

Immunologic Perturbations Exerted by Harmine and Foot Shock Stress

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Abstract

Pregnancy is a complex physiological state, in which the effect of any stress multiplies its impacts; in this study, we are interested in the effects of electrical stress on pregnant rats and an attempt to mitigate them using an alkaloid. Pregnant rats were divided into seven groups: control and two treated groups with harmine at 10, 15 mg/kg, psychological stressed group, two foot shocked groups 0,4 and 1,2 mA and a treated stressed group. Each group contains three sub-groups according to the stage of pregnancy. Rats have conducted to plus maze test and object recognition test. We marked increased time spent with new object and number of entries in all arms and a significant decrease in food consumption, the red blood cells RBC, Mean corpuscular hemoglobin content MCHC have increased. A significant decrease in monocytes and lymphocytes after treatment. The number of placentation and fetuses has increased significantly in treated group and treated stressed group even the significant decrease in stressed group. Harmine has enhanced the cognition of rats in object recognition test, and exerted its anxiolytic effect in the plus maze test even during pregnancy. It decreased food consumption and enhanced implantation, RBC and thrombocytes due to its enhancement of serotonin *via* its effect of monoaminoxidase inhibitor MAO I.

Keywords: Harmine; Footshock stress; Pregnant rats

About the Study

Treatment with ayahuasca did not affect the predictors of major depression, neither brain derived neurotrophic factor BDNF nor did cortisol levels, higher BDNF levels were detect even the existence of two types of BDNF. *Peganum harmala* well known in traditional Bedouin medicine used as an emmenagogue and abortifacient. In the case of an excess dose, the perfuse heart is arrested in diastolic phase and the contractions of smooth muscle are diminished with the exception of the uterus, which may be made to contract more powerfully. From a metabolic point of view, serotonin levels increase after MAO inhibition, stimulating the vagus nerve in the brain, which innervates the digestive tract; due to the toxic alkaloids characterized in the seeds of *P. harmala* 'Harmaline and harmine'.

Studies reported that harmine were responsible for inhibition of M.A.O. *in vivo* on rat's brain. Then it has reported to be a potent and selective inhibitor of MAO-A. Thus, treatment with harmine would expect to produce a general increase in serotonergic activity. A series of recent pharmacological studies indicate that the role of serotonin in the regulation of female sexual behavior may be considerably more complex than simple tonic inhibition of behavior. In addition, evidence suggests that both inhibitory and facilitators serotonergic effects are mediated postsynaptically. However, in a later series of experiments the agonists have found to facilitate lordosis in females primed with estrogen alone.

The hemolytic effect of total alkaloids of *Pharmala* on erythrocytes of the animals could explained by the interaction of alkaloids with the compounds of the membranes of erythrocytes of animals; by this way harmine is prone if it were be the main cause.

Most research has focused on lymphocyte cytokine production and we have previously shown that during pregnancy, the peripheral-specific immune response has shifted away from a type 1 (i.e. cellular)

immune response towards a type 2 (i.e. humoral) immune response. Moreover, in line with human experiments, we observed recently that during rat pregnancy both monocytes and granulocytes have shown an activated phenotype.

Previous works had suggested that these rats exhibit greater basal impulsivity but not high reactivity to novelty. Different cerebral structures participate in different types of memory, being the striatum related with procedural memory. It is a dopaminergic area involved to memory. However, work memory model included components not only for auditory and visual information, but also for tactile and kinesthetic information. Female rats characterized by their sensibility to stress, and face to pregnant stress, the possibility of harmine to prevent physical stress during gestation, in short work memory task, has been excluded.

Repeated stress results in decreased dendrite length and density of dendritic spines of cortical and hippocampal neurons. In our study, chronic foot-shock stress had no effect on the survival of hippocampal cells that were born several days before the start of the chronic stress protocol, but it cannot ensure that footshock stress does not affect the survival of cells that are born during the period of chronic stress.

Harmine produced an increase in dopamine release from rat striatal slices. In other hand footshock stress increased extracellular dopamine in the prefrontal cortex PFC. However, excessive MFC dopaminergic activity has a negative impact on the cognitive functions of primates, making them unable to select and process significant environmental stimuli. A single footshock session acutely activates dopamine systems in the frontal cortex, hypothalamus, nucleus accumbens, and striatum, but daily application of footshock sensitizes dopamine release only in the cortex, nucleus accumbens, and striatum, then harmine risks exerting its anti-stress effect.

The advancements in research aims to reveal the effect of harmine on memory and exploratory capacity of rats, blood quality and the fecundity parameters like immunity, number of fetuses after a treatment during three phases of pregnancy.