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# A new brain-based marker of stress susceptibility

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Some people can handle stressful situations better than others, and it's not all in their genes: Even identical twins show differences in how they respond.

Researchers have identified a specific electrical pattern in the brains of genetically identical mice that predicts how well individual animals will fare in stressful situations.

The findings, published July 29 in *Nature Communications*, may eventually help researchers prevent potential consequences of chronic stress—such as post-traumatic stress disorder, depression and other psychiatric disorders—in people who are prone to these problems.

"In soldiers, we have this dramatic, major stress exposure, and in some individuals it's leading to major issues, such as problems sleeping or being around other people," said senior author Kafui Dzirasa, M.D., Ph.D., an assistant professor of psychiatry and behavioral sciences at Duke University Medical Center and a member of the Duke Institute for Brain Sciences. "If we can find that common trigger or common pathway and tune it, we may be able to prevent the emergence of a range of mental illnesses down the line."

In the new study, Dzirasa's team analyzed the interaction between two interconnected brain areas that control fear and stress responses in both mice and men: the prefrontal cortex and the amygdala. The amygdala plays a role in the 'fight-or-flight' response. The prefrontal cortex is

involved in planning and other higher-level functions. It suppresses the amygdala's reactivity to danger and helps people continue to function in stressful situations.

Implanting electrodes into the brains of the mice allowed the researchers to listen in on the tempo at which the prefrontal cortex and the amygdala were firing and how tightly the two areas were linked—with the ultimate goal of figuring whether the electrical pattern of cross talk could help decide how well animals would respond when faced with an acute stressor.

Indeed, in mice that had been subjected to a chronically stressful situation—daily exposure to an aggressive male mouse for about two weeks—the degree to which the prefrontal cortex seemed to control amygdala activity was related to how well the animals coped with the stress, the group found.

Next the group looked at how the brain reacted to the first instance of stress, before the mice were put in a chronically stressful situation. The mice more sensitive to chronic stress showed greater activation of their prefrontal cortex-amygdala circuit, compared with resilient mice.

"We were really both surprised and excited to find that this signature was present in the animals before they were chronically stressed," Dzirasa said. "You can find this signature the very first time they were ever exposed to this aggressive dangerous experience."

Dzirasa hopes to use the signatures to come up with potential treatments for stress. "If we pair the signatures and treatments together, can we prevent symptoms from emerging, even when an animal is stressed? That's the first question," he said.

The group also hopes to delve further into the brain, to see whether the

circuit-level patterns can interact with genetic variations that confer risk for psychiatric disorders such as schizophrenia. The new study will enable Dzirasa and other basic researchers to segregate stress-susceptible and resilient animals before they are subjected to stress and look at their molecular, cellular and systemic differences.

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