

The claustrum neuronal ensembles that were activated by social defeat stress mediate anxiety-like behavior through regulating the activation of multiple stress-responsive nuclei

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Acute mental stress induces negative emotional states including anxiety. However, the neuronal mechanisms underlying stress responses remain unknown. Recently, we found that the neuronal activation in the claustrum prominently differs between control mice and mice received stress. Here we examined the role of the claustrum neuronal ensembles that were activated by social defeat stress in anxiety-like behavior and the underlying neuronal networks. We bilaterally co-injected adeno-associated virus vectors expressing the tamoxifen-dependent recombinase $ERT2^{ERT2}Cre^{ERT2}$ and Cre-dependent DREADDs into the claustrum. Chemogenetic re-activation of DREADDs-tagged claustrum neurons increased the anxiety-like behaviors and induced neuronal activations of anxiety-related nuclei including the amygdala. Chemogenetic inhibition of these neurons suppressed stress-induced anxiety-like behaviors and prevented neuronal activation by the defeat stress. In addition, the claustral neurons received innervation from stress-responsive neurons in the amygdala and the medial prefrontal cortex. The stress-responsive claustral neurons projects to the cortices including the medial prefrontal cortex. These results suggest that the claustrum neuronal ensembles regulate stress-induced anxiety through orchestrating activations in the multiple brain nuclei.