

Effect of 8-OH-DPAT on the Behavioral Indicators of Stress and on the Number of Astrocytes after Exposure to Chronic Stress

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Abstract : Prolonged exposure to stress can cause disorders related with dysfunction in the prefrontal cortex such as generalized anxiety and depression. These disorders involve alterations in neurotransmitter systems; the serotonergic system—a target of the drugs that are commonly used as a treatment to these disorders—is one of them. Recent studies suggest that 5-HT_{1A} receptors play a pivotal role in the serotonergic system regulation and in stress responses. In the same way, there is increasing evidence that astrocytes are involved in the pathophysiology of stress. The aim of this study was to examine the effects of 8-OH-DPAT, a selective agonist of 5-HT_{1A} receptors, in the behavioral signs of anxiety and anhedonia as well as in the number of astrocytes in the medial prefrontal cortex (mPFC) after exposure to chronic stress. They used 50 male Wistar rats of 250-350 grams housed in standard laboratory conditions and treated in accordance with the ethical standards of use and care of laboratory animals. A protocol of chronic unpredictable stress was used for 10 consecutive days during which the presentation of stressors such as motion restriction, water deprivation, wet bed, among others, were used. 40 rats were subjected to the stress protocol and then were divided into 4 groups of 10 rats each, which were administered 8-OH-DPAT (Tocris, USA) intraperitoneally with saline as vehicle in doses 0.0, 0.3, 1.0 and 2.0 mg/kg respectively. Another 10 rats were not subjected to the stress protocol or the drug. Subsequently, all the rats were measured in an open field test, a forced swimming test, sucrose consume, and a zero maze test. At the end of this procedure, the animals were sacrificed, the brain was removed and the tissue of the mPFC (Bregma: 4.20, 3.70, 2.70, 2.20) was processed in immunofluorescence staining for astrocytes (Anti-GFAP antibody - astrocyte maker, ABCAM). Statistically significant differences were found in the behavioral tests of all groups, showing that the stress group with saline administration had more indicators of anxiety and anhedonia than the control group and the groups with administration of 8-OH-DPAT. Also, a dose dependent effect of 8-OH-DPAT was found on the number of astrocytes in the mPFC. The results show that 8-OH-DPAT can modulate the effect of stress in both behavioral and anatomical level. Also they indicate that 5-HT_{1A} receptors and astrocytes play an important role in the stress response and may modulate the therapeutic effect of serotonergic drugs, so they should be explored as a fundamental part in the treatment of symptoms of stress and in the understanding of the mechanisms of stress responses.

Keywords : anxiety, prefrontal cortex, serotonergic system, stress

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