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T149. Novel Synergistic Actions of Multiple Stress Hormones Mediate Memory Impairments After Acute Simultaneous Stresses

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Background: Acute stress typically enhances memory, an adaptive process crucial for survival. Surprisingly, we recently found that several acute concurrent stresses provoke enduring memory problems. During stress, hippocampal synapses are bathed in a cocktail of stress-released molecules, yet it is unknown how these molecules interact to mediate the profound effects of stress on memory.

Methods: We employed in vivo and in vitro approaches including transgenic mice, slice electrophysiology and novel imaging methods such as wide-field confocal imaging and 3D deconvolution tomography, to examine the mechanisms of the enduring memory problems provoked by acute concurrent stresses.

Results: The multiple acute concurrent stresses led to the lost ability of hippocampal synapses to sustain a potentiated state. These physiological deficits derived from structural alterations of synapse-bearing dendritic spines. Investigating the mole-cular mediators of these effects of stress, we found that both physiological and structural defects were recapitulated by the combined actions of the steroid stress hormone corticosterone (CORT) and the peptide corticotropin-releasing hormone (CRH). Mechanistically, CORT and CRH converged on the stability and plasticity of the actin skeleton of dendritic spines. Specifically, CORT and CRH exerted synergistic effects on the spine actin-regulating Rho-GTPase enzyme, RhoA. Support-ing the convergent actions of CORT and CRH in mediating the effect of concurrent acute stresses on memory, blocking the brain actions of both hormones, but not each alone, rescued spatial memory in stressed mice.

Conclusions: Memory impairment by concurrent acute stresses requires interactions of multiple stress hormones at hippocampal synapses, with significant clinical impact.

Keywords: Memory, Hippocampus-mPFC pathway, Acute and Chronic Stress, Long-Term Potentiation, Rho Family GTPase.

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