UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: LaKisha Ladson
214-648-3404
lakisha.ladson@utsouthwestern.edu

New brain nerve cells key to stress resilience, UT Southwestern researchers find

DALLAS – March 31, 2010 – UT Southwestern Medical Center researchers have found new clues that might help explain why some people are more susceptible to stress than others.

In a study of mice, the researchers determined that weeks after experiencing a stressful event, animals that were more susceptible to stress exhibited enhanced neurogenesis – the birth of new nerve cells in the brain. Specifically, the cells that these animals produced after a stressful event survived longer than new brain cells produced by mice that were more resilient.

In addition, when researchers prevented neurogenesis in both stress-susceptible and resilient mice, the animals previously susceptible to stress became more resilient.

"This work shows that there is a period of time during which it may be possible to alter memories relevant to a social situation by manipulating adult-generated nerve cells in the brain," said Dr. Amelia Eisch, associate professor of psychiatry at UT Southwestern and senior author of the study in the *Proceedings of the National Academy of Sciences*. "This could eventually lead to a better understanding of why, in humans, there is an enormous variety of responses to stressful situations."

Mice that are susceptible to stress exhibit long-lasting social avoidance and depressive-like behavior after experiencing a stressful event, such as being placed in a cage with a more aggressive mouse. Resilient mice behave more like unstressed control animals. This animal model is commonly used in studies of stress and depression, as understanding the changes in the brain and behavior of the mice can shed light on stress-induced changes in the human brain and in human behavior.

In the study, the brain cells of both groups of mice responded in similar ways after a stressful event. But weeks later, researchers found that mice displaying social avoidance had more nerve cells in a region of the brain called the hippocampus that survived the stressful event than mice that were more resilient.

The study is the first to link the memory of a social experience with neurogenesis in the hippocampus, Dr. Eisch said. Recently, Dr. Eisch and her team have linked adult neurogenesis with addiction. Previously, neurogenesis was primarily associated with spatial learning and memory.

In this study, Dr. Eisch and her colleagues exposed some mice to social defeat by having the animals live in the same cage as larger, aggressor mice for five minutes a day, and in the same cage but

(MORE)

with a barrier in place the rest of the day. Researchers then tested the mice to see if they were susceptible to stress.

The researchers labeled the new cells of susceptible and unsusceptible mice so they could see how the cells divided. Both types of mice produced fewer dividing cells immediately after stress, but in the long run, mice susceptible to stress had more new adult cells than unsusceptible and control mice, who lived in cages with nonaggressor mice.

Dr. Eisch and her colleagues also used radiation to prevent hippocampal neurogenesis in all groups of mice. Mice susceptible to stress stopped producing new nerve cells and didn't display social avoidance in the long term.

Inhibiting social avoidance also had detrimental effects, however.

"Radiation in susceptible mice led to behavior that might be interpreted as harmful, such as approaching a potential aggressor mouse instead of avoiding it. We hypothesize that the survival of new nerve cells may be a compensatory event in the brain to allow the mouse to remember a socially relevant aggressor," Dr. Eisch said. "We're eager to see if these results carry over to other animal models and to explore the mechanisms underlying these changes, as these are critical steps to understanding how adult-generated neurons might be modulated to help humans in stressful situations."

Future studies also will help determine which genes are involved with increased survival of new nerve cells in mice susceptible to stress, Dr. Eisch said.

Other UT Southwestern researchers participating in this study were Nathan DeCarolis, student research assistant in psychiatry and Shveta Malhotra, senior research associate in psychiatry. Others involved in the work were lead author Dr. Diane Lagace, former instructor of psychiatry, now at the University of Ottawa, as well as investigators from the University of Pennsylvania School of Medicine and Mount Sinai School of Medicine.

The study was supported by the National Institutes of Health, NASA, the National Alliance for Research on Schizophrenia and Depression, and the Canadian Institutes of Health Research.

Visit http://www.utsouthwestern.org/neurosciences to learn more about UT Southwestern's clinical services in neurosciences, including psychiatry.

###