Learning what's dangerous is costly, but social animals have a way of lowering the price

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What would you do if the person standing next to you suddenly screamed and ran away? Would you be able to carry on calmly with what

you're doing, or would you panic? Unless you're James Bond, you're most likely to go for the second option: panic.

But now imagine another scenario: While out on the street, the person walking in front of you suddenly freezes—she stops moving and becomes perfectly still. What would you do?

"Here, the answer becomes more tricky," says Marta Moita, head of the Behavioral Neuroscience Lab at the Champalimaud Centre for the Unknown, in Lisbon, Portugal. "Even though freezing is one of the three basic instinctive defense behaviors [along with fight and flight], animals don't instinctively know that when others freeze, they are actually responding to a threat."

For social animals such as ourselves, being able to tell if a group member senses a threat can be a matter of life and death. How does this learning happen? To find an answer to this question, Moita and her team engaged in a series of studies. Their most recent findings are presented in two scientific articles, one that was published today (May 12th) in the journal *PLOS Biology* and another published a few months ago in *Current Biology*. Together, their results reveal a mechanism by which animals acquire fear of freezing and outline the neural circuitry that underlies the expression of that fear.

"No pain, no gain"

How is it that some fear responses are innate, while others must be learned? The answer is not fully known, but a good guess would be that because the world is ever-changing, animals must flexibly adapt to their environment.

For instance, when an animal freezes, it essentially stops moving. But is lack of motion necessarily a sign of danger? "The answer is no," says

Moita. "There are situations where an animal stops moving that are perfectly benign; it might be grooming or observing something. But then, this harmless cue can transform into a sign of danger. We wanted to find out how it happens."

In the study published in the journal *Current Biology*, Moita and her team tested various experimental scenarios with rats. They found out that first and foremost, the animal has to go through a process called auto-conditioning, meaning that the learning does not happen by observing others, but through first-hand experience. And more than that, it can only happen if specific criteria are fulfilled. "We were a bit surprised by the results, because it turns out that the learning mechanism is quite strict," says Andreia Cruz, the first author of the study.

The team discovered that for a rat to adopt freezing as a social cue, it has to go through a learning experience that consists of two key components: pain and immobility. Either one without the other is not enough.

"For instance, animals that experience a mild foot shock [which is a painful event] and then freeze as a result, learn to recognize freezing in other group members as a threat. But when we prevented the subsequent freezing response by removing the rat from the experimental box immediately after the foot shock, the learning didn't happen," Cruz explains.

It may seem harsh, but in fact, as Moita points out, this manner of learning is an enormously beneficial way for animals to avoid danger. "The rat underwent a single painful experience [a mild foot shock] that taught it that freezing is a response to a negative event. As a consequence, now it doesn't need to learn first-hand the full range of scenarios that can cause painful experiences. Instead, it just needs to be attentive to how its group members behave."

Hearing and fearing silence

Creating an association between freezing and danger means that new neural connections were formed in the brain. But before diving into the neural circuits, there was still an important question that needed to be addressed: Which brain areas might be involved in the expression of this newly learned fear?

"Learning happens by associating cognitive elements that were previously unrelated," Moita explains. "For instance, in the famous Pavlov experiment, dogs learned that the sound of a bell meant that they were about to receive food. So two previously unrelated things—bell sound and food—became associated in the brain."

Moita points out that several cognitive elements may be associated with this newly acquired defensive response, among which is a special kind of auditory cue—silence.

The team previously discovered that rats who learned to use freezing as an alarm cue were actually detecting the sudden onset of silence. "When a rat freezes, it stops moving. Which effectively means that it stops generating sound," Moita explains. "We found that this transition from sound to silence can become a social cue by which rats recognize that another group member is freezing."

Following this line of thought, the team focused on the brain's fear-learning center and the auditory system. Their results—describing a new neural map that spans these structures—were published today in the journal *Plos Biology*.

A newly discovered neural map

The first question that comes to mind is: How can the auditory system hear silence? Moita explains that to answer this question, you have to think about it in reverse. "We believe that it's not silence per se that the brain is detecting, it's actually the cessation of sound."

The auditory system is made up of many thousands of neurons, each of which has a preference for certain features of auditory information. For example, some neurons respond to high-frequency sounds, others to the onset of sound. And then, there are offset neurons that respond to the cessation of sound. Those are the neurons the team suspects to be the ones that detect silence.

"Offset neurons are abundant in a particular area within a brain region called the auditory thalamus. When we blocked the activity of this area, animals that have adapted freezing as a social cue and would normally respond to the sudden onset of silence, did not," explains Ana Perreira, the first author of the study.

Importantly, this same auditory region connects to the lateral amygdala—a brain area crucial for learning to respond to threatening sounds. Could it also be involved in fearing silence? The team discovered that the answer is yes. "Our results show that the lateral amygdala is not only important for associating sound and danger, but also silence and danger," says Perreira.

The team used these results together with others obtained in this study to generate a map of how the brain expresses fear of freezing. "The pathway we identified expands the network that processes auditory cues in the context of danger," says Moita. "More broadly, our work sets the stage to further our understanding of how sensory stimuli and their behavioral relevance are encoded in the brain," she concludes.

More information: Piray Atsak et al. Experience Modulates Vicarious

Freezing in Rats: A Model for Empathy, *PLoS ONE* (2011). DOI: 10.1371/journal.pone.0021855

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