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Brainstorm: Head Injuries and the NFL, Part 11: Microglial Cells

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We are trying to understand the biology of CTE at the most intimate level possible, the level of cells and molecules. The last entry dealt with the tau protein and its role in mediating closed-head neural damage. In this installment, let’s consider the role of microglial cells, a little wisp of a cell type with a great big job.

Microglia are small, non-neural cells that win my award for the Most Unusual Permanent Denizens of the Human Nervous System. Why do I say that? It might sound creepy to hear this, but microglia actually move around inside your brain. They migrate, possessing the only all-points access card that exists in your brain. And not just your brain. These migratory cells can crawl around all your central nervous system, which, as you might know, includes the spinal cord.

Why are they allowed to roam so freely? The reason comes from their job description. The brain’s very own local immune system, walled off from the rest of the body, comprises microglial cells. The nearest analogy would be one of your standard issue immune cells for the rest of the non-brain body (called a macrophage, which literally means “big eater”). Like their hungry cousins, microglial cells function as combination soldiers, police officers, and ambulance and garbage collectors for the entire brain. They keep the whole central nervous system under surveillance — that’s why they migrate — and can spring quickly into action if they detect a foreign organism, a damaged cell, or a localized injury (such as a stroke). Once activated, they are full capable of unleashing a broad spectrum of molecules onto brain cells, some that assist in destroying the bad guys, others that assist in promoting healing to the friendlies.

Most of the time microglial cells are not in this active state, and that’s a good thing. If the cells were constantly stimulated, even when there was nothing to worry about, the chemicals they dump might accumulate to toxic levels. Then they would become the source of the damage, not the source of the cure.
What do microglial cells have to do with repeated closed-head injury? Some researchers believe this inactive/active toggling state may explain why repeated injuries are so toxic. The idea goes like this:

1) The injury

The first closed-head injury occurs and brain cells become damaged.

2) The rescue

The microglial cells detect the injury and spring into action. They migrate to the damaged spot, releasing their powerful mixture of good-guy/bad-guy chemicals along the way.

3) Repeated blow

Another head injury occurs. The microglial cells, already partially activated from the previous wound, once again spring into action. More chemicals appear.

4) The microglia adapt

The repeated injuries communicate something to the microglia. They "get it" that other injuries are going to occur and decide to stay in a partially active state. This is formally called "priming." Priming means greater sensitivity; they are more likely to dump their elixir of good-guy/bad-guy chemicals all over the brain, perhaps even when there is no activating signal. The result? CTE.

Though this explanation is mostly speculation, it is based on something that is not at all far-fetched. Microglial priming has been shown to occur in many scenarios that the brain can experience, including exposure to environmental toxins and viral infections. It provides a series of testable hypotheses as one seeks to explain why repetitive injury is so important to consider in cases of this disorder.

Taken together, researchers have three potential mechanisms to explain the relationship of closed-head trauma to CTE: direct injury, changes in tau protein, and hyper-activation of the microglia. Are all three mechanisms in play in people suffering from CTE? Some smaller combination? Nobody knows at this point. But the fact that we can argue about which — if any — mechanisms are relevant to the disease state means we have come a long way in our understanding of it.

What problems some researchers have with this whole line of research (in the interest of full disclosure, I’m one of them), and exactly what issues lie ahead as the investigations continue, will be the subject of our final installments.

Comments