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Rapid response for inflammation control in songbirds' brains could lead to therapies in humans

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A biological process in the brains of zebra finches shows that the songbirds respond quickly to trauma and are capable of controlling the natural inflammation that occurs to protect the brain from injury.

Understanding the process well enough could lead to therapies in humans to control inflammation and hasten recovery from brain injury such as stroke, said American University Prof. Colin Saldanha, who presented new research findings during the annual meeting of the Society for Neuroscience. Through experiments, Saldanha and his colleagues' found that estrogen-producing glial cells play a role in the rapid response.

"The most surprising thing to me is that the inflammation control is happening within hours, and that estrogen is made in the brain around an injury site in response to an injury," Saldanha said. "These animals have evolved a mechanism to protect their brains from injury very quickly."

Preserving Brain Function

Inflammation is a normal part of the body's immune response. It affects the brain differently compared with other parts of the body. In the brain, too much inflammation can cause degenerative effects, or in the worst case scenario, death. Chronic inflammation causes cell damage and the loss of important neurons that regulate memory, mood and movement. Being able to control and limit inflammation in an injured brain may

preserve vital brain function.

As a neurobiologist and member of AU's Center for Behavioral Neuroscience, Saldanha studies estrogen in songbirds. The birds produce the common sex steroid in their brains, as do humans and other mammals. It's been known that hormones affect the brain since the 1850s, but realizing that similar hormones could be made in the brain itself, took until the 1980s. The animals make good research subjects for neuroscience for many reasons, including because of their brain plasticity.

Previous work by Saldanha and his colleagues explored how hormones communicate with neurons. They discovered a new method of communication, synaptocrine signaling, by which neurons create and feed high levels of estrogen to one another. That's when they also discovered which cells were synthesizing estrogen under conditions of brain injury: the glial cells, which are important, non-neuronal cells that live in the brain.

For more than a decade, National Institutes of Health has funded Saldanha's research because of the implications it has for treating neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, strokes and inflammatory diseases.

Controlling Inflammation

The release of estrogen in the brain to control inflammation is a natural process. It happens within about 24 hours in songbirds. The same process occurs in mammals over several days - perhaps far too late to stop brain degeneration or an end to life.

In the current experiments, Saldanha discovered another important function of glial cells—that they activated the rapid response to protect

the birds' brains. However more needed to be understood about how the protective process was keeping inflammation in check.

The researchers conducted three experiments using a type of acute injury, similar to a stroke. The injury spurred the secretion of small proteins called cytokines, which trigger an inflammatory response.

At certain points during the response, Saldanha and his colleagues controlled the levels of estrogen by preventing aromatase - the key protein needed for estrogen production - from working.

In the first experiment, researchers injured both sides of the brain, but flooded only one side with estrogen. The side flooded with estrogen showed less inflammation.

In a second experiment, researchers injured both sides of the songbird brain and limited aromatase function to only one side of the brain. On the side without aromatase, the inflammatory cytokines remained dangerously elevated. That's when researchers knew estrogen controls inflammation and its very production occurs in response to injury.

Estrogen is a complex chemical, which makes it exciting to study, Saldanha said. "We can't just pump people full of estrogen. It can have very bad effects on systems other than the brain," Saldanha said. "It's very tricky, which is why exploring this is so important, so we can figure out how to harness its power without any deleterious side-effects."

More information: Scientific Presentation: Tuesday, Nov. 18, 1-2 p.m., Halls A-C 640.09, Estradiol, synthesized by reactive glia, is a potent anti-inflammatory in the injured vertebrate brain A.L. PEDERSEN, L.H. NELSON, C.J. SALDANHA; Biology, Psychology, & Ctr. for Behavioral Neurosci., American Univ., Washington, D.C.

Provided by American University