Dying brain cells cue new brain cells to grow in songbird

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Gambel's white-crowned sparrows are about seven inches in length. Credit: T Larson/U of Washington

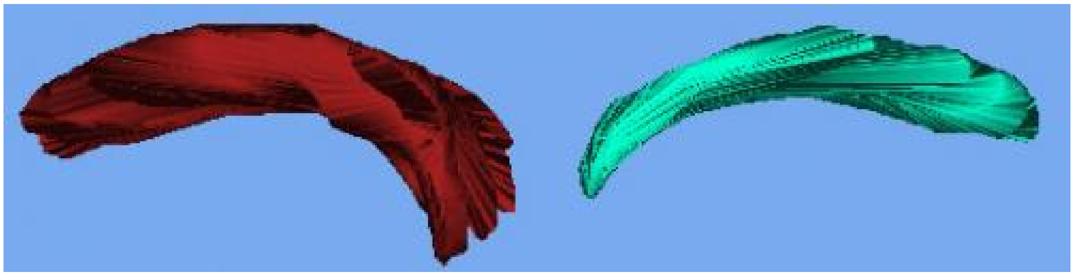
Brain cells that multiply to help birds sing their best during breeding season are known to die back naturally later in the year. For the first time researchers have described the series of events that cues new neuron growth each spring, and it all appears to start with a signal from the expiring cells the previous fall that primes the brain to start producing stem cells.

If scientists can further tap into the process and understand how those signals work, it might lead to ways to exploit these signals and encourage replacement of cells in human brains that have lost neurons naturally because of aging, severe depression or Alzheimer's disease, said Tracy Larson, a University of Washington doctoral student in biology. She's lead author of a paper in the Sept. 23 *Journal of Neuroscience* on brain cell birth that follows natural brain cell death.

Neuroscientists have long known that new neurons are generated in the adult brains of many animals, but the birth of new neurons – or neurogenesis – appears to be limited in mammals and humans, especially where new neurons are generated after there's been a blow to the head, stroke or some other physical loss of brain cells, Larson said. That process, referred to as "regenerative" neurogenesis, has been studied in mammals since the 1990s.

This is the first published study to examine the brain's ability to replace cells that have been lost naturally, Larson said.

"Many neurodegenerative disorders are not injury-induced," the co-authors write, "so it is critical to determine if and how reactive neurogenesis occurs under non-injury-induced neurodegenerative conditions."



Additional neurons make the part of the sparrow's brain that produces its song about twice as large during the breeding season, depicted here in red, compared to its size the rest of the year, shown in green. Credit: G Bentley/E Brenowitz/U of Washington

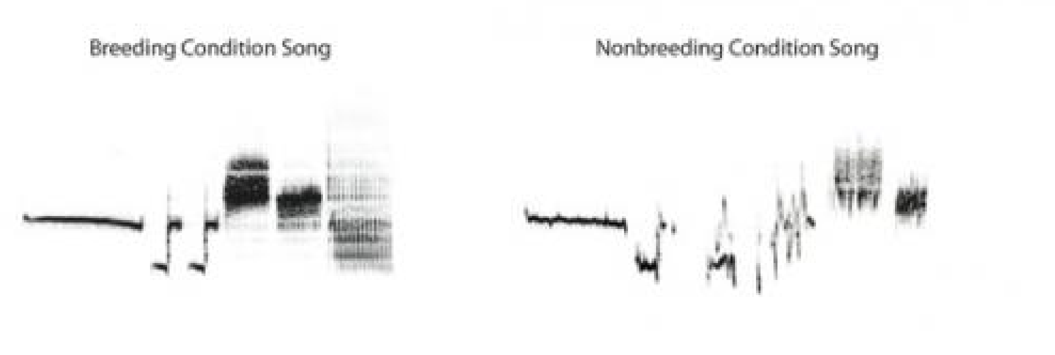
The researchers worked with Gambel's white-crowned sparrows, a medium-sized species 7 inches (18 centimeters) long that breeds in Alaska, then winters in California and Mexico. Sometimes in flocks of more than 100 birds, they can be so plentiful in parts of California that they are considered pests. The ones in this work came from Eastern Washington.

Like most songbirds, Gambel's white-crowned sparrows experience growth in the area of the brain that controls song output during the breeding season when a superior song helps them attract mates and define their territories. At the end of the season, probably because having extra cells exacts a toll in terms of energy and steroids they require, the cells begin dying naturally and the bird's song degrades.

Gambel's white-crowned sparrows are particularly good to work with because their breeding cycle is closely tied to the amount of sunlight they receive. Give them 20 hours of light in the lab, along with the right increase of steroids, and they are ready to breed. Cut the light to eight to 12 hours and taper the steroids, the breeding behavior ends.

"As the hormone levels decrease, the cells in the part of the brain controlling song no longer have the signal to 'stay alive,'" Larson said. "Those cells undergo programmed cell death – or cell suicide as some call it. As those cells die it is likely they are releasing some kind of signal that somehow gets transmitted to the stem cells that reside in the brain. Whatever that signal is then triggers those cells to divide and replace the loss of the cell that sent the signal to begin with."

The next spring, all that's needed is for steroids to ramp up and new cells start to proliferate in the song center of the brain.



The natural die off of neurons in the song center of a sparrow's brain as the breeding season concludes causes a measureable decline in the song that scientists can measure. Credit: T Larson/U of Washington

"This paper doesn't describe the exact nature of the signals that stimulate proliferation," Larson said. "We're just describing the phenomenon that there is this connection between cells dying and this stem cell proliferation. Finding the signal is the next step."

"Tracy really nailed this down by going in and blocking cell death at the end of the breeding season," said Eliot Brenowitz, UW professor of psychology and of biology, and co-author on the paper. "There are chemicals you can use to turn off the cell suicide pathway. When this was done, far fewer stem cells divided. You don't get that big uptick in new neurons being born. That's important because it shows there's something about the cells dying that turns on the replacement process.'

"There's no reason to think what goes on in a bird brain doesn't also go on in mammal brains, in human brains," Brenowitz says. "As far as we know, the molecules are the same, the pathways are the same, the hormones are the same. That's the ultimate purpose of all this, to identify these molecular mechanisms that will be of use in repairing human brains."

In mammals, the area of the brain that controls the sense of smell and the one that is thought to have a role in memories can produce tiny numbers of new brain cells but it is not understood how or why. The numbers of new cells is so low that trying to identify and quantify if dying cells are being replaced and if so, the steps that are involved, is much more difficult than when using a songbird like Gambel's white-crowned sparrow, Larson and Brenowitz said.

Provided by University of Washington