INVOLVEMENT OF THE CANNABINOID RECEPTOR TYPE-1 (CB_1) ON SALVINORIN-A-INDUCED EMOTIONAL RESPONSE IN RATS

Capurro Valeria, Braida Daniela, Zani Alessia, Sala Mariaelvina

Department of Pharmacology, Chemotherapy and medical Toxicology, University of Milan, Via Vanvitelli 32, 20129, Milan

Salvinorin A, a potent kappa-opioid receptor agonist (1) is the major active ingredient of *Salvia divinorum*,a hallucinogenic herb, usually smoked or buccally absorbed by chewing. Recently, salvinorin A has been shown to produce reinforcing effects in the zebrafish when given at low doses (2). About emotional reactivity, salvinorin A induces in humans both positive and negative effects. Until now, only a pro-depressant like-response in the forced swimming test (3), has been reported in rats. Thus, the aim of the present work was to investigate salvinorin A on emotional reactivity in male Sprague-Dawley rats using the elevated plus-maze (EPM) and the forced swimming test (FST) at doses not affecting motor activity. Salvinorin A (0.001-1000 μg/kg), was studied in EPM apparatus The test length was 5 min, the total time spent in each arm and the number of arm entries were scored, 20 min after treatment. The FST test, consisted in two swimming sessions where the time of immobility during the 2nd 5-min session was an indicator of antidepressant activity. Salvinorin A showed a dose-dependent increase in the mean number of entries and time spent in the open arms and a decrease of the mean time spent in immobility. Pre-treatment with the k opioid antagonist, nor-binaltorphimine (10 mg/kg i.p.), and with the CB1 cannabinoid receptor antagonist AM 251 (3 mg/kg i.p.), given 2 h and 40 min before salvinorin A respectively, significantly blocked the anxiolytic and antidepressant effect. These findings support for the first time the demonstration of the emotional response induced by salvinorin A through a mechanism cannabinoid CB_1 receptor mediated.

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