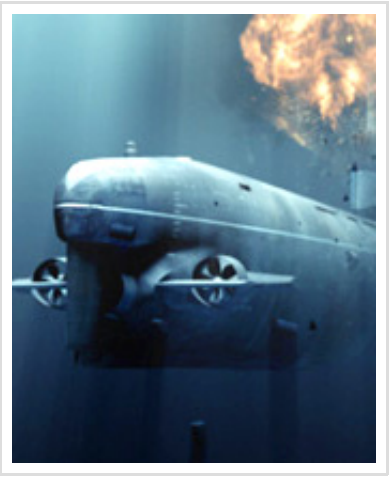
Summer October 4th, 2012

Brainstorm: Head Injuries and the NFL, Part 8: CuttingEdge Nerves

John J. Medina Ph.D.

Head Injuries and the NFL, Part 8: Cutting-Edge Nerves

By: John Medina | Posted: October 4, 2012



Armed with information from the last installment about nerve cells' basic biology, we can now talk about how they get injured in a more informed fashion. That's the subject of this post, and also the next two.

It was thought for a long time that cellular damage occurred for exactly the reason you'd suspect: the direct, mechanical tearing and/or shearing of nerves absorbing the fiercest force — especially at the surface. As the brain received a blow, nerve tissue was envisioned to scrape along the rough, inner surface of the skull, rupturing cells, causing what we call *primary axotomy*.

What is primary axotomy? *Primary* means "first," or "initial," of course.*Axotomy* comes from the word "axon," which — as you recall from last time — is the long, slender-looking structure typical of many nerve cells. Remember the handle of our cellular "mop"? An "axotomy" is a severing of this mop handle, and the destruction of neural function.

We no longer think that axotomy is an adequate cellular explanation for all of the damage that occurs in closed-head injuries. While this straightforward mechanism certainly occurs in the most severe accidents, we now have a clearer, and more nuanced, understanding of what happens to brain cells in the repeatedly traumatized brains. In most instances, absolute destruction is not what happens to cells at the moment of injury, but what occurs a few hours, 24 hours, even *weeks* later.

One of the most surprising discoveries is that many cells at or near the site of injury do not undergo primary axotomy as a direct result of the shearing forces of the blow. Instead, they undergo a series of internal changes, all lethal, but that can take a surprisingly long time to develop fully. Cell death eventually occurs, but there is a delay factor, which we describe by using the term*secondary axotomy*. It may be why so many symptoms of head-injury don't manifest themselves until long after the time the injury.

What happens during secondary axotomy, and why is there a delay? We now

know that cells that don't immediately die are still affected by the forces of the injury. They stretch. They twist. They get pinched. Their outer surfaces (the axolemma we discussed in the last entry) start to slowly rupture, and the cells begin to leak. Christopher Giza, a neurobiologist from UCLA, likens it to the damage a submarine might experience if it took an indirect hit from a depth charge. It may take a while for the vessel to fill up with enough ocean to sink it, or it may eventually recover, but it is still affected by the blast.

There are many bad things that happen when nerve cells leak.

I will outline three molecular/cellular processes many researchers believe are involved in the establishment of CTE. The first two will be covered in our next entry, focusing on the molecular biology of a little protein called "tau" and its relationship to the injury-induced leaking. The third, the most insidious by far, involves a cell type known as microglia. This mechanism has been invoked to explain why repetition must usually be involved in the CTE formation. It will take up most of the real estate of the entry after our discussion of tau. But the journey may be worth it. The data may go a long way toward explaining why repetitive injuries are so darned toxic.

Or not. As you may have guessed, not all scientists agree on exactly how that damage occurs.

Comments