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Persistent pain produces stress-like alterations in hippocampal neurogenesis and gene expression.

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Abstract

Clinical observations have shown that patients with chronic pain are often depressed, suggesting the importance of the affective or emotional component of pain and its impact on cognition. In this study we investigated pain-induced activation of the hippocampus to address possible molecular and cellular events that may underlie the comorbidity of chronic pain and depression. Rats received either an acute (formalin) or chronic (complete Freund's adjuvant) inflammatory stimulus to the hind paw or an acute or chronic immobilization. Results demonstrated that pain can alter hippocampal morphology and gene expression. Bromodeoxyuridine (BrdU) staining indicated that neurogenesis in the hippocampal dentate gyrus was significantly reduced after long-term inflammatory nociception, similar to previous observations after various stress models. Important activators of nociception-induced spinal central sensitization, the neurokinin-1 (NK-1) receptor and brain-derived neurotrophic factor (BDNF), have also been intimately associated with depressive processes in the limbic system. In situ hybridization assay results demonstrated that either pain or stress (acute or chronic treatments) reduced the levels of both NK-1 receptor and BDNF mRNAs in the cornu ammonis 1-3 sublayers of the hippocampus, suggesting a possible role of these neuromediators in processing of pain in higher brain centers.

PERSPECTIVE:

The findings in this study demonstrate that persistent pain induces stress-like damaging modulatory effects in the hippocampus, which is one of the limbic regions involved in the pathophysiology of depression. Targeting these mechanisms (which are potential contributors to the emotional impact of pain) may provide novel therapeutic approaches for relieving depression-like aspects of chronic pain.

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