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For the first time, scientists have directly linked social cues to an immediate genetic response in the brain, according to a new study in *PloS Biology*. Only minutes after subordinate male cichlid fish sense an opportunity to become socially dominant, they display dominant characteristics such as changes in color and behavior, and express *egr-1*, encoding a transcription factor that likely triggers enhanced fertility and other long-term dominance traits.

"People forget that social influences are pretty important," said study co-author Russell Fernald at Stanford University in California. "Here's the case where the social is everything. [It] regulates brain structure in a very direct way."

Characterized by a dynamic social hierarchy, the cichlid fish *Astatotilapia (Haplochromis) burtoni* can readily alter sexual capacities, and only dominant males are physiologically able to reproduce. "We were interested in understanding how this occurred at a mechanistic level, uncovering earliest steps that occur in the process," said first author Sabrina Burmeister, a former postdoctoral fellow in Fernald's lab, who is now at the University of North Carolina-Chapel Hill.

Previous work has shown that one week after males become dominant, neurons in the preoptic region of the brain become eight times larger and produce a great deal of gonadotropic-releasing hormone-1 (GnRH1), which regulates reproductive physiology in all vertebrates. To investigate what neural mechanisms rapidly connect social change to this physiological change, the researchers gave subordinate fish an opportunity to ascend in a familiar environment. Molecular analyses focused on *egr-1*, an immediate-early gene that codes for a transcription factor involved in neural plasticity. According to Burmeister, "it's poised in the cell to have a rapid response."

During the experiment, the researchers removed the dominant male from each observation tank containing four females and one other male, then turned on the lights an hour later so that the fish could see the dominant male was missing. Minutes later, the subordinate male changed body color and became more aggressive, with larger testes and other signs of heightened fertility following soon after. Burmeister said she was surprised to see the animals respond so quickly to a change in social environment.

Twenty minutes after they turned on the lights, the researchers used *in situ* hybridization to analyze gene expression in the fish's brains, and found that the ascending males had more than twice as much *egr-1* expression in the anterior preoptic region—especially where there are a lot of GnRH1 neurons—as males who had remained either subordinate or dominant. There was no *egr-1* expression in control brain regions that do not express GnRH1. Subsequent genetic analysis demonstrated that GnRH1 has recognition sites for *egr-1*, pointing out a logical target for the transcription factor. "[*Egr-1*] can turn on GnRH-1, so we're pretty clear that it's one of the things it's doing," Fernald said.

The work "speaks to how dynamic these [social] situations can be and how natural selection has probably selected for these very, very rapid responses," said Sigal Balshine at McMaster University in Ontario, who did not participate in the study. Because of its "amazing reversibility and capacity for dynamic change," she said, *A. burtoni* is a "really neat, effective model to study social changes that occur rapidly in nature."

In a previous experimental model, the researchers moved the subordinate male into a tank where he could become dominant. In this scenario, it took longer for him to respond to the change in environment, something Fernald suspected might be due to the disruptive nature of the experiment. This new system minimized these stresses. "It's as if you woke up one morning in your house, and the neighborhood bully had suddenly moved away," Fernald explained.

In the future, Fernald said, genetic researchers "can now use *egr-1* as a marker to what cells are being activated." His lab is studying transgenic fish to investigate the putative interaction between *egr-1* and GnRH1. Still, according to Fernald, several questions remain. For instance, "how does [the fish] put two and two together," combining internal and sensory cues to make a physiological decision? On a broader scale, Fernald said he hopes this work will "encourage people to look for structures related to how animals lead their social lives."

According to Burmeister, "the mechanisms that we're looking at are very fundamental" and could be extrapolated to other animals, particularly since both *egr-1* and GnRH1 are common in vertebrates. "All kinds of species use social information to make reproductive decisions," she said.

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