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Chronic stress causes excessive aggression by altering synaptic actin dynamics in the mPFC.

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Behavioral and psychological symptoms of dementia (BPSD) are an integral part of dementia syndrome. In particular, BPSD such as chronic stress induced excessive aggression is known to be more stressful to caregivers than the cognitive and functional problems of the patients with dementia. Therefore, the effective treatment for excessive aggressive behavior is required. There is evidence that functional circuits in the medial prefrontal cortex (mPFC) regulate social cognitive functions including aggressive behaviors. Also, social isolation, one form of chronic stress environment, can lead to the development of excessive aggression. However, the underlying cellular and molecular mechanisms of the mPFC neural network involved in chronic stress environment induced aggression is largely unknown.

To clarify the molecular mechanism of mPFC neuronal network with excessive aggression, we examined aggressive behavior in rat model of chronic social isolation focusing on mPFC synaptic plasticity. We further investigated the relationship between synaptic actin dynamics and AMPARs delivery in spines of mPFC of chronic stressed animals. Here, we show that chronic stress environment changes spines in the mPFC by reducing actin dynamics, leading to the decrease of synaptic AMPA receptor delivery and altered social cognition and aggressive behavior. Our study provides molecular and cellular mechanisms underlying the influence of chronic stress environment on social cognition and aggression.