helpless behaviors after stress exposure. Our observation is consistent with clinical reports of the interaction between mOR and depression. Therefore, we suggest that the selective activation of mORs in the LHb may serve as a possible therapeutic strategy for treating depressive disorders.

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Effect of agmatine on behavioral changes over time in post-traumatic stress disorder

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Abstract

Objective: Post-traumatic stress disorder (PTSD) is a persistent mental and emotional condition after life-threatening events. A single prolonged stress (SPS) induced animal model has demonstrated to result in neurological dysregulation and behavior abnormalities observed in PTSD. However, agmatine which was proposed as antidepressant and anxiolytic endogenous molecule was investigated in a rat model of PTSD.

Methods: Rats (200–260 g) were divided into Control (saline), SPS, SPS+Imipramine (20 mg/kg), SPS+Agmatine (20, 40 and 80 mg/kg) groups. In SPS model, rats were restrained for 2 h, 20 min of group forced swim in water, allowed 15 min in home cages then placed in an empty cage with a wire mesh floor under which petri dishes filled with ether were placed until loss of consciousness. Control animals were only handled. Animals were housed for 1, 7 and 14 days without disturbance. Animals were tested in open field (OFT), forced swimming test (FST) and elevated plus maze (EPM).

Results: We found that the SPS rats spent less time than the control rats in the center. General locomotor behavior was measured as the total distance traveled during the OFT test, was significantly lower in SPS rats than in controls. SPS rats spent less time grooming, longer immobility time in the FST and the highest mean value were detected at day 7. All PTSD related findings significantly reversed by imipramine and agmatine treatment. In EPM, agmatine increased time spent and number of entries in open arm, in a dose-dependent manner. The effect is comparable to imipramine which induced increase in the occupancy in the open arm.

Conclusion: Our results indicate that SPS would trigger a constant anxiety-like behaviors, and significant depressive behavior which was reversed by agmatine. Since all anxiety-like behavior is reversed by Agmatine, as an endogenous molecule, might have a regulatory function in PTSD.

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Establishing a fear extinction-impaired animal model of post-traumatic stress disorder

Establishing a fear extinction-impaired animal model of post-traumatic stress disorder

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Abstract

Post-traumatic stress disorder (PTSD), a common anxiety disorder, occurs less than 10 % of individuals after experiencing one or more terrifying accidents. One of key symptoms reported in PTSD patients is repeatedly and persistently re-experiencing the traumatic event due to the recurrent visits of fearful memory. The estimated lifetime prevalence of PTSD among adult Americans is 7.8 % while ~60 % of adults reported to have experienced at least one traumatic event. Currently available animal models include physical and social stress models, however stressor models cannot distinguish general trauma coping responses from persistent and selective PTSD symptoms. Therefore, we took advantage of a genetic strain of mouse, 129S1/SvImJ (129S1) to establish a convincing animal model for PTSD. 129S1 has been reported to have a trouble with fear memory forgetting or fear extinction after fear conditioning. Here, we evaluated 129S1 as a bona-fide, fear extinction-impaired animal model for PTSD at cellular, synaptic and behavioral levels. 129S1 shows reduced immediate early gene, c-Fos expression in infralimbic cortex of medial prefrontal cortex and basolateral amygdala compared to C57BL/6, both of which are parts of fear extinction circuitry. We found that 129S1 had no problem in fear memory formation while having impaired fear extinction in both auditory and contextual fear conditioning protocols. 129S1 exhibited comparable hippocampal dependent spatial memory in Morris water maze following contextual fear conditioning compared to C57BL/6, suggesting that fear memory impairment is only selective to fear extinction in 129S1. Therefore we propose that 129S1 could serve as a useful animal model for PTSD to study the etiology and pathophysiology underlying PTSD.

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Enhancement of forgetting remote contextual fear memory through increase in adult hippocampal neurogenesis in combination with reactivation of hippocampus by long-time memory recall

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Abstract

Approaches to develop treatment for PTSD using rodents have been targeted on extinction and reconsolidation of recent memory although traumatic memories associated with PTSD are remote. Recent study has shown that forgetting of recent fear memory is promoted by the treatment with memantine (MEM) that increases in hippocampal neurogenesis. Here we show that forgetting of remote contextual fear memory is enhanced by the MEM treatment only after long-time memory recall. Treatment with MEM for 4 weeks after contextual fear conditioning enhances forgetting but this treatment fails to enhance forgetting of remote fear memory. Interestingly, the same treatment promotes forgetting of remote memory only after long-time recall by the re-exposure to the conditioned stimulus (CS) for 10 min, but not 3 min. Similarly, exercise, another hippocampal-neurogenesis enhancer, also promotes forgetting of remote memory after the prolonged recall. As a possible mechanism by which long-time recall allows remote memory forgetting, we found that long-, but not short-, time recall of remote memory activates gene expression of hippocampus and induces hippocampus-dependent reconsolidation. More importantly, retrieval of remote contextual fear memory becomes hippocampus-dependent after the long-time recall. These observations suggest that remote fear memory returns into a hippocampus-dependent state after long-time retrieval, thereby allowing enhance forgetting by increased hippocampal neurogenesis. Our findings may contribute to develop a method for the PTSD treatment by enhancing forgetting of traumatic memory.