The Science of CTE

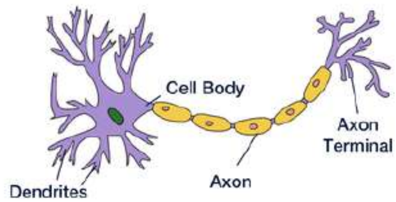
Information about the Science of CTE for suspected CTE patients and caregivers

CONCUSSION LegacyFoundation Canada

Brain cells 101

CTE is a disease of the brain. To really understand the science of what's going on, you'll need some background on what the brain is like when it is healthy. A good place to start is by looking at our brain cells, or neurons.

If you've ever heard someone talking about how brains are wired, or if you've heard someone talking about getting their brains firing, they were talking about their neurons.



Every neuron has three main parts:

- **The cell body**
- **The axon,**
- **and the axon terminal**

We'll focus mainly on the axon, a long, thin structure that behaves much like a wire in an electrical circuit. Neurons communicate with one another by sending electrical signals down their axons and off to adjacent cells.

Neurons are the basic building blocks of the brain. About 90 billion neurons form trillions of connections, creating a complex network that allows us to interpret and react to our environment.

Problems with the neuron

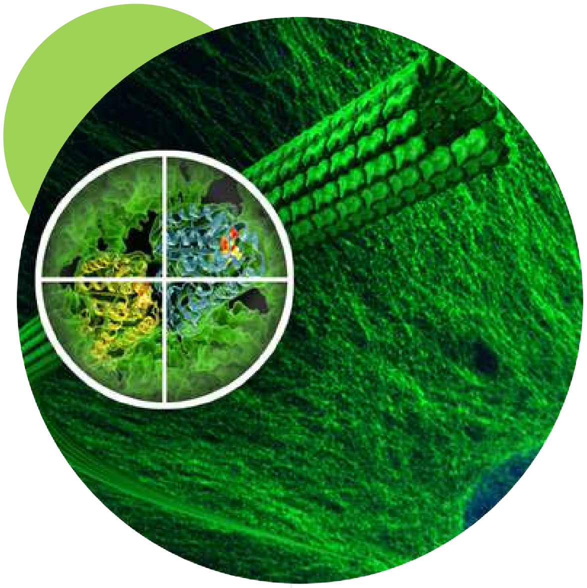
The axon's long and spindly shape helps the neuron reach faraway cells in different parts of the brain, but there are two problems that come with that shape:

1. It makes the axons fragile and prone to injury during a concussion. Things tend to break at their weakest point, and the axon is very often the weak point for the neuron. After a concussion, damage to axons is much more common than damage to other parts of the cell. A damaged axon has more trouble sending its signals, interfering with the brain's ability to do its job.

2. It makes it difficult for the cells to distribute chemicals and materials to all areas of the cell. Almost everything the cell needs to function is made in the cell body, but a lot of that stuff needs to be used along the axon or at the axon terminal. To get everything where it needs to go, the cell needs a transportation system.

Microtubules: a fragile transportation system

To help distribute molecules and materials throughout the cell, neurons have a special transportation system made up of tiny tubes called microtubules. These tubes run the length of the cell, helping materials move from one end to the other. If the axon were as big as a regular wire, each microtubule would only be as wide as a single strand of hair.



Remember, axons are the weakest point of the neuron, making them the first to break during a concussion. Microtubules are even smaller and weaker, making them vulnerable not only to concussions but also to smaller impacts that may leave axons intact, and because they are so small, they need support to maintain their structure.

A special protein called tau helps keep everything together by sticking to the outside of microtubules. In healthy brains, tau supports the microtubules, helping cells function and the brain operate normally.

In diseased brains, however, the same protein that helped keep everything together can actually cause things to fall apart.

Tau Proteins Going Haywire

If the microtubules are injured or break down, tau proteins can misfold, detach, and float freely inside the cell. Once proteins start misfolding, even without additional trauma they can cause other tau proteins within the same cell to misfold and malfunction, impairing cell function and eventually killing the cell

The misfolding tau appears to spread to connected cells when they cause those cells to malfunction as well through what is called prion-like spread.

Scientists are still trying to understand why this process leads to CTE in some people and not others. What scientists do know is that the tau in CTE spreads in a distinctive pattern that is unique to CTE. Scientists also believe that the slow spread of misfolding is likely one reason it takes so long for symptoms to show up. The slow spread also provides opportunities for effective treatment to slow or stop the disease.

Future directions of CTE research

One of the biggest questions in CTE research today is One of the biggest questions in CTE research today is: *How can we diagnose CTE in a living person?* Once this is possible, we can begin evaluating treatments and therapies to help those experiencing symptoms.

Scientists are working to develop such tests, with promising findings using a variety of techniques, **some of the most exciting aim to diagnose CTE using:**

Positron Emission Tomography (PET scans)

Researchers first inject a tracing chemical that binds to the tau proteins in CTE, then use a special brain scanner to trace where the chemical settles in the brain.

With a tracer chemical that binds to CTE tau (and only CTE tau), this technique could show us the tell-tale distribution of tau tangles while someone is still alive.

Several research groups have developed such a chemical, and early studies in athletes are already underway.

Fluid Based Biomarkers

New techniques in biochemistry have allowed researchers to develop extremely sensitive tests able to detect proteins and substances in the blood at extremely low levels. Researchers using these tests are looking for evidence of abnormal tau and other indicators in the blood of athletes at risk for CTE.

Normally, these indicators would be caught by a robust barrier between the bloodstream and the brain (called the blood-brain barrier), but repeated concussions and **nonconcussive impacts** that cause CTE can also damage this barrier, allowing clues to slip out of the brain.

Understanding Risk Factors

Another major field of inquiry is understanding risk factors for CTE and CTE progression – Why do some people get CTE while most do not, and why do some people appear to have worse symptoms associated with CTE?

Genetics play a role in every major neurodegenerative disease. The **BU CTE Center's** first CTE genetics study found that among those diagnosed with CTE, a variant of TMEM106B was associated with a 2.5 times greater risk of dementia, but not with developing CTE pathology—supporting the hypothesis that brain trauma exposure is the primary risk factor.

As the **Concussion and CTE Foundation Global Brain Bank grows**, our ability to detect the influence of genetics on CTE pathology and symptoms will grow. Understanding CTE genetics will provide insight into why it occurs and how it progresses, helping create better targets for treatment. You can support this effort by joining the **CLF Research Registry**. While the science isn't there yet, genetic profiles may one day help identify children who should not be exposed to contact sports.