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# What is CTE?

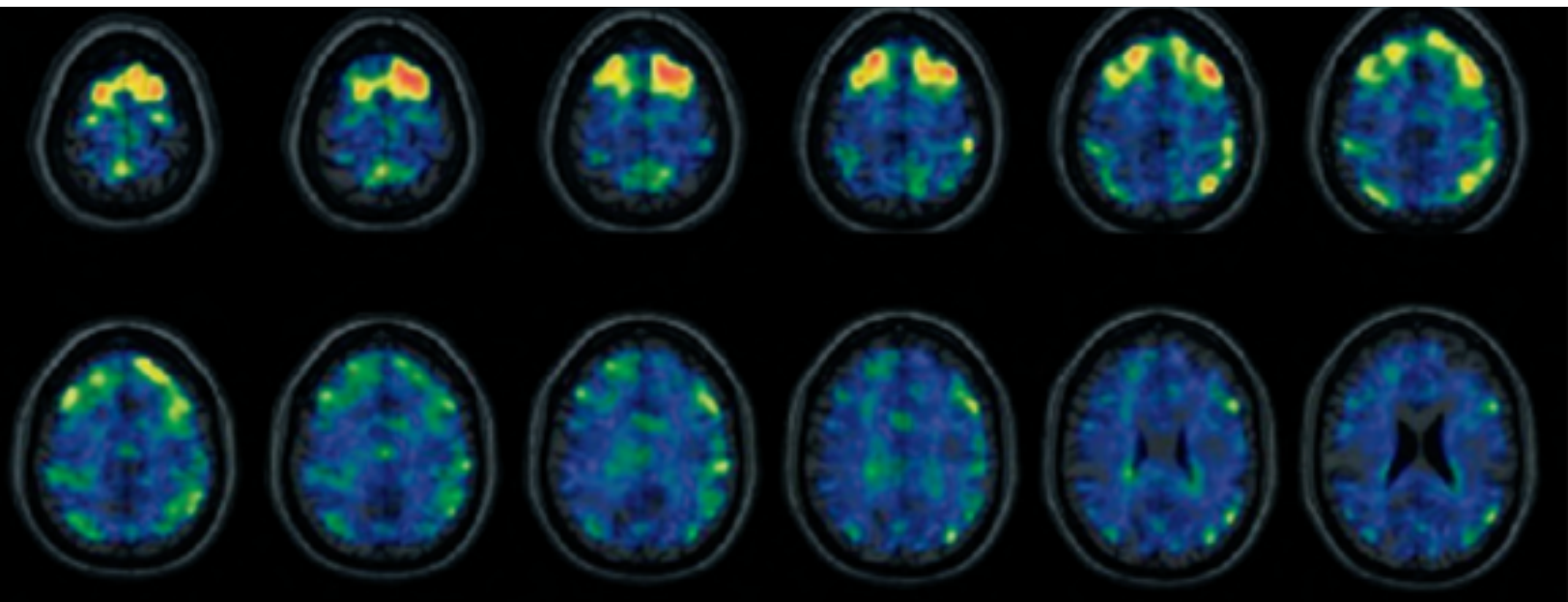
*Answers to common questions  
about chronic traumatic  
encephalopathy*

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# What is CTE?

Chronic traumatic encephalopathy (CTE) is a degenerative brain disease that can occur in people with a history of repetitive head impacts, such as contact and collision sport athletes, combat military service members, and others. The repetitive head impacts can result in symptomatic concussions or the more common subconcussive trauma, i.e., blows to the head without symptoms of a concussion. These repetitive head impacts result in rapid acceleration and deceleration of the brain inside the skull, and stretching, twisting, and shearing of the long connections (axons) between the brain cells (neurons). It is thought that these repetitive injuries start a cascade of changes in the brain, including the buildup of an abnormal form of a protein called tau. This, in turn, eventually leads to the slow, progressive destruction of brain tissue and associated changes in cognitive functioning, mood, and behavior. When these changes become severe enough, they lead to dementia (i.e., memory and other cognitive and behavioral impairments that get in the way of day-to-day living and independence). The symptoms of CTE often do not begin for years or decades following the cessation of the repetitive head impacts (e.g., end of playing football or boxing).



Stern et al. 2019



# What are the signs and symptoms of CTE?

In contrast to what might be thought based on the public attention and media focus that CTE has received in recent years, there remain several gaps in scientific and medical knowledge about the disease. One such gap is a clear understanding of the clinical manifestations of the underlying brain changes. At this time, CTE can only be diagnosed after death through careful neuropathological examination of the brain. Much of what we currently know about the signs and symptoms of CTE is based on interviews of next of kin of deceased individuals whose brains have been examined postmortem and found to have CTE. Based on these reports, the clinical features of CTE can be broken down into four major areas: mood, behavior, cognition, and movement.

**Mood:** Problems with mood and emotion can include feelings of depression, hopelessness, or anxiety. Some people are described as having apathy, i.e., the lack of motivation, emotional connection, or drive. Others have been described as being angry and irritable.

**Behavior:** Behavioral changes can include acting impulsively, having a short fuse, being out of control, or having excessive rage. Some individuals become physically and verbally explosive and can become violent. Addictive behaviors are not uncommon.

**Cognition:** Cognitive difficulties include problems with memory, specifically difficulty learning and recalling new information. This can result in forgetting conversations or experiences that happened just hours or days earlier, or repeating oneself. Forgetting things that occurred years earlier (prior to the symptoms) is rare. Other problems include difficulties with attention, as well as what is referred to as “executive functions.” This includes problems with planning, organization, multitasking, judgment, and decision-making. As these problems worsen and have a negative impact on routine daily functioning, the person can be described as having dementia

**Movement:** Movement difficulties are not seen in all cases of CTE but are more likely in individuals who participated in boxing, mixed martial arts, or other forms of hand-to-hand fighting. Movement problems can include tremors and issues with walking, balance, and speaking.

Having all or even some of these signs and symptoms may be indicative of having CTE. There is no one uniform expression of how and when these symptoms will present in an affected individual. Research suggests that in some people, the behavioral and mood changes may begin earlier in life (30s to 50s) compared with cognitive problems that may start later. However, the research into CTE is in its early stages, so it is important to note that while the signs and symptoms described above can be caused by CTE, they can also be caused by several other diseases and illnesses. Our picture of CTE may change as new research comes out; the specific symptoms of CTE may be different from what scientists currently believe. In the meantime, it is important to know that just because someone has many of the clinical features of CTE described above, that does not mean they have CTE.

## **If people with CTE have dementia, doesn't that just mean they have Alzheimer's?**

Having all or even some of these signs and symptoms may be indicative of having CTE. There is no one uniform expression of how and when these symptoms will present in an affected individual. Research suggests that in some people, the behavioral and mood changes may begin earlier in life (30s to 50s) compared with cognitive problems that may start later. However, in the later stages of CTE, as more and more brain tissue is destroyed and the cognitive and other symptoms worsen, an individual can develop difficulties with routine social or occupational functioning, as well as with household chores and activities. This would mean the person has dementia. It is important to note that dementia is not the same thing as Alzheimer's disease, as it is so often viewed. Rather, dementia merely refers to problems with memory

and other cognitive skills and behavior that are severe enough to get in the way of routine activities, daily functioning, and independence. Dementia is not an illness or a disease. Rather, it is a clinical syndrome that occurs in the later stages of many different neurodegenerative diseases. Alzheimer's disease is the most common disease that eventually leads to dementia, but CTE can also eventually lead to dementia, without any evidence of Alzheimer's disease in the brain.

## **How is CTE diagnosed?**

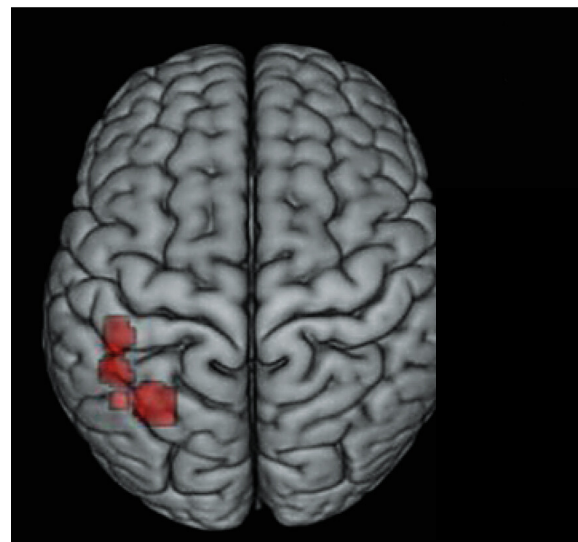
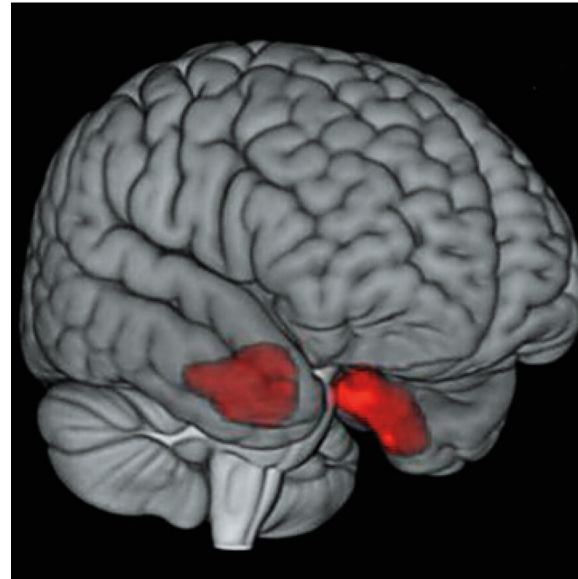
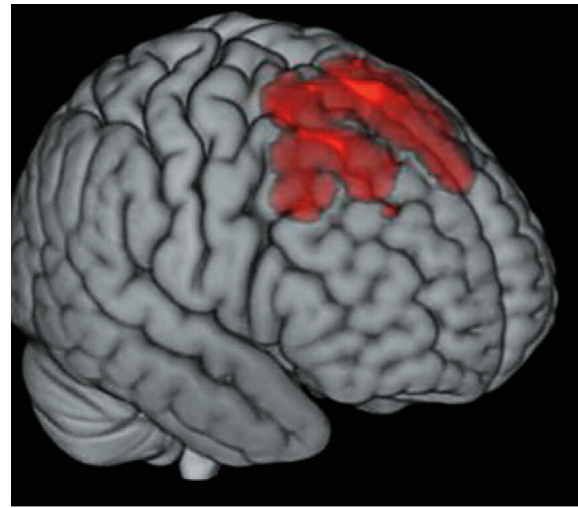
Currently, the only way to diagnose CTE is after death through an autopsy and neuropathological examination of the brain. After putting special chemicals on the brain tissue that stain the abnormal tau protein, the neuropathologist examines the brain tissue under a microscope and looks for the telltale diagnostic findings of accumulation of tau protein around small blood vessels, preferentially in the depths of the cortical sulci (i.e., the valleys and crevices in the outer layer of the brain). They also determine whether the abnormal tau protein has spread to other areas of the brain, and they examine the degree to which there is atrophy of the brain and where that atrophy is. Neuropathologists use all of this information to determine if the person had CTE, in addition to determining the severity of the disease.

## **Can CTE be diagnosed during life?**

Scientists are currently unable to diagnose CTE during life. This is similar to other neurodegenerative diseases, including Alzheimer's disease, that cannot accurately be diagnosed during life and require postmortem examination of brain tissue. However, over the past decade, there have been tremendous advances in the ability to diagnose these types of diseases during life due to the creation and refinement of objective biological tests of the underlying changes in the brain. These types of tests, called biomarkers, include measurements of

proteins and other molecules in the cerebrospinal fluid and, more recently, in blood, as well as the use of MRI scans to examine the structures and functioning of the brain. None of these tests is yet validated or approved for the diagnosis of CTE and requires additional research. There is a special type of PET scan that is approved to help doctors rule out Alzheimer's disease as the cause of an individual's cognitive decline. That PET scan measures the amount of amyloid-beta plaque buildup in the brain. Because amyloid-beta plaque is a necessary part of the diagnosis of Alzheimer's disease, if a patient with significant cognitive impairment does not exhibit the elevated amyloid-beta on the PET scan, they would likely not be diagnosed with Alzheimer's disease as the cause of the problems. Rather, other conditions (including CTE in an individual with extensive history of repetitive head impact exposure) would have to be considered.

More recently, an experimental PET scan that detects the amount and location of abnormal tau protein in the brain has been studied as a possible biomarker for CTE. Preliminary findings published in the *New England Journal of Medicine* showed that former NFL players with cognitive, mood, and behavioral symptoms had significantly higher amounts of abnormal tau detected on the PET scan than same-aged men without any history of traumatic brain injury, and the tau accumulations were in areas in the brain seen in neuropathological



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examinations of CTE brains. Moreover, the amount of abnormal tau detected on the PET scan was associated with the total number of years playing tackle football. Although these results are promising, this PET scan remains experimental and requires a great deal of additional research before it might be able to be used to diagnose individual patients.

Researchers are hopeful that diagnosing CTE during life will be possible within a few years, based on a combination of increased research, validation of provisional clinical diagnostic criteria, and advances in biomarker development.

## How do I get CTE?

In recent years, it has become clear that the most significant risk factor for developing CTE is a history of repetitive head impacts. The symptoms of CTE may not show up for many years after exposure to these hits, but in almost all autopsy cases of confirmed CTE, the individual experienced repetitive hits to the head over an extended period of time. Most people think of contact or collision sports, like American football or boxing, as being the main activities that can lead to CTE, but other sports, such as soccer (because of heading the ball) and rugby, have been linked to CTE. In addition, CTE has been found in the brains of combat military veterans, a victim of domestic abuse, and a developmentally disabled person who was a headbanger, as well as others. Persons with CTE may have had several diagnosed concussions, or they may not have had even a single concussion.

Repeated concussions are certainly a factor in the development of CTE, but researchers believe that the main concern is with subconcussive hits—impacts that happen with some force but do not necessarily result in any concussive symptoms. Someone who has had a subconcussive impact will often feel fine and can continue their activity without any problem. Think of a lineman in American tackle football who, at every play of every game and every practice, hits their head against their opponent. The hard plastic helmet and facemask prevent the player from feeling pain and allow the player to keep receiving these repetitive subconcussive blows.

It remains unclear what aspects of the repetitive head impacts (e.g., type, severity, cumulative amount, duration, age of first exposure to the hits) lead to the development of CTE. And, not everyone with even tremendous exposure to these hits gets CTE. It is likely that there are modifying factors, such as genetic predisposition or other variables, leading to increased resilience. Like all neurodegenerative diseases, the elements that cause CTE and its symptoms are complex. Each individual has a different level of risk and resilience that will influence the disease progression and presentation.

## **Will I get CTE from one concussion?**

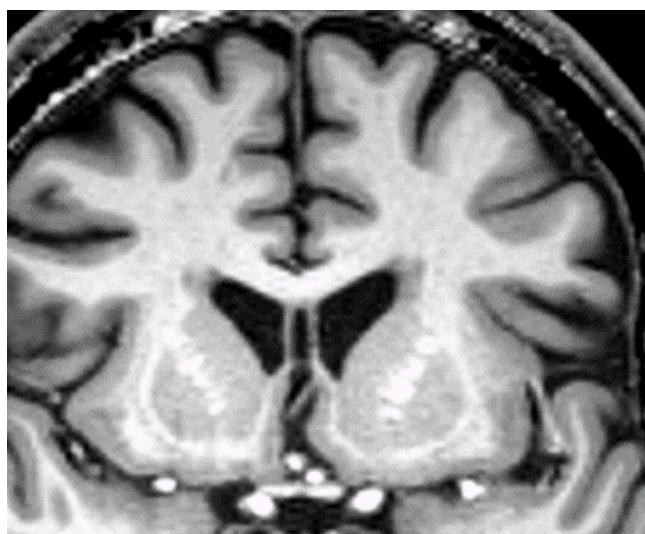
A concussion is caused by a jolt to the head or the body that makes the brain move rapidly in the skull, leading to a variety of symptoms (e.g., “seeing stars,” headache, dizziness, nausea, vomiting, trouble sleeping, fatigue, confusion, difficulty remembering and concentrating). Less than 10% of concussions involve loss of consciousness or blacking out. Concussion symptoms can occur immediately after impact or can be delayed for hours. Most people fully recover from the symptoms of a concussion in 1–3 weeks. Although a concussion should be taken seriously and diagnosed and monitored by trained clinicians, it is important to note that a single concussion (e.g., from a fall or other accident) will not lead to CTE. The risk for CTE appears to be from experiencing repetitive concussive and subconcussive hits over a period of time.

## **How common is CTE?**

It is unclear how common CTE is in the general population. Autopsy studies on CTE have shown that a high percentage of people whose brains have been donated (especially former college and professional American football players) have had the disease. However, these studies are susceptible to potential biases due to the fact that the majority of brains may have been donated to research because the individual had been experiencing symptoms associated



with CTE. For this reason, it is difficult to generalize these autopsy studies to the general population. Future research on individuals with a wide range of types of



Koerte et al. 2016

repetitive head impact exposure will allow for better estimates of how common it is. Some researchers believe that CTE may become more common in the years to come as large numbers of individuals who played American tackle football since the advent of the large plastic helmet and facemask (late 1950s) and the development of organized youth tackle football (late 1960s to early 1970s) become older.

## Is CTE a new disease?

CTE is not a new disease. CTE is the same thing as what had been referred to as “punch drunk syndrome,” a term first used in 1928 in a paper by Dr. Harrison Martland in the *Journal of the American Medical Association* to describe the long-term problems former professional boxers had. It was similarly referred to as “dementia pugilistica” (the dementia of fighters) starting in the 1930s. Although some people think that CTE is a newly discovered disease or a newly coined term, it has, in fact, been used in the medical and scientific literature since the 1940s and 1950s, when it was used as a more general (and more scientific) term for “punch drunk” because it wasn’t seen only in boxers. However, it was not until the 1970s that the actual changes in the brains of CTE patients (through postmortem neuropathological examination) were first described in the scientific literature. CTE became better known to the public when, in 2002, it was found through postmortem brain examination of a well-known former NFL player, Mike Webster, who died at age 50 from a heart attack after years of significant memory decline and behavioral change. It has only been since 2009 or 2010 that the scientific and medical literature has shown a tremendous increase in research on CTE.

## Does CTE cause suicide?

Many news articles and media outlets have reported that CTE causes suicide because several athletes who died from suicide had then been diagnosed with CTE through postmortem examination. However, the relationship between CTE and suicide is unclear and complex. There is no single cause that results in suicide. Suicide is, tragically, all too common and is one of the most complex of human behaviors. Having CTE does not inevitably make a person take their own life. However, symptoms of CTE can cause changes in mood (including sadness, hopelessness, and anger) as well as an inability to control one's impulses. Therefore, it is hypothetically possible that someone with CTE may be at a higher risk of suicide or suicidal behavior, but this does not mean that just because someone has CTE they will attempt or commit suicide. Regardless of an underlying cause, suicide is preventable. Refer to: *National Suicide Prevention Lifeline at 1-800-273-8255 or [www.suicidepreventionlifeline.org](http://www.suicidepreventionlifeline.org).*

## What should I do if I think I have CTE?

If you believe you have CTE, it is important to first speak to a doctor. Even if CTE cannot be diagnosed, some of the symptoms of CTE, such as depression, anxiety, or attention problems, can be treated or alleviated with medical help. Additionally, a doctor may find that these symptoms are caused by another issue that is not necessarily related to CTE. It can be helpful to speak to a clinician who may have more specialized knowledge than your general practitioner. This specialist could be a clinician who is familiar with dementia or memory or mood disorders. You should pick a clinician by deciding what symptom or symptoms are causing the most trouble and finding a professional with experience in that field. The actual title of the clinician, whether they are a neurologist, neuropsychologist, or psychiatrist, is not as crucial as their background. Most medical professionals will have their area of expertise or prior work publicly

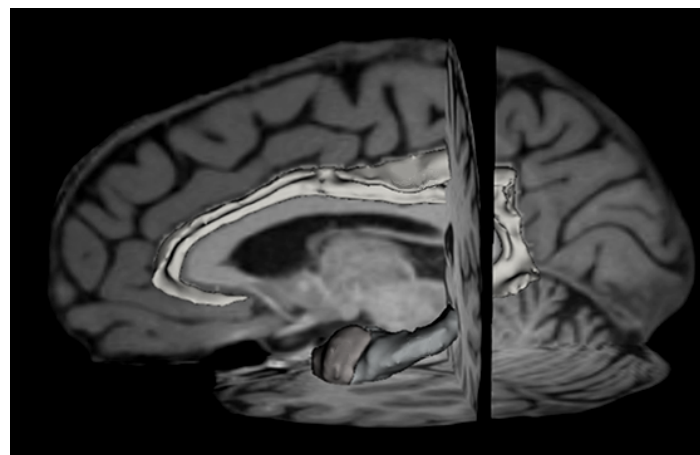
available, and you can use that information to decide if a doctor is right for you. Be aware that while repetitive head impacts cause CTE, it is a degenerative disease and not the same thing as a traumatic brain injury. Therefore, a specialist in head or brain injury (e.g., a neurosurgeon) may not be the best choice unless that person also has a background in CTE. Once you have made your appointment and are speaking to a clinician, make sure they have a good understanding of your background (i.e., history of repetitive head impacts, family history of neurologic or psychiatric illness) so that they can evaluate your risk of CTE. It is also always helpful to bring a loved one or friend who knows you well to the appointment; sometimes they have helpful observations or can help with providing history.

## What can I do to treat CTE?

There are no medications available yet that can prevent, stop, or slow down the accumulation of the abnormal tau protein and associated destruction of brain tissue in CTE. However, several new medications aimed at just that are being studied in various phases of clinical trials for other tauopathies. There is hope that one or more of these medications will be approved as an effective treatment to

modify the disease course. In the meantime, there are effective treatments for many of the symptoms associated with CTE, such as reducing symptoms of depression, anxiety, irritability, and poor emotional regulation. There are treatments to improve attention and provide some boost to memory. There are ways to reduce out-of-control behavior. These treatments may take some trial and error to find the most effective. The most important thing is being aware of your symptoms and actively seeking ways to improve them.

There are several changes to one's lifestyle that have been demonstrated through research studies to provide some improvement of symptoms as well as maintain overall brain health. These include the following:



LePage et. al 2018

**Exercise:** routine aerobic exercise that gets your heart beating faster (such as going on a brisk walk, using a stationary bicycle) for 20-30 minutes several days each week.

**Mediterranean Diet:** follow a diet with lots of fruits and vegetables, nuts and legumes, olives and extra virgin olive oil, fish high in omega-3 fatty acids (e.g., salmon), and little or no red meat.

**Reduce Vascular Disease Risk:** prevent or control diabetes, high blood pressure, and/or high (bad) cholesterol (what's good for the heart is good for the brain!).

**Intellectual Stimulation:** keeping one's mind active by doing new things in new ways, such as starting a new hobby or rekindling an old one, doing activities that require multiple ways of thinking or responding (complexity is great), trying out new recipes or reading a new genre of book, doing crossword puzzles (or Sudoku or other word games) but try new types of puzzles and games and don't just keep doing what has become routine.

**Social Networks:** retain old social groups and friendships and/or build new ones, interacting with people (preferably in person) on a regular basis for social and fun purposes.

## How do I care for a loved one who may have CTE?

There are several ways that you can support someone who may have CTE. First, you can help that person seek appropriate evaluation and treatment for their symptoms. Speak to your doctor or do some research to find a clinician in your area. Second, support your loved one in their treatment. Make sure they take prescribed medication and help assist with changes in diet or encourage



participation in exercise or other healthy activities. Perhaps one of the most important things that a caregiver for someone who may have CTE can do is to understand that your loved one has a different “reality” from you and others with an intact brain.

As a caregiver, it is also important to take care of yourself. An individual with CTE can suffer from symptoms that may impact those around them. They might act differently, be more prone to outbursts, or be unable to do simple tasks. It is essential to not only be understanding of the person’s struggles but also build a support system for yourself. This system can include attending support groups, getting outside aid for day-to-day tasks, or even relying on in-home or out-of-home assistance for your loved one. If a loved one becomes physically violent and explosive, it is important for the caregiver to take care of themselves as well as their loved one. Practicing relaxation methods and stress relief, seeing one’s own doctor, getting exercise, eating well, and finding some alone time are all critical. You cannot take care of someone else if you are physically or emotionally ill. By taking the right steps to support yourself and your loved one, you can improve the quality of life for you both.

## **How can I help improve our knowledge of CTE?**

The most important way to help improve our understanding of CTE is by participating in research. Several studies are seeking volunteers to join in research, and the number of CTE-related research studies will be growing over the next few years. Researchers are seeking volunteers with a history of repetitive head impacts (such as through contact or collision sports) as well as individuals with no history of blows to the head to participate as a part of comparative groups. Studies vary in their requirements but can include anything from extensive in-person clinical examinations to online surveys. Our knowledge of CTE is still limited. As we continue to understand more about CTE, we will be able to provide better answers to your questions and identify effective methods to diagnose, treat, and even prevent CTE.

## Acknowledgments

We thank Olivia Haller and Nicole Gullotti for their assistance in developing this guide.

The Boston University School of Medicine – CurePSP CTE Research Initiative seeks funding for BUSM’s groundbreaking research into chronic traumatic encephalopathy (CTE), a neurodegenerative disease that may strike athletes and combat veterans in the prime of their lives. While there is currently no treatment or cure for CTE, BUSM scientists are now focused on the discovery of biomarkers, genetic factors, and clinical diagnostic criteria. Your contributions to this program will help to accelerate research into this debilitating disease.