

Traumatic Brain Injury



National Institute of Neurological Disorders
and Stroke
National Institutes of Health

Hope Through Research

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Table of Contents

Introduction	1
What is a TBI?	3
How does TBI affect the brain?	4
What are the leading causes of TBI?	9
What are the signs and symptoms?	11
Effects on consciousness	14
How is TBI diagnosed?	15
How is TBI treated?	19
Treating mild TBI	19
Treating severe TBI	21
Other factors that influence recovery	23
Can a TBI be prevented?	25
What research is NINDS funding?	26
Clinical trials	28
Animal models	31
How is NINDS coordinating research efforts?	32
How can I support TBI research?	34
Where can I get more information?	38
Glossary	41

Introduction

Traumatic brain injury (TBI) is the leading cause of death and disability in children and young adults in the United States. TBI is also a major concern for elderly individuals, with a high rate of death and hospitalization due to falls among people age 75 and older. Depending on the severity of injury, TBI can have a lasting impact on quality of life for survivors of all ages — impairing thinking, decision making and reasoning, concentration, memory, movement, and/or sensation (e.g., vision or hearing), and causing emotional problems (personality changes, impulsivity, anxiety, and depression) and epilepsy.

Annually, TBI injuries cost an estimated \$76 billion in direct and indirect medical expenses. According to the U.S. Centers for Disease Control and Prevention:

- TBIs were a factor in the deaths of more than 50,000 people in the United States
- More than 280,000 people with TBI were hospitalized
- 2.2 million people with TBI visited an emergency department¹.

These figures are likely an underestimate of the true number of TBIs as they exclude people who did not seek medical attention at the emergency room. Although approximately 75 percent of brain injuries are considered mild (not life-threatening),

¹ Traumatic Brain Injury in the United States Fact Sheet. *Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention.* January 12, 2015.



According to the CDC, 2.2 million people with TBI visited an emergency department in one year.

as many as 5.3 million people in the United States are estimated to be living with the challenges of long-term TBI-related disability.

2

Not every TBI is alike. Each injury is unique and can cause changes that affect a person for a short period of time, or sometimes permanently.

The majority of people will completely recover from symptoms related to *concussion*², a mild type of TBI. However, persistent symptoms do occur for some people and may last for weeks or months. The long-term effects of TBI may vary depending on the number and nature of “hits” to the head, the age and gender of the individual, the speed with which the person received medical attention, and genetic and other factors.

Over the past few decades preventive measures, such as seatbelts and helmets, and better critical care have substantially increased survival from severe TBI.

² Words in *Italic* appear in a Glossary at the end of this document.

Recently, research has expanded from a singular focus on severe TBI to a greater awareness about potential long-term consequences and the need to find better ways to diagnose, treat, and prevent all forms of TBI. Many questions remain unanswered regarding the impact of TBIs, the best treatments, and the most effective methods for promoting recovery of brain function. This publication outlines what is known about TBI, as well as directions for future research.

What is a TBI?

A TBI occurs when physical, external forces impact the brain either from a penetrating object or a bump, blow, or jolt to the head. Not all blows or jolts to the head result in a TBI. For the ones that do, TBIs can range from mild (a brief change in mental status or consciousness) to severe (an extended period of unconsciousness or amnesia after the injury). There are two broad types of head injuries: penetrating and non-penetrating.

Penetrating TBI (also known as *open TBI*) occurs when the skull is pierced by an object (for example, a bullet, shrapnel, bone fragment, or by a weapon such as hammer, knife, or baseball bat). With this injury, the object enters the brain tissue.

Non-penetrating TBI (also known as *closed head injury* or *blunt TBI*) is caused by an external force that produces movement of the brain within the skull. Causes include falls, motor vehicle crashes, sports injuries, or being struck by an object. Blast

injury due to explosions is a focus of intense study but how it causes brain injury is not fully known.

Some accidents such as explosions, natural disasters, or other extreme events can cause both penetrating and non-penetrating TBI in the same person.

How does TBI affect the brain?

TBI-related damage can be confined to one area of the brain, known as a *focal injury*, or it can occur over a more widespread area, known as a *diffuse injury*. The type of injury is another determinant of the effect on the brain. Some injuries are considered *primary*, meaning the damage is immediate. Other consequences of TBI can be *secondary*, meaning they can occur gradually over the course of hours, days, or weeks. These secondary brain injuries are the result of reactive processes that occur after the initial head trauma.

There are a variety of immediate effects on the brain, including various types of bleeding and tearing forces that injure nerve fibers and cause inflammation, metabolic changes, and brain swelling.

- *Diffuse axonal injury (DAI)* is one of the most common types of brain injuries. DAI refers to widespread damage to the brain's white matter. White matter is composed of bundles of axons (projections of nerve cells that carry electrical impulses). Like the wires in a computer, axons connect various areas of the brain to one another. DAI is the result of *shearing* forces, which stretch or tear these axon bundles. This

damage commonly occurs in auto accidents, falls, or sports injuries. It usually results from rotational forces (twisting) or sudden deceleration. It can result in a disruption of neural circuits and a breakdown of overall communication among nerve cells, or *neurons*, in the brain. It also leads to the release of brain chemicals that can cause further damage. These injuries can cause temporary or permanent damage to the brain, and recovery can be prolonged.

- *Concussion* — a type of mild TBI that may be considered a temporary injury to the brain but could take minutes to several months to heal. Concussion can be caused by a number of things, including a bump, blow, or jolt to the head, sports injury or fall, motor vehicle accident, weapons blast, or a rapid acceleration or deceleration of the brain within the skull (such as the person having been violently shaken).

5



Concussions can have a number of causes including motor vehicle accidents.

The individual either suddenly loses consciousness or has sudden altered state of consciousness or awareness, and is often called “dazed” or said to have his/her “bell rung.” A second concussion closely following the first one causes further damage to the brain — the so-called “second hit” phenomenon — and can lead to permanent damage or even death in some instances.

- *Hematomas* — a pooling of blood in the tissues outside of the blood vessels. Hematomas can develop when major blood vessels in the head become damaged, causing severe bleeding in and around the brain. Different types of hematomas form depending on where the blood collects relative to the *meninges*. The meninges are the protective membranes surrounding the brain, which consist of three layers: dura mater (outermost), arachnoid mater (middle), and pia mater (innermost).
 - *Epidural hematomas* involve bleeding into the area between the skull and the dura mater. These can occur with a delay of minutes to hours after a skull fracture damages an artery under the skull, and are particularly dangerous.
 - *Subdural hematomas* involve bleeding between the dura and the arachnoid mater, and, like epidural hematomas, exert pressure on the outside of the brain. Their effects vary depending on their size. They are very common in the elderly after a fall.
 - *Subarachnoid hemorrhage* is bleeding that occurs between the arachnoid mater and the pia mater and their effects vary depending on their size.

— Bleeding into the brain itself is called an *intracerebral hematoma* and damages the surrounding tissue.

- *Contusions* — a bruising or swelling of the brain that occurs when very small blood vessels bleed into brain tissue. Contusions can occur directly under the impact site (i.e., a *coup injury*) or, more often, on the complete opposite side of the brain from the impact (i.e., a *contrecoup injury*). They can appear after a delay of hours to a day.
- *Coup/Contrecoup lesions* — contusions or subdural hematomas that occur at the site of head impact as well as directly opposite the coup lesion. Generally they occur when the head abruptly decelerates, which causes the brain to bounce back and forth within the skull (such as in a high-speed car crash). This type of injury also occurs in *shaken baby syndrome*, a severe head injury that results when an infant or toddler is shaken forcibly enough to cause the brain to bounce back and forth against the skull.
- *Skull fractures* — break cracks in one or more of the bones that form the skull. They are a result of blunt force trauma and can cause damage to the underlying areas of the skull such as the membranes, blood vessels, and brain. One main benefit of helmets is to prevent skull fracture.



Skull fractures result from blunt force trauma and can cause damage to underlying areas of the skull.

The first 24 hours after mild TBI are particularly important because subdural hematoma, epidural hematoma, contusion, or excessive brain swelling (edema) are possible and can cause further damage. For this reason doctors suggest watching a person for changes for 24 hours after a concussion.

- *Hemorrhagic progression of a contusion (HPC)* contributes to secondary injuries. HPCs occur when an initial contusion from the primary injury continues to bleed and expand over time. This creates a new or larger lesion — an area of tissue that has been damaged through injury or disease. This increased exposure to blood, which is toxic to brain cells, leads to swelling and further brain cell loss.
- Secondary damage may also be caused by a breakdown in the *blood-brain barrier*. The blood-brain barrier preserves the separation between the brain fluid and the very small capillaries that bring the brain nutrients and oxygen through the blood. Once disrupted, blood, plasma proteins, and other foreign substances leak into the space between neurons in the brain and trigger a chain reaction that causes the brain to swell. It also causes multiple biological systems to go into overdrive, including inflammatory responses which can be harmful to the body if they continue for an extended period of time. It also permits the release of neurotransmitters, chemicals used by brain cells to communicate, which can damage or kill nerve cells when depleted or over-expressed.
- Poor blood flow to the brain can also cause secondary damage. When the brain sustains

a powerful blow, swelling occurs just as it would in other parts of the body. Because the skull cannot expand, the brain tissue swells and the pressure inside the skull rises; this is known as *intracranial pressure (ICP)*. When the intracranial pressure becomes too high it prevents blood from flowing to the brain, which deprives it of the oxygen it needs to function. This can permanently damage brain function.

Additional information about TBI and its causes can be found on the U.S. Centers for Disease Control and Prevention TBI website: <http://www.cdc.gov/TraumaticBrainInjury/>.

What are the leading causes of TBI?

According to data from the Centers for Disease Control and Prevention (CDC), falls are the most common cause of TBIs and occur most frequently among the youngest and oldest age groups. From 2006 to 2010 alone, falls caused more than half (55 percent) of TBIs among children aged 14 and younger. Among Americans age 65 and older, falls accounted for more than two-thirds (81 percent) of all reported TBIs.

The second and third most common causes of TBI are unintentional blunt trauma (accidents that involved being struck by or against an object), followed closely by motor vehicle accidents. Blunt trauma is especially common in children younger than 15 years old, causing nearly a quarter of all TBIs. Assaults account for an additional 10 percent of TBIs, and include abuse-related TBIs, such



Among girls, TBI occurs most often while playing sports such as soccer or basketball.

as head injuries that result from shaken baby syndrome.

Unintentional blunt trauma includes sports-related injuries, which are also a major cause of TBI. Overall, bicycling, football, playground activities, basketball, and soccer result in

the most TBI-related emergency room visits. The cause of these injuries does vary slightly by gender. According to the CDC, among children age 10 to 19, boys are most often injured while playing football or bicycling. Among girls, TBI occur most often while playing soccer or basketball or while bicycling. Anywhere from 1.6 million to 3.8 million sports- and recreation-related TBIs are estimated to occur in the United States annually.

TBIs caused by blast trauma from roadside bombs became a common injury to service members in recent military conflicts. From 2000 to 2014 more than 320,000 military service personnel sustained TBIs, though these injuries were not all conflict related. The majority of these TBIs were classified as mild head injuries and due to similar causes as those that occur in civilians.

Adults age 65 and older are at greatest risk for being hospitalized and dying from a TBI, most likely from a fall. TBI-related deaths in children aged 4 years and younger are most likely the result of assault. In young adults aged 15 to 24 years, motor vehicle accidents are the most likely cause. In every age

group, serious TBI rates are higher for men than for women. Men are more likely to be hospitalized and are nearly three times more likely to die from a TBI than women.

What are the signs and symptoms?

The effects of TBI can range from severe and permanent disability to more subtle functional and cognitive difficulties that often go undetected during initial evaluation. These problems may emerge days later. Headache, dizziness, confusion, and fatigue tend to start immediately after an injury, but resolve over time. Emotional symptoms such as frustration and irritability tend to develop later on during the recovery period. Many of the signs and symptoms can be easily missed as people may appear healthy even though they act or feel different. Many of the symptoms overlap with other conditions, such as depression or sleep disorders. If any of the following symptoms appear suddenly or worsen over time following a TBI, especially within the first 24 hours after the injury, people should immediately see a medical professional.

People should seek immediate medical attention if they experience any of the following symptoms:

- loss of or change in consciousness anywhere from a few seconds to a few hours
- decreased level of consciousness, i.e., hard to awaken
- convulsions or seizures

- unequal dilation in the pupils of the eyes or double vision
- clear fluids draining from the nose or ears
- nausea and vomiting
- new neurologic deficit, i.e., slurred speech; weakness of arms, legs, or face; loss of balance.

Other common symptoms that should be monitored include:

- mild to profound confusion or disorientation
- problems remembering, concentrating, or making decisions
- headache
- light-headedness, dizziness, vertigo, or loss of balance or coordination
- sensory problems, such as blurred vision, seeing stars, ringing in the ears, bad taste in the mouth
- sensitivity to light or sound
- mood changes or swings, agitation (feeling sad or angry for no reason), combativeness, or other unusual behavior
- feelings of depression or anxiety
- fatigue or drowsiness; a lack of energy or motivation
- changes in sleep patterns (e.g., sleeping a lot more or having difficulty falling or staying asleep); inability to wake up from sleep.



TBI symptoms including headache, dizziness, confusion, and fatigue generally start immediately after an injury, but resolve over time.

Diagnosing TBI in children can be challenging because they may be unable to let others know that they feel different. A child with a TBI may display the following signs or symptoms:

13

- changes in eating or nursing habits
- persistent crying, irritability, or crankiness; inability to be consoled
- changes in ability to pay attention; lack of interest in a favorite toy or activity
- changes in the way the child plays
- changes in sleep patterns
- sadness or depression
- loss of a skill, such as toilet training
- loss of balance or unsteady walking
- vomiting.

In some cases, repeated blows to the head can cause *chronic traumatic encephalopathy (CTE)* — a progressive neurological disorder associated with a variety of symptoms, including cognition and communication problems, motor disorders, problems with impulse control and depression, confusion, and irritability. CTE occurs in those with extraordinary exposure to multiple blows to the head and as a delayed consequence after many years. Studies of retired boxers have shown that repeated blows to the head can cause a number of issues, including memory problems, tremors, and lack of coordination and dementia. Recent studies have demonstrated rare cases of CTE in other sports with repetitive mild head impacts (e.g., soccer, wrestling, football, and rugby). A single, severe TBI also may lead to a disorder called *post-traumatic dementia (PTD)*, which may be progressive and share some features with CTE. Studies assessing patterns among large populations of people with TBI indicate that moderate or severe TBI in early or mid-life may be associated with increased risk of dementia later in life.

Effects on consciousness

A TBI can cause problems with arousal, consciousness, awareness, alertness, and responsiveness. Generally, there are four abnormal states that can result from a severe TBI:

- *Brain death* — The lack of measurable brain function and activity after an extended period of time is called brain death and may be confirmed by studies that show no blood flow to the brain.

- *Coma* — A person in a coma is totally unconscious, unaware, and unable to respond to external stimuli such as pain or light. Coma generally lasts a few days or weeks after which an individual may regain consciousness, die, or move into a vegetative state.
- *Vegetative state* — A result of widespread damage to the brain, people in a vegetative state are unconscious and unaware of their surroundings. However, they can have periods of unresponsive alertness and may groan, move, or show reflex responses. If this state lasts longer than a few weeks it is referred to as a *persistent vegetative state*.
- *Minimally conscious state* — People with severely altered consciousness who still display some evidence of self-awareness or awareness of one's environment (such as following simple commands, yes/no responses).

How is TBI diagnosed?

Although the majority of TBIs are mild they can still have serious health implications. Of greatest concern are injuries that can quickly grow worse. All TBIs require immediate assessment by a professional who has experience evaluating head injuries. A neurological exam will assess motor and sensory skills and the functioning of one or more cranial nerves. It will also test hearing and speech, coordination and balance, mental status, and changes in mood or behavior, among other abilities.



The most common imaging technology used to evaluate people with suspected TBI is computed tomography or CT.

Screening tools for coaches and athletic trainers can identify the most concerning concussions for medical evaluation.

Initial assessments may rely on standardized instruments such as the *Acute Concussion Evaluation (ACE)* form from the Centers for Disease Control and Prevention or the *Sport Concussion Assessment Tool 2*, which provide a systematic way to assess a person who has suffered a mild TBI. Reviewers collect information about the characteristics of the injury, the presence of amnesia (loss of memory) and/or *seizures*, as well as the presence of physical, cognitive, emotional, and sleep-related symptoms. The ACE is also used to track symptom recovery over time. It also takes into account risk factors (including concussion, headache, and psychiatric history) that can impact how long it takes to recover from a TBI.

When necessary, medical providers will use brain scans to evaluate the extent of the primary brain injuries and determine if surgery will be needed to help repair any damage to the brain. The need for imaging is based on a physical examination by a doctor and a person's symptoms.

Computed tomography (CT) is the most common imaging technology used to assess people with suspected moderate to severe TBI. CT scans create a series of cross-sectional x-ray images of the skull and brain and can show fractures, hemorrhage, hematomas, hydrocephalus, contusions, and brain tissue swelling. CT scans are often used to assess the damage of a TBI in emergency room settings.

Magnetic resonance imaging (MRI) may be used after the initial assessment and treatment as it is a more sensitive test and picks up subtle changes in the brain that the CT scan might have missed.

17

Unlike moderate or severe TBI, milder TBI may not involve obvious signs of damage (hematomas, skull fracture, or contusion) that can be identified with current neuroimaging. Instead, much of what is believed to occur to the brain following mild TBI happens at the cellular level. Significant advances have been made in the last decade to image milder TBI damage. For example, diffusion tensor imaging (DTI) can image white matter tracts, more sensitive tests like fluid-attenuated inversion recovery (FLAIR) can detect small areas of damage, and susceptibility-weighted imaging very sensitively identifies bleeding. Despite these improvements, currently available imaging technologies, blood tests, and other measures remain inadequate for

detecting these changes in a way that is helpful for diagnosing the mild concussive injuries.

Neuropsychological tests to gauge brain functioning are often used in conjunction with imaging in people who have suffered mild TBI. Such tests involve performing specific cognitive tasks that help assess memory, concentration, information processing, executive functioning, reaction time, and problem solving. The *Glasgow Coma Scale* is the most widely used tool for assessing the level of consciousness after TBI. The standardized 15-point test measures a person's ability to open his or her eyes and respond to spoken questions or physical prompts for movement. A total score of 3-8 indicates a severe head injury; 9-12 indicates moderate injury; and 13-15 is classified as mild injury. (For more information about the scale, see <http://glasgowcomascale.org/>).

Many athletic organizations recommend establishing a baseline picture of an athlete's brain function at the beginning of each season, ideally before any head injuries have occurred. Baseline testing should begin as soon as a child begins a competitive sport. Brain function tests yield information about an individual's memory, attention, and ability to concentrate and solve problems. Brain function tests can be repeated at regular intervals (every 1 to 2 years) and also after a suspected concussion. The results may help health care providers identify any effects from an injury and allow them make more informed decisions about whether a person is ready to return to their normal activities.

How is TBI treated?

Many factors, including the size, severity, and location of the brain injury, influence how a TBI is treated and how quickly a person might recover. One of the critical elements to a person's prognosis is the severity of the injury. Although brain injury often occurs at the moment of head impact, much of the damage related to severe TBI develops from secondary injuries which happen days or weeks after the initial trauma. For this reason, people who receive immediate medical attention at a certified trauma center tend to have the best health outcomes.

Treating mild TBI

Individuals with mild TBI, such as concussion, should focus on symptom relief and “brain rest.” In these cases, headaches can often be treated with over-the-counter pain relievers. People with mild TBI are also encouraged to wait to resume normal activities until given permission by a doctor. People with a mild TBI should:

- Make an appointment for a follow-up visit with their health care provider to confirm the progress of their recovery.
- Inquire about new or persistent symptoms and how to treat them.
- Pay attention to any new signs or symptoms even if they seem unrelated to the injury (for example, mood swings, unusual feelings of irritability). These symptoms may be related even if they occurred several weeks after the injury.



Even after symptoms resolve entirely, people should return to their daily activities gradually. Brain functionality may still be limited despite an absence of outward symptoms. Very little is known about the long-term effects of concussions on brain function. There is no

Individuals with mild TBI should focus on symptom relief and “brain rest,” and are encouraged to wait to resume normal activities until given permission from their health care provider.

clear timeline for a safe return to normal activities although there are guidelines such as those from the *American Academy of Neurology* and the *American Medical Society for Sports Medicine* to help determine when athletes can return to practice or competition. Further research is needed to better understand the effects of mild TBI on the brain and to determine when it is safe to resume normal activities.

20

Preventing future concussions is critical. While most people recover fully from a first concussion within a few weeks, the rate of recovery from a second or third concussion is generally slower.

In the days or weeks after a concussion, a minority of individuals may develop *post-concussion syndrome (PCS)*. People can develop this syndrome even if they never lost consciousness. The symptoms include headache, fatigue, cognitive impairment, depression, irritability, dizziness and balance trouble, and apathy. These symptoms usually improve without medical treatment within one to a few weeks but some people can have longer lasting symptoms.

In some cases of moderate to severe TBI, persistent symptoms may be related to conditions triggered by imbalances in the production of hormones required for the brain to function normally. Hormone imbalances can occur when certain glands in the body, such as the pituitary gland, are damaged over time as result of the brain injury. Symptoms of these hormonal imbalances include weight loss or gain, fatigue, dry skin, impotence, menstrual cycle changes, depression, difficulty concentrating, hair loss, or cold intolerance. When these symptoms persist 3 months after their initial injury or when they occur up to 3 years after the initial TBI, people should speak with a health care provider about their condition.

Treating severe TBI

Immediate treatment for the person who has suffered a severe TBI focuses on preventing death; stabilizing the person's spinal cord, heart, lung, and other vital organ functions; and preventing further brain damage. Persons with severe TBI generally require a breathing machine to ensure proper oxygen delivery and breathing.

During the acute management period, health care providers monitor the person's blood pressure, flow of blood to the brain, brain temperature, pressure inside the skull, and the brain's oxygen supply. A common practice called intracranial pressure ICP monitoring involves inserting a special catheter through a hole drilled into the skull. Doctors frequently rely on ICP monitoring as a way to determine if and when medications or surgery are needed in order to prevent secondary

brain injury from swelling. People with severe head injury may require surgery to relieve pressure inside the skull, get rid of damaged or dead brain tissue (especially for penetrating TBI), or remove hematomas.

In-hospital strategies for managing people with severe TBI aim to prevent conditions including:

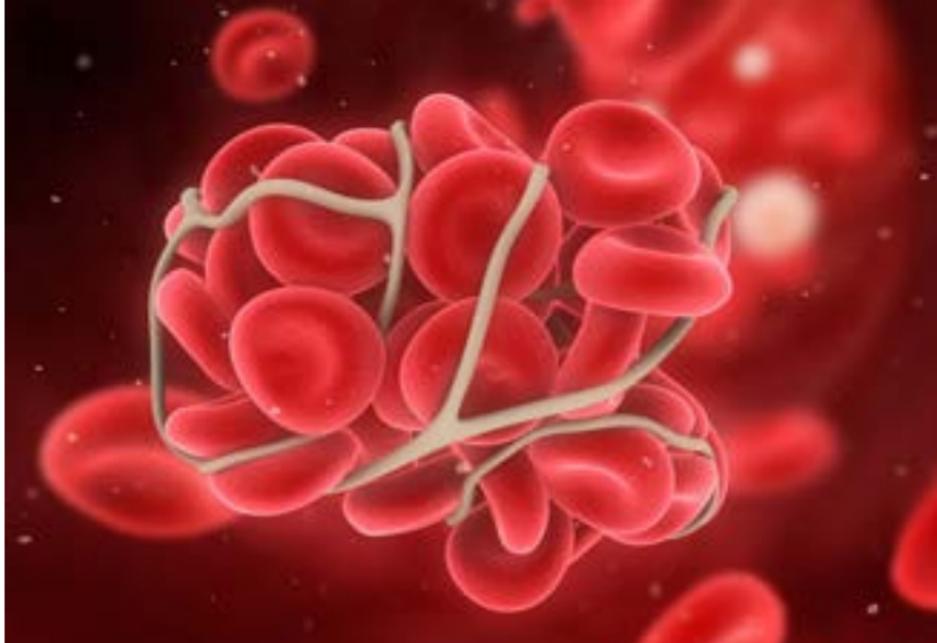
- infection, particularly pneumonia
- deep vein thrombosis (blood clots that occur deep within a vein; risk increases during long periods of inactivity) .

People with TBIs may need nutritional supplements to minimize the effects that vitamin, mineral, and other dietary deficiencies may cause over time. Some individuals may even require tube feeding to maintain the proper balance of nutrients.

22

Following the acute care period, people with severe TBI are often transferred to a rehabilitation center where a multidisciplinary team of health care providers help with recovery. The rehabilitation team includes neurologists, nurses, psychologists, nutritionists, as well as physical, occupational, vocational, speech, and respiratory therapists.

Cognitive rehabilitation therapy (CRT) is a strategy aimed at helping individuals regain their normal brain function through an individualized training program. Using this strategy, people may also learn compensatory strategies for coping with persistent deficiencies involving memory, problem solving, and the thinking skills to get things done. CRT programs tend to be highly individualized and their success varies. A 2011 Institute



In-hospital strategies for managing people with severe TBI focus on preventing infection and deep vein thrombosis or blood clots (like the one shown above) that occur deep within a vein.

of Medicine report concluded that cognitive rehabilitation interventions need to be developed and assessed more thoroughly.

23

Other factors that influence recovery

Genes

Evidence suggests that genetics play a role in how quickly and completely a person recovers from a TBI. For example, researchers have found that apolipoprotein E 4 (ApoE4) — a genetic variant associated with higher risks for Alzheimer’s disease — is associated with worse health outcomes following a TBI. Much work remains to be done to understand how genetic factors, as well as how specific types of head injuries in particular locations, affect recovery processes. It is hoped that this research will lead to new treatment strategies and improved outcomes for people with TBI.

Age

Studies suggest that age and the number of head injuries a person has suffered over his or her lifetime are two critical factors that impact recovery. For example, TBI-related brain swelling in children can be very different from the same condition in adults, even when the primary injuries are similar. Brain swelling in newborns, young infants, and teenagers often occurs much more quickly than it does in older individuals. Evidence from very limited CTE studies suggest that younger people (ages 20 to 40) tend to have behavioral and mood changes associated with CTE, while those who are older (ages 50+) have more cognitive difficulties.

24

Compared with younger adults with the same TBI severity, older adults are likely to have less complete recovery. Older people also have more medical issues and are often taking multiple medications that may complicate treatment (e.g., blood-thinning agents when there is a risk of bleeding into the head). Further research is needed to determine if and how treatment strategies may need to be adjusted based on a person's age.

Researchers are continuing to look for additional factors that may help predict a person's course of recovery.

Can a TBI be prevented?

The best treatment for TBI is prevention. Unlike most neurological disorders, head injuries can be prevented. According to the CDC, doing the following can help prevent TBIs:

- Wear a seatbelt when you drive or ride in a motor vehicle.
- Wear the correct helmet and make sure it fits properly when riding a bicycle, skateboarding, and playing sports like hockey and football.
- Install window guards and stair safety gates at home for young children.
- Never drive under the influence of drugs or alcohol.
- Improve lighting and remove rugs, clutter, and other trip hazards in the hallway.

25



Wearing a seatbelt when you drive or ride in a motor vehicle can help prevent TBI.

- Use nonslip mats and install grab bars next to the toilet and in the tub or shower for older adults.
- Install handrails on stairways.
- Improve balance and strength with a regular physical activity program.
- Ensure children’s playgrounds are made of shock-absorbing material, such as hardwood mulch or sand.

What research is NINDS funding?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world. NINDS funds research on the full range of severity of TBI to understand the mechanisms that result in immediate and delayed effects in the brain and to develop therapies that can prevent or reverse brain damage.

NINDS-supported researchers are working to better understand the factors that contribute to chronic traumatic encephalopathy (CTE). Brain tissue studies suggest that people with CTE have abnormal microscopic deposits of a protein known as tau. Accumulations of tau are also found in the brains of people known to have other neurodegenerative disorders such as Alzheimer’s disease. NINDS-

funded researchers are working to define a clear set of criteria for the various stages of CTE and to distinguish it from Alzheimer's and other neurodegenerative disorders in post-mortem brain



NINDS funds a wide range of TBI research in an effort to find better ways to safely detect, treat, and ultimately prevent TBI.

tissue. Once researchers characterize CTE in brain tissue they may then be able to correlate certain changes with findings from advanced brain scanning technologies. If this were possible then individuals with CTE would be able to be diagnosed while they are still alive. One promising research strategy uses a radioactive biochemical substance known as a ligand to bind to tau, which can then be detected using positron emission tomography (PET scan).

27

It is currently not known how many people either have CTE or are at greatest risk for developing the condition. Researchers are conducting studies to better understand the lasting effects of a single head injury vs. repetitive injuries to the brain, how repetitive TBI might lead to CTE, and how commonly these changes occur among adults. A key objective is to identify and develop noninvasive ways of detecting and monitoring brain injuries. For example, NINDS researchers are currently working to develop consensus criteria for diagnosis as well as objective biomarkers (signs that may indicate risk of a disease and aid in diagnosis) for CTE in order to detect this and similar disorders in living people.

NIH has also funded research to develop sensors to determine the type of acceleration and rotation that can lead to brain injuries. Researchers hope these sensors can help determine the effect of head injuries over time on cognitive performance and aid in new ways to diagnose concussions.

NINDS, along with the NIH's National Institute of Mental Health and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, supports the NIH NeuroBioBank (NBB) (<https://neurobiobank.nih.gov>). The repository brings together multiple stakeholders to enable and advance research by collecting and distributing human post-mortem brain tissue. This research improves our understanding of the long-term consequences of brain trauma and the development of conditions such as CTE.

Other studies focus on substances found in the body or in nature that are believed to prevent cell death and inflammation. For example, naturally occurring substances in plants called flavonoids have been shown to reduce inflammation and cell toxicity.

Clinical trials

Despite recent progress in understanding what happens in the brain following TBI, more than 30 large clinical trials have failed to identify specific treatments that make a dependable and measurable difference in people with TBI. A key challenge facing doctors and scientists is the fact that each person with a TBI has a unique set of circumstances

based on such multiple variables as the location and severity of the injury, the person's age and overall health, and the time between the injury and the initiation of treatment. These factors, along with differences in care across treatment centers, highlight the importance of coordinating research efforts so that the results of potential new treatments can be confidently measured.

Among such efforts to coordinate researchers worldwide is the *International Initiative for Brain Injury Research (InTBIR)*, a collaboration between the NIH, the European Commission, and the Canadian Institutes of Health Research. The U.S. Department of Defense (DOD) also participates. InTBIR's goal is to advance TBI research by establishing and promoting the use of consistent standards for TBI clinical data collection. One component of InTBIR that NINDS supports is the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study. This large, multi-center study aims to test, refine, and develop standards and best practices for TBI research across the entire spectrum of TBI severity among adults. TRACK-TBI has a sister study in Europe called Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI). Researchers hope that these projects have the potential to substantially advance and revolutionize TBI clinical research. InTBIR is also building a large registry of people with TBI to track the results of various treatment strategies over time.

NIH has funded research to develop sensors to determine the type of acceleration and rotation that can lead to brain injuries.

NINDS-funded researchers are also coordinating a large international study aimed at evaluating

treatments for children with moderate to severe TBI. Most of the treatments for TBI are based on studies involving adults. Children are rarely included in research studies so the best course of treatment in pediatric TBI cases is often not clear. The five-year study, called the Approaches and Decisions for Acute Pediatric TBI (ADAPT) Trial, aims to develop evidence-based guidelines that can immediately improve recovery and disability rates among children with TBI. The study will include 1,000 children from more than 36 locations in the United States and abroad. Researchers are looking at the effectiveness of immediate interventions, such as lowering intracranial pressure, as well as strategies to prevent secondary injuries and deliver nutrients to the brain.

NINDS is also leading the establishment of a collaborative emergency care research network, Strategies to Innovate EmeRgENcy Care Clinical Trials (SIREN). SIREN will be responsible for simultaneously conducting at least four large clinical trials that focus on improving care in emergency room settings for individuals suffering from traumatic and medical conditions, including TBI. Other participating NIH organizations are the National Heart, Lung and Blood Institute, the National Center for Advancing Translational Science, and the Office of Emergency Care Research in the National Institute of General Medical Sciences.

Animal models

NINDS-supported researchers conduct numerous studies using animal models in order to test potential new therapies and to better understand the nature of TBI.

One major challenge to delivering drug therapies for TBI is dealing effectively with the blood-brain barrier. This important barrier plays a key role in protecting the brain from potentially harmful substances. However, it also limits the ability of potentially beneficial agents from reaching the brain. Researchers are exploring ways of combining neuroprotective agents with membrane transporters that are able to carry medications across the blood-brain barrier.

Other researchers are exploring ways to promote the brain's innate ability to adapt and repair itself, known as *neuroplasticity*. For example, they are stimulating deep brain structures with electricity or magnetic fields and combining such therapy with exercises to see if it improves functionality in animals with TBI.

A newly developed mouse model of TBI is enabling researchers to look at potential treatments for concussion. Using the model, they found that applying glutathione (an antioxidant that is normally found in our cells) directly on the skull surface after brain injury reduced the amount of brain cell death.

In addition to NINDS, other NIH Institutes fund research on TBI. Among them, the National Center for Medical Rehabilitation Research (NCMRR)

coordinates rehabilitation research; the National Institute on Drug Abuse supports investigations into TBI and drug abuse; the National Institute of Biomedical Imaging and Bioengineering funds studies on head impact detection technologies, imaging technologies, regenerative medicine, and prosthetics; and the National Institute of Mental Health supports research on post-traumatic stress disorder associated with TBI. Research projects on TBI and other disorders can be found using NIH RePORTER (<http://projectreporter.nih.gov>), a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications from these projects and other resources.

32 How is NINDS coordinating research efforts?

Harnessing the efforts of the many physicians and scientists working on developing better treatments for TBI requires everyone to collect the same types of information from people including details about injuries and treatment results. To lay the groundwork for these studies, NINDS started the ***Common Data Elements*** project. This effort brings the research community together to develop data collection standards.



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Closely linked to the Common Data Elements project is the data sharing platform, ***Federal Interagency Traumatic Brain Injury***

Research (FITBIR). Born out of a partnership between DOD and NIH, the database provides a central repository for information on TBI and allows researchers to compare study results worldwide. With FITBIR researchers can collectively pursue answers to common problems. Together, FITBIR and the Common Data Elements project provide the tools that make large-scale research on TBI possible.

NINDS also works with DOD and the Departments of Health and Human Services, Veterans Affairs, and Education to coordinate TBI research for military members. This National Research Action Plan (NRAP) aims to improve prevention, diagnosis, and treatment of TBI and other mental health conditions such as PTSD that effect veterans and their families. The findings resulting from NRAP will be rapidly translated into new effective prevention strategies and clinical innovations, as well as identify biomarkers to detect these disorders early and accurately.

Expediting the development of better treatments for TBI also requires collaboration between private and public organizations dedicated to preventing and managing the consequences of TBI. NIH, through its Foundation for NIH, has built an innovative private-public partnership known as the Sports and Health Research Program (SHRP). Through SHRP, the National Football League has committed millions of dollars to furthering TBI research to improve the lives of all athletes.

SHRP projects include developing and testing a portable eye tracking instrument that can be used on the sidelines to help diagnose concussions and monitor injury progression. SHRP-funded investigators also are looking at other options for detecting mild TBI brain changes with biomarkers such as those on imaging or by measuring levels of substances in the blood. The potential to improve TBI care through these projects will extend beyond the athletic field and be of value to anyone who sustains a TBI.

How can I support TBI research?

If you or someone you know has been diagnosed with a TBI, enrolling in a clinical trial or brain bank are the best ways to support research toward new and better treatment options.

Clinical trials are research studies that involve people. Studies involving individuals with TBI and healthy individuals offer researchers the opportunity to greatly increase our knowledge of TBI and find better ways to safely detect, treat, and ultimately prevent TBI. By participating in a clinical study, healthy individuals and those with TBI can greatly benefit the lives of those living with this disorder. Talk with your doctor about clinical studies and help to make the difference in the quality of life for all people with TBI. Trials take place at medical centers across the United States and elsewhere. For information about NINDS-funded studies on TBI, see *www.clinicaltrials.gov*



Clinical research studies involving healthy people and those with TBI give researchers the opportunity to greatly increase our knowledge of TBI.

and search for “TBI AND NINDS.” For additional studies on TBI and information about participating in clinical studies, visit the “NIH Clinical Trials and You” website at (www.nih.gov/health/clinicaltrials). Always talk with your health care provider before enrolling in a clinical trial.

35

People with a TBI also can support TBI research by designating the donation of brain tissue before they die. The study of human brain tissue is essential to increasing the understanding of how the nervous system functions.

The NIH NeuroBioBank is an effort by the National Institutes of Health to coordinate the network of brain banks it supports in the United States to facilitate advances in research through the collection and distribution of post-mortem brain tissue. Stakeholder groups include brain and tissue repositories, researchers, NIH program staff,

information technology experts, disease advocacy groups, and most importantly individuals seeking information about opportunities to donate. It ensures protection of the privacy and wishes of donors. Creating a network of these centers makes it more likely that precious tissue can be made available to the greatest number of scientists. Six current brain and tissue repositories include:

University of Miami Brain Endowment Bank

University of Miami Department of Neurology
1951 N.W. 7th Avenue, Suite 240

Miami, FL 33136

305-243-6219

800-862-7246

brainbank.med.miami.edu

University of Maryland Brain and Tissue Bank

(formerly NICHD Brain and Tissue Bank for
Developmental Disorders)

University of Maryland, School of Medicine
655 West Baltimore Street, Room 13-0313 BRB

Baltimore, MD 21201-1559

410-706-1755

800-847-1559

www.medschool.umaryland.edu/BTBank/

Harvard Brain Tissue Resource Center

McLean Hospital

115 Mill Street

Belmont, MA 02478

617-855-2400

800-272-4622

www.brainbank.mclean.org

**The Human Brain and Spinal Fluid Resource
Center (HBSFRC)**

Building 212, Room 16

West Los Angeles Health Care Center

11301 Wilshire Blvd. (127A)

Los Angeles, CA 90073

310-268-3536

Pager: 310-636-5199

brainbank.ucla.edu

Mount Sinai NIH Brain and Tissue Repository

James J. Peters VA Medical Center

130 West Kingsbridge Road

Room 4F-33A

Bronx, NY 10468

718-584-9000 x6083

*icahn.mssm.edu/research/labs/neuropathology-and-
brain-banking*

**Brain Tissue Donation Program at the University
of Pittsburgh**

Translational Neuroscience Program

Biomedical Service Tower 1654

3811 O'Hare Street

Pittsburgh, PA 15213-2582

412-383-8548

www.tnp.pitt.edu

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN

P.O. Box 5801
Bethesda, MD 20824
301-496-5751
800-352-9424

www.ninds.nih.gov

Additional information about TBI is available from the following organizations:

Brain Injury Association of America

1608 Spring Hill Road, Suite 110
Vienna, VA 22182
703-761-0750
800-444-6443

www.biausa.org

Brain Injury Resource Center

P.O. Box 84151
Seattle, WA 98124
206-621-8558

www.headinjury.com

Brain Trauma Foundation

1 Broadway, 6th Floor
New York, NY 10004-1007
212-772-0608

www.braintrauma.org

**Uniformed Services University of the Health
Sciences (USUHS)**

Center for Neuroscience and Regenerative
Medicine (CNRM)

NIH-USUHS TBI Center

4301 Jones Bridge Road
Bethesda, MD 20814-4799

www.usuhs.mil/cnrm

U.S. Centers for Disease Control and Prevention

Heads Up to Concussion

National Center for Injury Prevention and
Control (NCIPC)

Division of Unintentional Injury Prevention

1600 Clifton Road

Atlanta, GA 30329-4027

800-232-4636

TTY: 888-232-6348

http://www.cdc.gov/headsup/index.html

National Rehabilitation Information Center

8400 Corporate Drive, Suite 500

Landover, MD 20785

800-346-2742

www.naric.com

ThinkFirst

National Injury Prevention Foundation

1801 N. Mill Street, Suite F

Naperville, IL 60563

630-961-1400

800-844-6556

www.thinkfirst.org

National Library of Medicine

National Institutes of Health

8600 Rockville Pike

Bethesda, MD 20894

301-594-5983

888-346-3656

www.nlm.nih.gov

Glossary

blood-brain barrier — a protective barrier around brain blood vessels designed to keep the environment in the brain as stable as possible

brain death — a lack of measurable brain function activity and blood flow after an extended period of time

chronic traumatic encephalopathy (CTE) — brain damage caused by cumulative and repetitive head trauma

cognitive rehabilitation therapy (CRT) — a strategy aimed at helping individuals with severe TBI regain their normal brain function through an individualized training program

coma — a state of unconsciousness in which a person cannot be wakened and does not respond to external stimuli, such as pain or light

41

concussion — injury to the brain caused by a hard blow or violent shaking of the brain within the skull, which produces a sudden and temporary impairment of brain function, such as amnesia, short loss of consciousness, or disturbance of vision and equilibrium

contrecoup lesions — contusions or subdural hematomas that occur directly opposite the point of head impact

contusion — a distinct area of swollen or bruised brain tissue mixed with blood released from broken blood vessels

coup injury — a head injury that occurs under the site of impact with an object

diffuse axonal injury (or traumatic axonal injury) — widespread damage to the brain's white matter; the result of shearing forces that stretch or tear the nerve fibers that connect brain regions

diffuse injury — a brain injury that covers a widespread area; most often associated with injuries resulting from rapid acceleration or deceleration of the skull such as in a car crash or to a blast injury

epidural hematomas — bleeding into the area between the skull and the dura

focal injury — a brain injury that occurs in a specific area; most often associated with an injury in which the head strikes or is struck by an object

42

Glasgow Coma Scale — a widely-used clinical tool used to assess the degree of consciousness and neurological functioning after a brain injury by testing motor responsiveness, ability to respond to verbal questions, and eye opening

hematoma(s) — heavy bleeding in or around the brain caused by damage to a large blood vessel in the head

hemorrhagic progression of a contusion (HPC) — occurs when an initial contusion from the primary injury continues to bleed and expand over time, creating a new or larger lesions. This contributes to secondary injuries.

intracerebral hematoma — bleeding within the brain caused by damage to a major blood vessel

increased intracranial pressure (ICP) — buildup of pressure in the brain as a result of swelling and/or bleeding in the brain

meninges — the protective membranes surrounding the brain, which consist of three layers: dura mater (outermost), arachnoid mater (middle), and pia mater (innermost)

minimally conscious state — people with severely altered consciousness who still display some evidence of self-awareness or awareness of one's environment

neuron(s) — nerve cells that process and transmit information through electrical and chemical signals; these cells are core components of the brain and nervous system

neuroplasticity — ability of the brain to adapt to deficits and injury by creating new connections to uninjured brain regions

non-penetrating head injury or (closed head injury) — an injury that occurs when the head suddenly and violently hits an object but the object does not break through the skull

penetrating head injury (or open head injury) — a brain injury in which an object pierces the skull and enters the brain tissue

persistent vegetative state — an ongoing state of severely impaired consciousness, in which the patient is incapable of voluntary motion

primary injury — an injury that occurs during the initial brain trauma

post-concussion syndrome (PCS) — a set of symptoms that may occur after a concussion, including cognitive impairment, depression, irritability, persistent sensory problems, anger, apathy, or paranoia

post-traumatic dementia (PTD) — a condition with symptoms that are very similar to those of chronic traumatic encephalopathy (CTE) except that it caused by a single, severe TBI that results in a coma.

post-traumatic stress disorder (PTSD) — a condition that may develop after a person has experienced or witnessed a traumatic or terrifying event in which serious physical harm occurred or was threatened. PTSD can be caused by a number of different events including war, assaults, car crashes, and natural disasters.

44

secondary injury — a gradual injury that occurs in the hours and days following a primary head injury; these injuries are a major factor in TBI-related brain damage and death

shaken baby syndrome — a severe form of head injury that occurs when an infant or small child is shaken forcibly enough to cause the brain to bounce against the skull; the degree of brain damage depends on the extent and duration of the shaking. Minor symptoms include irritability, lethargy, tremors, or vomiting; major symptoms include seizures, coma, stupor, or death.

shearing — forces that stretch or tear axons as a result of the head rapidly accelerating or decelerating; the cause of diffuse axonal injuries (DAIs)

skull fractures — breaks or cracks in one or more of the bones that form the skull, which can damage the underlying areas of the skull including the brain, membranes, and blood vessels

subdural hematoma — bleeding confined to the area between the dura and the arachnoid membranes

subarachnoid hemorrhage — bleeding that occurs between the arachnoid mater and the pia mater

vegetative state — a condition in which people are unconscious and unaware of their surroundings, but can have periods of alertness and may groan, move, or show reflex responses



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