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**Title:** Exploring the Hypothesis that False Context Fear Memories Drive Traumatic Memory Generalization

**Background and Purpose:** Fearful experiences often occur suddenly, leaving little time to process contextual information, which can lead to distorted or false fear memories in non-traumatic environments. We hypothesize that such false fear memories underlie traumatic memory generalization, and that early exposure to a similar but distinct environment after fear experiencing promotes their formation while gradually reducing the precision of the original memory, demonstrating a time-dependent enhancement. We focused on glucocorticoid receptors (GR) and mineralocorticoid receptors (MR) in the hippocampus to clarify their roles in the formation and potentiation of false context fear memories, aiming to elucidate the mechanisms by which stress-related signaling contributes to the generalization of traumatic memories.

**Research Outline:** We investigated how false context fear memories are formed and strengthened over time in mice. When mice were exposed to a similar but distinct environment shortly after a fear-inducing experience, they later exhibited a strong fear response in that novel environment, indicating the formation of false fear memory. Importantly, this false memory became progressively stronger over time, highlighting a time-dependent enhancement. Meanwhile, the accuracy of the original memory gradually declined. At the molecular level, activation of glucocorticoid receptors (GR) shortly after fear exposure promoted the formation of false memories, whereas inactivation of mineralocorticoid receptors (MR) contributed to their later potentiation. Pharmacological interventions further revealed that GR and MR play distinct and time-dependent roles in this process. Our findings highlight the importance of hippocampal GR and MR in regulating the balance between accurate and false fear memories. Exposure to a similar context shortly after fear learning may integrate new contextual elements into the original memory trace, leading to time-dependent consolidation of false memories and reduced specificity of the original memory. This mechanism aligns with theories of systems consolidation and may help explain the generalized or intrusive fear memories observed in post-traumatic stress disorder (PTSD).

**Future Prospects:** Future studies using region-specific receptor modulation and memory engram-based approaches will be required to clarify the neural circuits and cellular ensembles responsible for integrating or separating contextual information. In addition, we aim to investigate whether key memory processes—consolidation, destabilization, and reconsolidation—are involved in the formation of false contextual fear memories, with the goal of identifying therapeutic strategies that could prevent the development of generalized traumatic memories.

**Reference:** Time-dependent Potentiation of False Context Fear Memory through Glucocorticoid Receptor Activation and Mineralocorticoid Receptor Inactivation, *Journal of Integrative Neuroscience.* 2025, 2025 Sep 28;24(9):40000