

**Abstract for 6th Chinese Computational and Cognitive Neuroscience Conference (CCCN 2024)
(July 3-5, 2024)**

Microglia Govern the Extinction of Acute Stress-induced Anxiety-like Behaviors

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Anxiety-associated symptoms following acute stress usually become extinct gradually within a period of time. However, the mechanisms underlying how individuals cope with stress to achieve the extinction of anxiety are not clear. Here we show that acute restraint stress causes an increase in the activity of GABAergic neurons in the CeA (GABA^{CeA}) in male mice, resulting in anxiety-like behaviors within 12 hours; meanwhile, elevated GABA^{CeA} neuronal CX3CL1 secretion via MST4 (mammalian sterile-20-like kinase 4)-NF- κ B-CX3CL1 signaling consequently activates microglia in the CeA. Activated microglia in turn inhibit GABA^{CeA} neuronal activity via the engulfment of their dendritic spines, ultimately leading to the extinction of anxiety-like behaviors induced by restraint stress. These findings reveal a dynamic molecular and cellular mechanism in which microglia drive a negative feedback to inhibit GABA^{CeA} neuronal activity, thus facilitating maintenance of brain homeostasis in response to acute stress.