

# Coming Undone: How Stress Unravels the Brain's Structure

The helpless behavior that is commonly linked to depression and post-traumatic stress disorder (PTSD) is preceded by stress-related losses of synapses-microscopic connections between brain cells-in the brain's hippocampal region, researchers at Yale School of Medicine report in the March 1 issue of *Biological Psychiatry*.

The team used a six-day treatment with the antidepressant desipramine to reverse helpless behavior and restore hippocampal synapses in rats.

"In clinical practice, the main problem with antidepressants is that they require weeks to exert their effect," said lead scientist on the project Tibor Hajszan, M.D., associate research scientist in the Department of Obstetrics, Gynecology & Reproductive Sciences at Yale School of Medicine. "Because there are ways to restore these lost hippocampal synapses in as little as hours or even minutes, our laboratory is currently testing rapid-acting antidepressants that could provide immediate relief from depressive symptoms."

Mental health disorders, including depression, are rapidly becoming the second largest public health problem, said Hajszan. "This is magnified by the fact that current antidepressant drugs remain ineffective in the majority of patients," he said.

Researchers have suspected for years that changes in synapses may play a role in depression neurobiology. In this study, Hajszan and his team studied helpless behavior in rats and used electron microscopy to analyze directly what happens to hippocampal synapses in the presence or absence of helpless behavior.

"Because synapses have the potential for rapid response, synapse loss probably underlies the rapid deterioration of mood that depressed patients sometimes experience," said Hajszan.

"Thus, it is possible to elevate mood rapidly by generating new hippocampal synapses, which is attainable by certain drugs we are testing."