. Linear acceleration damage is due to a blow on a stationary head, and rotational acceleration is due to trauma that causes the tethered, suspended brain to move out of phase relative to the skull. Rotational trauma includes an angled blow to a stationary, but not stabilized, head, as from uppercut blows in boxing, and the rapid deceleration-acceleration of a moving brain, as from motor vehicle accidents. Even whiplash injuries without loss of consciousness can produce some rotational acceleration of the brain with reversible attention and concentration deficits (Ettlin et al 1992; Radanov et al 1993). Repeated minor rotational injuries lead to cumulative brain damage, as in dementia pugilistica. Further brain injury
results from subdural hematoma, obstructive hydrocephalus, cerebral edema, traumatic vascular injury with scattered punctate lesions, subarachnoid hemorrhage, disseminated intravascular coagulation, systemic fat emboli, and microcirculatory disruption.

Pathogenesis and pathophysiology

Following the mechanical insult in traumatic brain injury, there are multiple cascades of neuropathological processes (Pearl 1998). These include axonal injury, disturbed vascular autoregulation, disturbed ionic fluxes (especially for calcium and potassium), neurotransmitter changes, inflammatory changes, oxygen free-radical formation, and alterations in the expression of amyloid precursor proteins (Lewen et al 1995). Impairment in cerebral vascular autoregulation may occur even after mild traumatic brain injury (Strebel et al 1997). Diffuse axonal injury has been associated with persistent cognitive impairment (Scheid et al 2006). Furthermore, diffuse axonal injury may result in damage to the thalamic projection fibers, potentially contributing to the observed defects in cognition (Little et al 2010).

In general, the more severe the traumatic brain injury, the greater the structural damage. Long-term cerebral atrophy has been correlated with injury severity and duration of posttraumatic amnesia (Wilde et al 2006). Rotational movement causes the greatest and most diffuse brain damage by shearing nerve axons in the subcortical white matter, corpus callosum, upper dorsolateral brainstem, superior cerebellar peduncle, and basal ganglia (Adams et al 1982). The location and extension of white matter abnormalities can partially predict cognitive function (Kinnunen et al 2011). In severe traumatic brain injury, there is widespread axonal tearing, particularly of long tracts projecting from the brain stem, with a breakdown of myelin and extensive neuronal loss (Hammoud and Wasserman 2002). In mild traumatic brain injury, there may be brief physiologic disruption with loss of consciousness; however, there can still be some neuropathological shearing of neuronal tissue (Povlishock and Coburn 1989). The corpus callosum is frequently damaged by closed head injuries, and the resulting deficits of interhemispheric communication may vary according to the specific position of the lesion within the corpus callosum. These disconnection deficits are usually transient, but occasionally, they may be found several years after the trauma (Peru et al 2003). For instance, it has been reported that severe traumatic brain injury is associated with a significant reduction in the volumes of the fornix, the hippocampus, and the corpus callosum; approximately 8 years later, further significant reduction of the corpus callosum, but not the fornix and the hippocampus, is observed (Tomaiuolo et al 2012).

Specific areas of the brain are susceptible to contusion. Both linear and rotational movement result in frontotemporal contusions as the moving brain collides with the adjacent rough surfaces of the skull. Marked cell loss may occur in the memory structures of the hippocampal CA3 region. Orbitofrontal damage is associated with disinhibition and executive disturbances, and hippocampal damage in the temporal poles is associated with memory impairment. Linear acceleration may contuse cortical gray matter located under the place of impact (coup) or near the opposite pole (contrecoup) and results in corresponding higher cortical deficits. Organic mental syndromes may arise from specific contusions, such as major depression arising from left frontal injury (Jorge et al 1993), anxious depression or mania from involvement of the right hemisphere (Starkstein et al 1990; Jorge et al 1993), and hypersexuality from damage to the septal nuclei (Gorman and Cummings 1992). Cortical atrophy in frontal and temporal lobes significantly correlates with deficits in memory and executive
functions (Bergeson et al 2004), and ventromedial prefrontal damage correlates with deficits in social knowledge (Mah et al 2005). Impulsivity has been associated with orbitofrontal gyrus, insula, and caudate abnormalities; disordered performance on rational choices has been related to bilateral involvement of the dorsolateral prefrontal cortices and the superior frontal gyri, right ventrolateral prefrontal cortex, dorsal and ventral striatum, and left hippocampus (Newcombe et al 2011). Decreases in executive functioning are related to damage to the ventral striatum and its associated structures (Shah et al 2012). On the other hand, orbitofrontal cortex damage has been related to defects in temporal context memory (Duarte et al 2010).

Further neuropathological findings arise from cumulative blows to the head. In dementia pugilistica, there is a cavum septum pellucidum, a detached fornix, a thinned corpus callosum, Purkinje cell loss, pigment loss in the substantia nigra, an atrophic midbrain, evidence of prior perivascular hemorrhage, and ventricular enlargement (Roberts et al 1990). Moreover, these patients may have abundant neurofibrillary tangles in the absence of neuritic plaques and profuse beta protein immunoreactive deposits (Roberts et al 1990).

Neurochemical changes occur. Traumatic brain injury can affect the neurotransmitter systems that mediate mood and affect, including norepinephrine, serotonin, dopamine, and acetylcholine. Traumatic brain injury may affect neurohormones that mediate fluid balance and sexuality such as antidiuretic hormone and gonadotrophins. Moreover, neuronal damage could result from free radicals, glutamate, and other excitotoxic neurotransmitters released during hypoxia (Becker et al 1988; Faden et al 1989).

Epidemiology

Head injury is the most common cause of neurologic illness in young people (Fisher 1985; Bond 1986). In the United States, there are more than 2 million traumatic brain injuries per year; 500,000 of these are sufficiently serious to require hospitalization (Goldstein 1990). In addition, different sports have been associated with brain injury (Toth et al 2005). An estimated 300,000 sports-related traumatic brain injuries occur in the United States each year (Anonymous 1997). Potential head injuries in any sport can result in neurobehavioral consequences. Traumatic brain injury is particularly associated with men between the ages of 15 years and 24 years and with motor vehicle accidents and the use of alcohol. Of all traumatic brain injuries, 70% are mild, 20% are moderate or severe, and 10% are fatal (Williams et al 1990).

Prevention

Preventive efforts emphasize protective headgear, seat belts, and education about the dangers of alcohol use when driving. Bicycle and motorcycle helmets reduce the risk of severe traumatic brain injury. Seatbelts significantly reduce the severity of head injuries (Smith-Seemiller et al 1997). Unbelted drivers have severe traumatic brain injuries about twice as often as belted drivers. Approximately 50% of traumatic brain injury cases from motor vehicle accidents involve the use of alcohol, and most of these patients are legally intoxicated at the time of the traumatic brain injury. Use of other drugs besides alcohol can contribute to head injuries. Paradoxically, traumatic brain injury may lead to pathological intoxication and, hence, to further traumatic brain injuries. Other preventive measures include regulations for sports activities involving repeated blows to the head and the avoidance of falls, particularly falls from ladders by the
elderly. Finally, there are specific recommended standards for the assessment of sports-related concussion (McCrea et al 1997; Field et al 2003).

Differential diagnosis

An important differential diagnostic consideration is the presence of intracranial hematomas, obstructive hydrocephalus, or other secondary causes of posttraumatic neurobehavioral changes. Suspicion of these potentially correctable causes may lead to repeat evaluation and neuroimaging.

A second diagnostic consideration is whether there are neurobehavioral changes at all. Mild traumatic brain injury patients are often dismissed as "neurotic," when in fact they may have subtle deficits in attention, memory, and executive functions (Weight 1998). These deficits can be difficult to detect even with the usual neuropsychological measures. Mild traumatic head injury may be mistaken for posttraumatic stress disorder with intrusive recollections and hyperarousal. Traumatic head injury and posttraumatic stress disorder are not mutually exclusive. However, victims of accidents are unlikely to develop a posttraumatic stress disorder if the impact to the head had resulted in an extended period of unconsciousness (Glaesser et al 2004). Postconcussional disorder in children is often mistaken as attention deficit or conduct disorder (Mittenberg et al 1997). Moreover, there may be difficulty in distinguishing posttraumatic changes from preexisting behaviors, especially because traumatic brain injury patients tend to be premorbidly aggressive and risk-taking people.

The differential diagnosis of traumatic brain injury involves questions about the contribution of psychogenic factors to the neurobehavioral aspects. It can be difficult to separate the direct neurobehavioral effects of trauma on the brain from these secondary reactive processes. Patients can develop anxiety, depression, or other neuropsychiatric changes consequent to the injury, the disability from the injury, and the disruption of their lives, including an inability to work or to function at their usual level (Thurber 1998). Subjective somatic, cognitive, emotional, and behavioral complaints are more common with traumatic brain injury than with other types of traumatic injuries (Lannoo et al 1998).

Many patients are involved in posttraumatic brain injury legal cases. For neurologists and others involved in these cases, it can be difficult to disentangle issues of secondary gain from the symptoms of postconcussional disorder. These distinctions are facilitated by the presence of the characteristic clinical profile of postconcussional disorder and neuropsychological deficits in complex attention and other measures. Although most patients do not have litigation as a major component (Leininger et al 1990), a subgroup of patients appear to have secondary gain and a poorer prognosis because of potential compensation (Szymanski and Linn 1992). Clinical evaluation of patients with traumatic head injury must include consideration of the effect of financial incentives on symptoms and disability.

Diagnostic workup

The evaluation of patients who have sustained traumatic brain injury includes an assessment of cognition. In addition to an evaluation of mental status, measures of orientation and attention, such as digits or months forward and backward, various scales and instruments are helpful. The Rivermead Post-Concussion Symptoms Questionnaire and the Galveston Orientation-Attention Test are two particularly useful instruments (King et al 1995; Crawford et al 1996). Specific cognitive tests of value include the Paced Auditory Serial Addition Test, the Symbol Digit Modalities Test, the Digit Symbol Substitution Test, the Speed of
Comprehension Test, double simultaneous stimulation, decision time, and measures of dual task performance (Vilkki et al 1996; Hinton-Bayre et al 1997). General intellectual test batteries can be useful to monitor the patient's changes (Langeluddecke and Lucas 2003). For example, the WAIS-III is a valid and sensible tool to detect cognitive deficits associated with brain injury. Almost all patients with severe brain injury show abnormal IQs with a slow processing speed as a predominant symptom. Some degree of ecological validity (or real-world relevance) is observed in these cognitive measures (Garcia-Molina et al 2012).

Measures have been developed to determine well-being after brain injury; for instance, the European Brain Injury Questionnaire (EBIQ) is a clinically reliable instrument to determine the subjective well-being of individuals with brain injury and to assess change of subjective concerns over time (Teasdale et al 1997; Sopena et al 2007). Length of coma and posttraumatic amnesia seem to be the most relevant parameters related to intelligence in severe brain-injured patients (Ferri et al 2004).

The diagnostic workup includes neuroimaging, neuropsychological testing, and rehabilitation assessments. CT or MRI may be normal or may show cerebral edema or intracranial hemorrhage (Mittl et al 1994). MRI shows diffuse axonal injury in some patients with mild traumatic brain injury (Mittl et al 1994) and additionally shows damage to the corpus callosum, dorsolateral rostral brainstem, and more extensive white matter injury on severe traumatic brain injury (Kampfl et al 1998). Neuroimaging can further define the injury by showing the effects of frontotemporal contusions or of coup-contrecoup contusions. MRI, more than CT, reveals white matter abnormalities, particularly in the frontal and temporal lobes (Levin et al 1987a). Delayed neuroimaging can reveal cerebral atrophy, ventricular enlargement, porencephalic cysts, chronic subdural hematomas, and, in boxers, a cavum septum pellucidum. In addition, neuropsychological testing defines the cognitive effects of traumatic brain injury and forms part of the rehabilitation work up.

Chen and colleagues observed that symptomatic concussed athletes demonstrate task-related activations in some but not all the brain regions, even when they performed as well as the control subjects (Chen et al 2004). Quantitative analysis of fMRI signals within regions of interest revealed that, in general, concussed athletes had different fMRI responses compared to the control subjects. These results demonstrate the potential of fMRI to identify an underlying pathology in symptomatic concussed individuals with normal structural imaging results.

Other less routine tests can be used selectively to clarify the nature of the head trauma. Cerebral blood flow studies, SPECT, and PET can demonstrate focal areas of reduced cerebral perfusion and decreased metabolism even when CT and MRI are normal (Gray et al 1992). SPECT is more sensitive in detecting cerebral abnormalities after mild traumatic brain injury than either CT or MRI (Kant et al 1997). MRI spectroscopy studies may reveal changes that predict neuropsychological dysfunction or the presence of diffuse axonal atrophy (Friedman et al 1999; Huisman et al 2003). Neurophysiological measures and evoked potential studies have revealed abnormalities in patients with traumatic brain injury (Watson et al 1995; Fenton 1996; Doi et al 2007). In particular, middle and long-latency auditory evoked potentials may show abnormal latencies in these patients (Drake et al 1996).

**Prognosis and complications**

Patients with severe traumatic brain injury have a poor prognosis. After the posttraumatic amnesia, there is a 6- to 12-month period of rapid recovery, after
which deficits persist with little change (Bond 1986). Most severe traumatic brain injury patients have cognitive and neuropsychiatric changes years after the trauma, and these deficits are significant in more than half (Thomsen 1984). Furthermore, mood disorders and frustration tolerance may be even more disabling than the cognitive difficulties (Rappaport et al 1989). Only one third eventually return to work and most have decreased social contacts and interests (Prigatano et al 1984; Thomsen 1984). Children with moderate to severe head trauma have significant long-term reduction in their quality of life as well as reduced communication skills, self-care ability, and participation in social activities (Rivara et al 2011). Good recovery depends on a diversity of factors, including shorter duration of posttraumatic amnesia, less fatigue, absence of intracranial pathology, higher education, and better performance on cognitive measures (Sigurdardottir et al 2009). The poorest outcomes are associated with severe diffuse axonal injury, significant frontal contusions, or increased width of the third ventricle on CT or MRI. Radiographically detectable intracranial pathology represents a reliable predictor of poor recovery during the first year following the injury (Levin et al 2008). Interestingly, females seem to present a better cognitive recovery than males (Ratcliff et al 2007).

Mild or moderate traumatic brain injury patients have a much better prognosis. Factors such as posttraumatic amnesia are variable predictors of prognosis with mild injury (King 1997). After mild traumatic brain injury, about half of postconcussional disorder symptoms are resolved at 3 months after the trauma, and most are gone at 6 months (Szymanski and Linn 1992). At 1 year after mild traumatic brain injury, up to 15% of patients may still experience headaches, fatigability, dizziness, irritability, memory loss, and depression (Levin et al 1987; Schoenhuber and Gentilini 1988; Leininger et al 1990). Long-term effects of mild head injury (approximately 8 years post injury), including complex attention and working memory defects, have been reported (Vanderploeg et al 2005). Keenan and colleagues reported that children with mild to severe traumatic head injury before the age of 2 years were at risk of presenting global cognitive defects and below normal scores on adaptive behavior tests at the age of 3 years (Keenan et al 2007).

There are other important prognostic factors. Pre-injury intelligence has been reported as the most consistent predictor of cognitive outcome recovery and decline after such traumatic head injury (Raymont et al 2008). Cognitive impairments are more likely to develop with recurrent traumatic brain injuries, a history of alcoholism, advanced age, the presence of an apolipoprotein 4-epsilon genotype, and the presence of significant anxiety (Chen et al 1997). Patients with cognitive dysfunction are more likely to sustain head injuries (Teasdale and Engberg 1997). Prior emotional adjustment is also a factor in recovery. Alcohol use is a particularly poor prognostic factor (Sparadeo and Gill 1989). Increasing age is associated with poorer outcome, and children may have a better cognitive prognosis. Children, however, may be left with behavioral problems and social maladjustment (Cattelani et al 1998). Hawley and colleagues followed up at a mean of 2.2 years post-injury with 526 injured children (419 mild, 58 moderate, 49 severe) aged 5 to 15 years at injury (mean 9.8) (Hawley et al 2004). Frequent behavioral, emotional, memory, and attention problems were reported by one third of the severe, one quarter of the moderate, and 10% to 18% of the mild groups. Personality change since head injury was reported in 148 children (28%), (21% mild head injury, 46% moderate, 69% severe). Following the head injury, 252 (48%) had moderate disability (43% mild head injury, 64% moderate, 69% severe), whereas 270 (51%) made a good recovery (57% mild head injury, 36% moderate, 22% severe). Difficulties in academic achievement scores have been
documented 5 years following the head injury in youth aged 5 to 15 years (Ewing-Cobbs et al 2004). In a long term follow-up it was found that children sustaining mild head injuries may be more vulnerable to development of chronic mild neuropsychological disorders than adults sustaining similar damage (Hessen et al 2007). However, young children with mild head injuries can make age-appropriate progress at least to 10 years post-trauma (Anderson et al 2012).

Patients who have sustained frontal-executive impairments are particularly unlikely to attain social autonomy and return to work (Mazaux et al 1997). In addition, there may be a higher-than-average incidence of traumatic brain injury in patients who later develop Alzheimer disease, suggesting a role for traumatic brain injury in the development of that dementia (Sullivan et al 1987; Nandoe et al 2002; Suhanov et al 2006). Whole-brain atrophy occurs after mild or moderate head injury and is evident at an average of 11 months after trauma, partially accounting for the long-term behavioral and cognitive sequelae (MacKenzie et al 2002). The presence of primitive reflexes also predicts performance in cognitive tests and the future level of functional independence (Wortzel et al 2009).

An instrument that specifically assesses the quality of life in patients with traumatic brain injury (QOLIBRI: Quality of Life after Brain Injury) has been developed (Bullinger et al 2002; von Steinbüchel et al 2010). It is a comprehensive questionnaire with 37 items covering 6 dimensions (cognition, self, daily life and autonomy, social relationships, emotions, and physical problems), together with an overall score. The dimension scores can be used separately, or they can be combined to give a profile of quality of life.

**Management**

Early rehabilitation results in greater improvement in emotional and social functions than in cognitive functions (Prigatano et al 1984). The specific rehabilitation measures vary with each patient's needs, and guidelines are needed to better identify patients who will respond to neuropsychological rehabilitation (Cicerone et al 1996). For mild traumatic brain injury with postconcussional disorder, patients benefit from education, counseling, and support. Other useful techniques included graded resuming of activity and cognitive restructuring of patients' environments to compensate for their deficits (Mittenberg and Burton 1994). For more severe traumatic brain injury, patients additionally benefit from various therapies including occupational, physical, speech, relaxation, biofeedback, and behavior modification therapies. The newer techniques of cognitive rehabilitation include the substitution of alternative means, such as teaching strategies to compensate for lost or impaired functions. In general, routine medical follow-up of patients with severe traumatic brain injury is beneficial to recovery (Wade et al 1997; Prigatano 1999). Evidence supports the use of certain cognitive and behavioral rehabilitation strategies for individuals with traumatic head injury (Anonymous 1999; Chua et al 2007; Cicerone et al 2008; Rohling et al 2009; Shum et al 2011).

Posttraumatic brain injury neurobehavioral problems may respond to the range of psychoactive medications including psychotropics, antidepressants, beta-adrenergics, lithium, and psychostimulants. Psychotropics may slow cognitive recovery; however, clozapine and other psychotropics may be useful in the treatment of posttraumatic brain injury psychosis and aggression (Michals et al 1993). Antidepressants may induce sedation and anticholinergic side effects; however, fluoxetine, bupropion, desipramine, carbamazepine, and others may ameliorate major depression due to traumatic brain injury (Varney et al 1987). Valproate, lithium, and beta-adrenergic receptor antagonists such as propranolol are particularly useful in treating agitation and aggression (Wroblewski et al
Psychostimulant medications have helped attention deficits, fatigue, and inertia (Gualtieri 1988). However, preliminary studies do not support the use of methylphenidate or other stimulants in the treatment of traumatic brain injury patients (Speech et al 1993). It has been suggested that cholinergic enhancers may represent a treatment of cognitive deficits in cases of traumatic head injury (Salmond et al 2005). Arciniegas and Silver have proposed that patients with defects in arousal and speed of processing may benefit from treatment with agents that increase catecholaminergic function, whereas patients with memory defects may improve from treatment with cholinesterase inhibitors (Arciniegas and Silver 2006). Finally, bromocriptine given to individuals with attentional difficulties does not seem to improve attentional ability, and it may be even associated with an excess of adverse consequence (Whyte et al 2008).

Pregnancy
Pregnancy may complicate hypoxia, increased intracranial hypertension, and other acute effects of traumatic brain injury.

Anesthesia
Anesthesia may also complicate hypoxia, increased intracranial hypertension, and other effects of traumatic brain injury.

ICD codes
ICD-9:
Frontal lobe syndrome: 310.0
Personality change due to conditions classified elsewhere: 310.1
Post concussion syndrome: 310.2
Other specified nonpsychotic mental disorders following organic brain damage: 310.8
Unspecified nonpsychotic mental disorder following organic brain damage: 310.9

ICD-10:
Organic personality disorder due to brain disease, damage and dysfunction: F07.0
Postencephalitic syndrome: F07.1
Postconcussional syndrome: F07.2
Other organic personality and behavioural disorders due to brain disease, damage and dysfunction: F07.8
Unspecified organic personality and behavioural disorder due to brain disease, damage and dysfunction: F07.9

Associated disorders
Subdural hematoma
Alzheimer disease

Related summaries
Affective disorders in neurologic disease
Dementia in Parkinson disease
Dementia pugilistica

Differential diagnosis
intracranial hematomas
obstructive hydrocephalus
other secondary causes of posttraumatic neurobehavioral changes
neurosis
posttraumatic stress disorder with intrusive recollections and hyperarousal
attention deficit disorder
conduct disorder
preexisting behaviors
secondary reactive processes
faked symptoms for financial gain

Demographics
For more specific demographic information, see the Epidemiology, Etiology, and Pathogenesis and pathophysiology sections of this clinical summary.

Age
0-01 month
01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years
65+ years

Population
None selectively affected.

Occupation
Boxers

Sex
male>female, >2:1
male>female, >1:1

Family history
None

Heredity
None

References cited


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**References especially recommended by the author or editor for general reading