SOCIAL NEUROSCIENCE

The social transmission of stress

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The effects of stress on the body are pretty well documented. To prepare for flight-or-fight, muscles tense, heart rate increases, blood pressure rises; in the brain, the hypothalamus instructs the kidneys to ramp up the production and release of stress hormones, like cortisol and epinephrine, which spur the liver to produce more glucose for energy. Stress also changes the brain; synapses become primed to respond more effectively should the stressor be encountered again. As a result, intense or prolonged exposure to stress could be a contributing factor to conditions like anxiety, depression, and post-traumatic stress disorder.

That's all going on within an individual, but there's been plenty of anecdotal evidence (and increasingly, experimental results too) that suggest that if one social creature—be it rodent, primate, or human—feels stressed, others nearby can feel it too. But does transmitted stress cause the same kinds of changes in the brain observed in animals that experience an aversive event directly? New research from the lab of Jaideep Bains at the University of Calgary points to "yes."

Bains' lab has been interested in stress and its impact on neural circuits for several years. They've previously observed evidence of plasticity in corticotropin-releasing hormone (CRH) neurons (these control the hormonal responses to stress—if they don't fire, stress hormones aren't released) in the hypothalamus of mice. But these were animals that were singly-housed during the experiments. "That's not how the animals really live," says Bains, and they wondered what would happen if a stressed mouse was returned to the company of other stress-naive cage mates.

In the current study, published in *Nature Neuroscience*, Bains and his lab designed a series of experiments to test how male and female mice responded to an acute stress—either a small foot shock or isolation in a novel environment—, how the presence of stress-naive cage mates altered those responses, and how the cage mates themselves were affected by their stressed conspecifics. They measured the short term potentiation (STP) of glutamate synapses on CRH neurons, a measure of synaptic metaplasticity, as well as corticosterone levels in the different mice to gauge the changes.

Two results stuck out to Bains. "One is that it doesn't really matter whether it's your stress or somebody else's," he says. "A transmitted stress changes the brain in the exact same way as a real stress." And stress can even propagate beyond the stressed mouse-naive mouse pairs. Though exact mechanisms are still unclear, further experiments presented in the paper that blocked anogenital sniffing and altered the activation of the CRH neurons suggest that stress transmission is accomplished via pheromones. A chemical alarm signal released by a stressed mouse can be picked up by its naive partner, which in turn produces an alarm signal of its own that can even affect a tertiary mouse that never met the original. Along the way, synapses in each mouse in the chain are changing and being "amped up" to respond to the next stressful event.

"From an evolutionary perspective, we think these types of signals were likely critical in the formation of social groups," Bains explains. The ability to transmit stress means a given animal doesn't have to experience an aversive event itself to be able to derive information about it from others in its group.

As for the second interesting observation, it seems that sex matters. By the measures recorded, male mice only responded to foot shocks, while females and their cage mates had elevated STP and corticosterone levels following both physical stress and the stress of isolation. But notably, the presence of a naive female appeared to buffer the responses observed in the original mouse: stressed female mice that were given a partner had lower measures than females left alone after the aversive event. No such buffering was observed in post-foot shocked males, regardless of whether they were given a companion. The paired mice of both sexes behaved similarly, leaving questions of whether other means of communication, such as ultrasonic vocalizations, contribute to females' buffering abilities.

Just how long the synaptic priming lasts and the extent of its impacts on behavior, as well as the exact mechanisms behind both the transmission of stress and its buffering by females, all still need to be worked out, but the results suggest that stress in an individual animal is not the only variable other researchers may need to consider. Particularly in areas like addiction research, Bains wonders how housing could affect outcomes, of the addicted animal itself and any of its naive cage mates. "I think these can be really interesting avenues to pursue and I think for the most part, people haven't really considered it," he says.

Bains' lab itself only turned to the social aspects of stress about a year and a half ago, but that initial spark of curiosity about whether stress might be transmitted between animals may one day bear relevance for better understanding the effects of stress in people. In the meantime, there's lots left to decipher in mice first. "For us, it's moving more towards asking these questions in the context of freely behaving animals where we can get real-time information about what specific cells are doing," Bains says.

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